Extracorporeal Blood Purification Therapies for Sepsis and Immune Dysregulation – Are we there yet?

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Disclosures

Relevant Financial Relationships

None

Relevant Non-Financial Relationships

Board Member, American Society for Apheresis 2013-16, 16-19

Senior Editor, Principles of Apheresis Technology 7th Edition 2019-

Member, JCA Special Issue Committee 2012-2019

Off Label Usage

None

Outline: Extracorporeal Blood Purification

- Definition: Extracorporeal Therapies
- Historical Perspectives. Extracorporeal Therapies: Blood Purification Techniques TAM vs Hemodialysis
- Existing Evidence Base: JCA Special Issue, Clinical Trials.

Extracorporeal Therapies:

procedures …. include .. diversion of blood through an external artificial circuit for … blood "purification," gas exchange, or correction of metabolic abnormalities.

Stegmayr B, Ramlow W, Balogun RA. Semin Dial. 2012 Mar-Apr;25(2):207-13.

Extracorporeal Therapies RPA 2001

- Hemodialysis
- Hemofiltration
- Hemodiafiltration
- Continuous renal replacement therapies
- Hemoperfusion
- Apheresis (TPE)
- Immunoadsorption
- Liver dialysis

Humans treating Disease

Bloodletting

- Bloodletting is the removal or large amounts of blood from a patient's body.
- The practice of bloodletting began in the ancient world.
- Ancient Greeks, Aztecs, and Egyptians used bloodletting because they believed that many diseases were caused by having too much blood.

Adapted from http://peer.tamu.edu/NSF_Files/Revolutionary%20Medical%20Treatment.ppt.

Manual "Plasmapheresis"

PLASMA REMOVAL WITH RETURN OF CORPUSCLES
(PLASMAPHAERESIS)

FIRST PAPER

JOHN J. ABEL, L. G. ROWNTREE AND B. B. TURNER
From the Pharmacological Laboratory of the Johns Hopkins University

Received for publication, July 16, 1914

I. In connection with our experiments on vividiffusion with a view to the ultimate use of the method for the relief of toxaemia the idea suggested itself to try the effects of the repeated removal of considerable quantities of blood, replacing the plasma by Locke's solution and reinjecting this together with the sedimented corpuscles.

J. Pharmacol Exp Ther, 5:625, 1914

J Clin Apher. 2010 00;25(5):240-249. Okafor C, Ward DM …. Balogun RA.

John Jacob Abel (1857–1938)

Father of (American) pharmacology and the Inventor of the artificial kidney machine (vividiffusion)

ON THE REMOVAL OF DIFFUSIBLE SUBSTANCES FROM THE CIRCULATING BLOOD OF LIVING ANIMALS BY DIALYSIS

JOHN J. ABEL, LEONARD G. ROWNTREE AND B. B. TURNER
From the Pharmacological Laboratory of the Johns Hopkins University

Received for publication, December 18, 1913

J Pharmacol Exp Ther July 1914 5:611-623

Principles of Separation: Indications and Therapeutic Targets for Plasma Exchange

Mark E. Williams and Rasheed A. Balogun†*

Summary

Extracorporeal "blood purification," mainly in the form of hemodialysis has been a major portion of the clinical activity of many nephrologists for the past 5 decades. A possibly older procedure, therapeutic plasma exchange, separates and then removes plasma as a method of removing pathogenic material from the patient. In contrast to hemodialysis, therapeutic plasma exchange preferentially removes biologic substances of high molecular weight such as autoantibodies or alloantibodies, antigen-antibody complexes, and Ig paraproteins. These molecular targets may be cleared through two alternative procedures: centrifugal separation and membrane separation. This review presents operation these plasma constituents specific to each molecula targets for common renal

Table 4. Examples of pathogenic target molecules for TPE in kidney disease

Kidney Disease	Target Molecule
Anti-GBM disease	Autoantibody reactive with type IV collagen; rapid decline in anti-GBM antibodies with TPE
Thrombotic thrombocytopenic purpura	Acquired autoantibody reactive with ADAMTS13 enzyme
Pauci-immune rapidly progressive GN	Autoantibodies against components of the cytoplasm of neutrophils-sequential ANCA levels have not been performed
Multiple myeloma	Free κ and λ light chains
Cryoglobulinemia	IgM anti-IgG antibody, immune complexes
Recurrent FSGS	Circulating glomerular permeability factor, suPAR (clinical remission correlated with reduction in suPAR levels below approximately 2000 pg/ml (45)
Atypical HUS	Complement regulatory components or autoantibodies; not specifically shown
Kidney transplantation	Alloantibodies reactive with HLA antigens; DSAs can be removed from plasma by TPE

See the text for specific characteristics of molecules. TPE, therapeutic plasma exchange; GBM, glomerular basement membrane; ADAMTS13, a disintegrin-like and metalloprotease with thrombospondin type 1 motifs-13; suPAR, soluble urokinase receptor; HUS, hemolytic uremic syndrome; DSA, donor-specific antibody. Adapted from Sanchez and Ward (4).

UNIVERSITY of VIRGINIA SCHOOL OF MEDICINE

Blood Purification; Size Matters

Molecular Weight kD

Immunoglobulin G
160kDa; 2 LC: 23-25 kDa each; 2 HC:~53 kDa each

BUN	Cr	VitB12	B2-mic	K Lig C	L Lig C	Album	IgG
0.06	0.113	1.355	11.8	25	50	66	160

Small Molecules | Middle Molecules | Large Molecules

Hemodialysis: Diffusion Clearance

Hemofiltration: Convective Clearance

Therapeutic Plasma Exchange

Williams ME, Balogun RA.
Clin J Am Soc Nephrol. 2013 Oct 31.

UNIVERSITY of VIRGINIA SCHOOL OF MEDICINE

Therapeutic APHERESIS Academy

Destructive Immunologic Dissonance

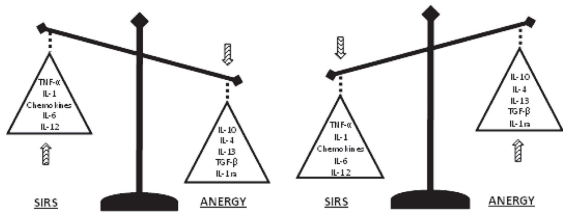
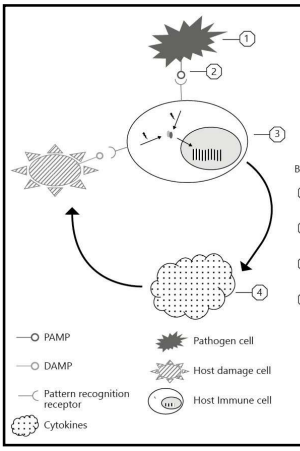


Figure 1 Sepsis is a state of disrupted inflammatory homeostasis often initiated by infection with a multifactorial progression.Overreactivity of pro- and anti-inflammatory processes can interfere with each other, creating a state of destructive immunologic dissonance and risk of death.

Extracorporeal Therapies in Sepsis
Anthi Panagiotou, MD, Sérgio Gaiao, MD, Dinna N. Cruz, MD, MPH



Blood purification therapy targets:
1. Removing pathogens from the blood
2. Removing endotoxins or other PAMPs
3. Removing activated leucocytes or reprogramming leucocytes
4. Reducing cytokine blood levels

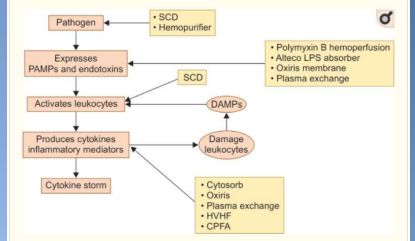
Extracorporeal Blood Purification Therapies for Sepsis
Monard C, Rimmelé T, Ronco C.

Blood Purification 2019, Vol.47, Suppl. 3 May 2019

Therapeutic APHERESIS Academy

Extracorporeal Therapy in Sepsis 2020

Glover & Kumar Indian J Crit Care Med. 2020 Apr; 24(Suppl 3): S117–S121.



Flowchart 1

Immune response to sepsis and extracorporeal therapies

SCD, selective cytopheretic device; PAMPs, pathogen-associated molecular patterns; DAMPs, damage-associated molecular patters; HVHF, high-volume hemofiltration; CPFA, coupled plasma filtration adsorption

Table 1. Substances removed by various adsorbers and techniques

Adsorbers	Plasma removal (33)
Polymyxin-B (22–24)	Toxins, free and protein-bound
Endotoxin	Free myoglobin, hemoglobin
T, IL-6, IL-10, PAI-1 activity	Activated complement components
MDS-microspheres (25–27)	Activated coagulation components
Endotoxin	C-reactive protein
TNF-α, IL-1β, IL-6	Cytokines, cytokine-complexes
HELP (29)	Amylase
Endotoxin	Proteases
C-reactive protein	Ghost cells
Fibrinogen	Cell debris
TNF-α	Lysosomal enzymes
BioLogic sorbent (28)	Physiologically essential substances
Cytokines, protein-bound toxins	Plasma exchange
Fresenius adsorber (31)	Removal of adverse products
Endotoxin (LPS), TNF-α	Substitution of essential substances by e.g., plasma from healthy donors

Apheresis as Therapy for Patients with Severe Sepsis and Multiorgan Dysfunction Syndrome

Bernd G. Stegmayr,

Volume5, Issue2
April 2001
Pages 123-127

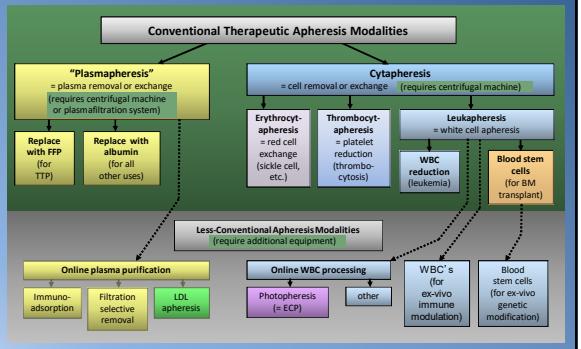
Table 1. Extracorporeal Blood Purification Techniques in Sepsis.

Technique	Aim	Principle	Reported Results
High-volume hemofiltration (HVHF)	Nonselective removal of inflammatory mediators	Convection	Reduces vasopressor requirements, reduces concentrations of inflammatory mediators in blood, and observed mortality lower than predicted mortality
High cutoff membranes (HCOM)	Nonselective removal of inflammatory mediators	Convection	Reduces vasopressor requirements, high clearance of inflammatory mediators moderates leukocyte proliferation, normalizes PMN phagocytosis
Polymyxin-B column (PMX-F)	Selective removal of endotoxin	Adsorption	Reduces vasopressor requirement, increases blood pressure, ameliorates organ dysfunction, reduces short-term mortality
Coupled plasma filtration adsorption (CPFA)	Nonselective removal of inflammatory mediators	Plasma adsorption	Reduces concentrations of inflammatory mediators in blood, restores leukocyte responsiveness
Cytokine adsorbing columns	Nonselective removal of inflammatory mediators	Plasma adsorption	Reduces cytokine levels, improvement in respiratory parameters
Renal assist device (RAD)	Substitute the filtration, transport, metabolic, endocrine and immunologic functions of the kidney	Cell-based therapy	Ameliorates the cytokine profile, improves calcium, phosphate, urea, and creatinine levels
Extracorporeal immune support system (EISS)	Attenuation of excessive antiinflammatory response	Cell-based therapy	Reduces vasopressor requirement, reduces concentrations of endotoxin and inflammatory markers (eg CRP, procalctonin) in blood
Leukocyte inhibition module (LIM)	Attenuation of excessive proinflammatory response	Antibody-based therapy	No studies in sepsis

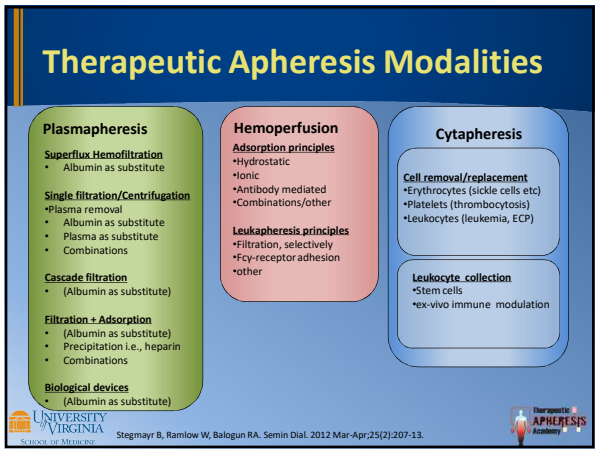
Abbreviations: CRP, C-reactive protein; PMN, polymorphonuclear.

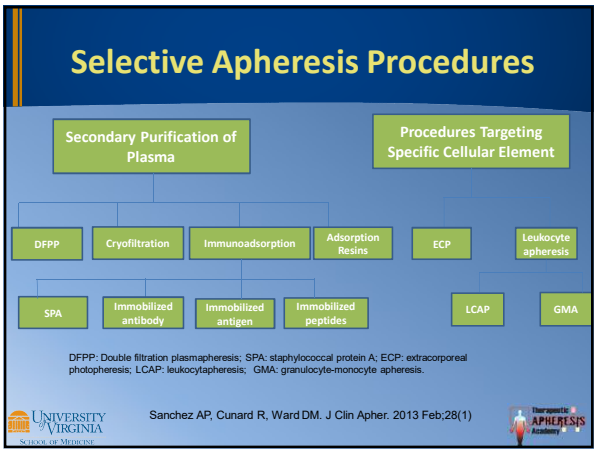
Table 1. Extracorporeal Blood Purification Techniques in Sepsis.

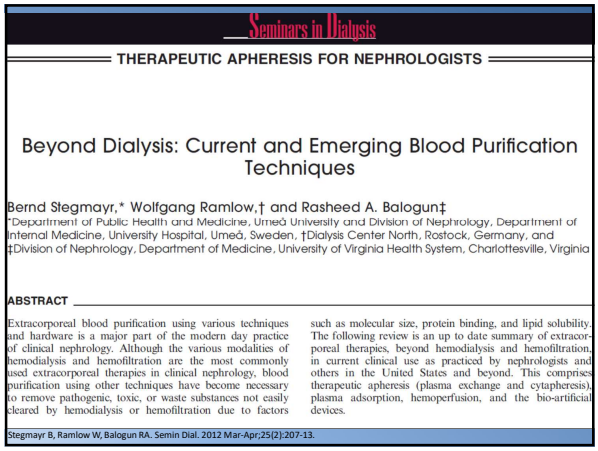
Extracorporeal Therapies in Sepsis



from Okafor C, Ward DM, Mokrzycki MH, Weinstein R, Clark P, Balogun RA. : J Clin Apheresis, 25:240-249, 2010






Seminars in Dialysis

THERAPEUTIC APHERESIS FOR NEPHROLOGISTS

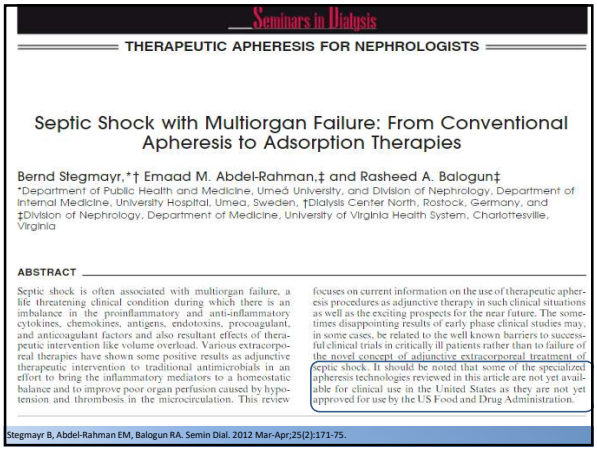
Beyond Dialysis: Current and Emerging Blood Purification Techniques

Bernd Stegmayr,* Wolfgang Ramlow,† and Rasheed A. Balogun‡
*Department of Public Health and Medicine, Umeå University and Division of Nephrology, Department of Internal Medicine, University Hospital, Umeå, Sweden, †Dialysis Center North, Rostock, Germany, and ‡Division of Nephrology, Department of Medicine, University of Virginia Health System, Charlottesville, Virginia

ABSTRACT

Extracorporeal blood purification using various techniques and hardware is a major part of the modern day practice of clinical nephrology. Although the various modalities of hemodialysis and hemofiltration are the most commonly used extracorporeal therapies in clinical nephrology, blood purification using other techniques have become necessary to remove pathogenic, toxic, or waste substances not easily cleared by hemodialysis or hemofiltration due to factors such as molecular size, protein binding, and lipid solubility. The following review is an up to date summary of extracorporeal therapies, beyond hemodialysis and hemofiltration, in current clinical use as practiced by nephrologists and others in the United States and beyond. This comprises therapeutic apheresis (plasma exchange and cytapheresis), plasma adsorption, hemoperfusion, and the bio-artificial devices.

Stegmayr B, Ramlow W, Balogun RA. Semin Dial. 2012 Mar-Apr;25(2):207-13.


Seminars in Dialysis

THERAPEUTIC APHERESIS FOR NEPHROLOGISTS

Septic Shock with Multiorgan Failure: From Conventional Apheresis to Adsorption Therapies

Bernd Stegmayr,*† Emaad M. Abdel-Rahman,‡ and Rasheed A. Balogun‡
*Department of Public Health and Medicine, Umeå University, and Division of Nephrology, Department of Internal Medicine, University Hospital, Umea, Sweden, †Dialysis Center North, Rostock, Germany, and ‡Division of Nephrology, Department of Medicine, University of Virginia Health System, Charlottesville, Virginia

ABSTRACT

Septic shock is often associated with multiorgan failure, a life threatening clinical condition during which there is an imbalance in the proinflammatory and anti-inflammatory cytokines, chemokines, antigens, endotoxins, procoagulant, and anticoagulant factors and also resultant effects of therapeutic intervention like volume overload. Various extracorporeal therapies have shown some positive results as adjunctive therapeutic intervention to traditional antimicrobials in an effort to bring the inflammatory mediators to a homeostatic balance and to improve poor organ perfusion caused by hypotension and thrombosis in the microcirculation. This review focuses on current information on the use of therapeutic apheresis procedures as adjunctive therapy in such clinical situations as well as the exciting prospects for the near future. The sometimes disappointing results of early phase clinical studies may, in some cases, be related to the well known barriers to successful clinical trials in critically ill patients rather than to failure of the novel concept of adjunctive extracorporeal treatment of septic shock. It should be noted that some of the specialized apheresis technologies reviewed in this article are not yet available for clinical use in the United States as they are not yet approved for use by the US Food and Drug Administration.

Stegmayr B, Abdel-Rahman EM, Balogun RA. Semin Dial. 2012 Mar-Apr;25(2):171-75.

Septic Shock with Multiorgan Failure: From Conventional Apheresis to Adsorption Therapies

TABLE 2. Various clinical studies using adsorption techniques in the treatment of sepsis, severe sepsis, and in MODS

Study/adsorber	*n*	Main mode of therapy	Survival (%)	*p*
Polymyxin B				
Tani et al. (36)	37/33c	AdsPmx	54/36	< 0.05
Nemoto et al. (21)	98	AdsPmx	41/11c	< 0.05
Suzuki et al. (37)	24/24c	AdsPmx	75/25c	< 0.05
Vincent et al. (23)	17/19c	AdsPmx	71/72c	ns
Cruz et al. (22)	34/30	AdsPmx	68/47c	< 0.05
Albumin as adsorber				
Staubach et al. (19)	67/76c	Albu adsc		

AdsPmx, adsorption column using group; ns, not significant.

TABLE 3. Various randomized studies using plasma exchange/plasmapheresis in the treatment of severe sepsis and in MODS

Study	*n*	Main mode of therapy	Survival (%)	*p*
Reeves et al. (26)	14/16c	PF	57/50	ns
Busund et al. (27)	54/52c	PE	67/44	0.05
Nguyen et al. (28)	5/5c	PE	100/20	< 0.05

PE, plasma exchange by centrifugation technique; PF, plasma exchange by filtration; c, control.

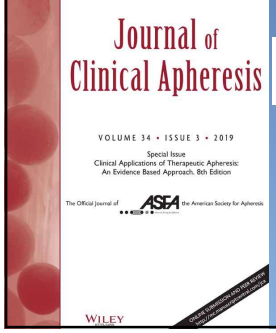
Septic Shock with Multiorgan Failure: From Conventional Apheresis to Adsorption Therapies

HD is necessary …. severe MOD, including AKI to survive…. uremic solutes, cytokines, chemokines, superantigens, modulators of apoptosis, endotoxins, drugs, and fluid overload.

….. prognosis is poor in severe cases. In the future…. additional approach …….. may be the use of apheresis procedures (centrifugation, filtration or adsorption).

Stegmyr, Abdel-Rahman and Balogun 2012

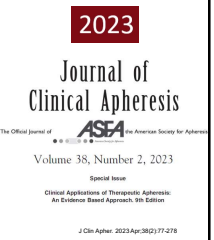
Apheresis Practice Guidelines

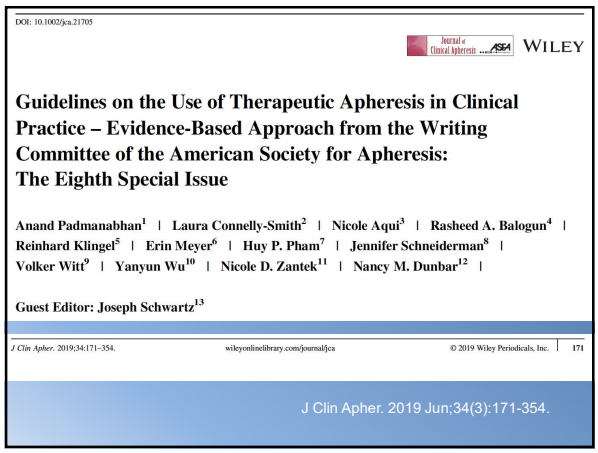


- Fact sheets renamed to co-locate similar disorders
- Select fact sheets merged, one fact sheet retired
- Several category recommendations changed based on new evidence or reassessment of existing evidence

J Clin Apher. 2019 Jun;34(3):171-354

APHERESIS PRACTICE GUIDELINES





DOI: 10.1002/jca.21705

Journal of Clinical Apheresis ASFA WILEY

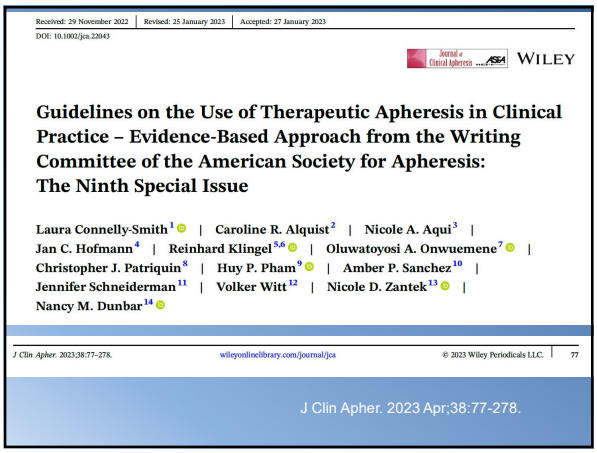
Guidelines on the Use of Therapeutic Apheresis in Clinical Practice – Evidence-Based Approach from the Writing Committee of the American Society for Apheresis: The Eighth Special Issue

Anand Padmanabhan[1] | Laura Connelly-Smith[2] | Nicole Aqui[3] | Rasheed A. Balogun[4] | Reinhard Klingel[5] | Erin Meyer[6] | Huy P. Pham[7] | Jennifer Schneiderman[8] | Volker Witt[9] | Yanyun Wu[10] | Nicole D. Zantek[11] | Nancy M. Dunbar[12] |

Guest Editor: Joseph Schwartz[13]

J Clin Apher. 2019;34:171–354. wileyonlinelibrary.com/journal/jca

J Clin Apher. 2019 Jun;34(3):171-354.



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Journal of Clinical Apheresis ASFA WILEY

Guidelines on the Use of Therapeutic Apheresis in Clinical Practice – Evidence-Based Approach from the Writing Committee of the American Society for Apheresis: The Ninth Special Issue

Laura Connelly-Smith[1] | Caroline R. Alquist[2] | Nicole A. Aqui[3] | Jan C. Hofmann[4] | Reinhard Klingel[5,6] | Oluwatoyosi A. Onwuemene[7] | Christopher J. Patriquin[8] | Huy P. Pham[9] | Amber P. Sanchez[10] | Jennifer Schneiderman[11] | Volker Witt[12] | Nicole D. Zantek[13] | Nancy M. Dunbar[14]

J Clin Apher. 2023;38:77–278. wileyonlinelibrary.com/journal/jca

J Clin Apher. 2023 Apr;38:77-278.

Category Definitions: 2023

Category	Description
I	Disorders for which apheresis is **accepted as first-line therapy**, either as a primary standalone treatment or in conjunction with other modes of treatment.
II	Disorders for which apheresis is **accepted as second-line therapy**, either as a standalone treatment or in conjunction with other modes of treatment.
III	Optimum **role of apheresis therapy is not established**. Decision making should be individualized.
IV	Disorders in which **published evidence demonstrates or suggests apheresis to be ineffective or harmful**. IRB approval is desirable if apheresis treatment is undertaken in these circumstances.

J Clin Apher. 2019 Jun;34(3):171-354.

University of Virginia School of Medicine

Therapeutic Apheresis Academy

ASFA Guidelines Fact Sheets 2016, 2019, 2023

2016

Journal of Clinical Apheresis 31:149–338 (2016)

SEPSIS WITH MULTIORGAN FAILURE

		Procedure	Recommendation	Category
Incidence: 300/100,000/yr (US)		TPE	Grade 2B	III
No. of reported patients: >300	RCT	CT	CS	CR
	4(194)	5(155)	12(231)	11

2019

Journal of Clinical Apheresis ASFA WILEY

SEPSIS WITH MULTIORGAN FAILURE

J Clin Apher. 2019;34:171–354.

		Procedure	Recommendation	Category
Incidence: Severe sepsis in adults 300/100,000/yr (US); 8% prevalence in pediatric intensive care		TPE	Grade 2B	III
# reported patients: >300	RCT	CT	CS	CR
	4(194)	6(215)	16(1,216)	NA

2023

Journal of Clinical Apheresis ASFA WILEY

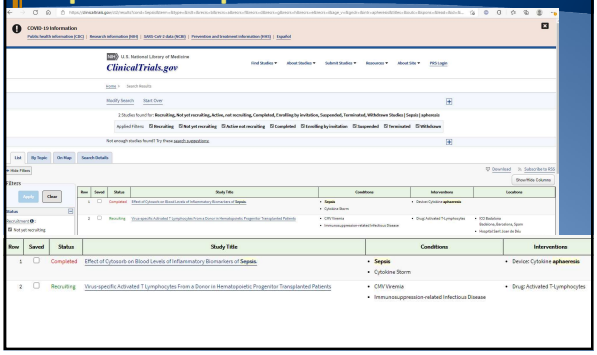
SEPSIS WITH MULTIORGAN FAILURE

Incidence: severe sepsis in adults 300/100,000/year (United States); 8% prevalence in pediatric intensive care

Indication	Procedure	Category		Grade	
	TPE	III		2A	
# reported patients: >300	**Procedure**	**RCT**	**CT**	**CS**	**CR**
Sepsis*	TPE	5 (234)	7 (295)	NA	NA
Sepsis, COVID-19 related	TPE	1 (87)	6 (359)	NA	NA

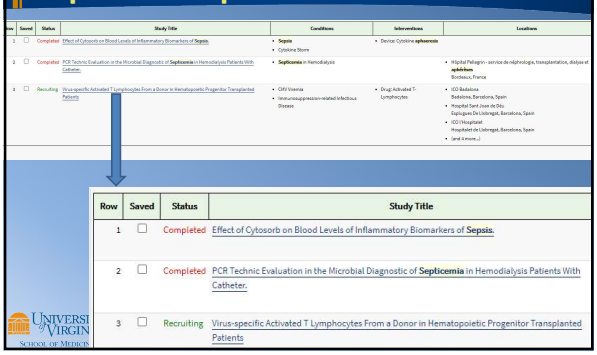
*excluding sepsis due to COVID-19

ClinicalTrials.gov October 9, 2021 Sepsis and Apheresis



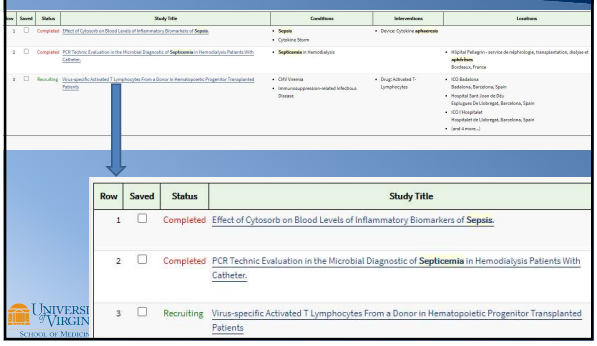
Row	Saved	Status	Study Title	Conditions	Interventions
1		Completed	Effect of Cytosorb on Blood Levels of Inflammatory Biomarkers of Sepsis.	• Sepsis • Cytokine Storm	• Device: Cytokine apheresis
2		Recruiting	Virus-specific Activated T Lymphocytes From a Donor in Hematopoietic Progenitor Transplanted Patients	• CMV Viremia • Immunosuppression-related Infectious Disease	• Drug: Activated T-Lymphocytes

ClinicalTrials.gov October 9, 2021 Sepsis and Apheresis



Row	Saved	Status	Study Title
1		Completed	Effect of Cytosorb on Blood Levels of Inflammatory Biomarkers of Sepsis.
2		Completed	PCR Technic Evaluation in the Microbial Diagnostic of Septicemia in Hemodialysis Patients With Catheter.
3		Recruiting	Virus-specific Activated T Lymphocytes From a Donor in Hematopoietic Progenitor Transplanted Patients

ClinicalTrials.gov October 9, 2021 Sepsis and Extracorporeal



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2		Completed	PCR Technic Evaluation in the Microbial Diagnostic of Septicemia in Hemodialysis Patients With Catheter.
3		Recruiting	Virus-specific Activated T Lymphocytes From a Donor in Hematopoietic Progenitor Transplanted Patients

ClinicalTrials.gov October 9, 2021 Sepsis and "Extracorporeal" All Phases, All Time

- Sepsis and Extracorporeal Results 45 all time
- Suspended or Terminated: 2
- Completed: 17
- Completed + Has Results: 3

Row	Saved	Status	Study Title	Conditions
1	☑	Completed Has Results	Inflammatory Cytokine Quantification in Infants	• Sepsis • Congenital Diaphragmatic Hernia • Neonatal Cardiopulmonary Failure
2	☑	Completed Has Results	Safety and Efficacy of Polymyxin B Hemoperfusion (PMX) for Septic Shock	• Septic Shock • Endotoxemia
3	☑	Completed Has Results	The Effects of Polymyxin-B Protects on Sepsis Induced Kidney Dysfunction: a Randomized Clinical Trial	• Gram-Negative Bacterial Infections • Sepsis

ClinicalTrials.gov Nov 28, 2023
Sepsis and "Extracorporeal" All Phases, All Time

- Sepsis and Extracorporeal Results 71 all time
- Suspended or Terminated: 4
- Completed: 22
- Recruiting: 26
- Completed + Has Results: 4

Research

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effect of Targeted Polymyxin B Hemoperfusion on 28-Day Mortality in Patients With Septic Shock and Elevated Endotoxin Level
The EUPHRATES Randomized Clinical Trial

R. Phillip Dellinger, MD, MSc; Sean M. Bagshaw, MD, MSc; Massimo Antonelli, MD; Debra M. Foster, BSc; David J. Klein, MD, MBA; John C. Marshall, MD; Paul M. Palevsky, MD; Lawrence S. Weisberg, MD; Christa A. Schorr, DNP, MSN, RN; Stephen Trzeciak, MD, MPH; Paul M. Walker, MD, PhD; for the EUPHRATES Trial Investigators

JAMA Network

From: **Effect of Targeted Polymyxin B Hemo… Elevated Endotoxin Level: The EUPHRATES**

JAMA. 2018;320(14):1455-1463. doi:10.1001/jama…

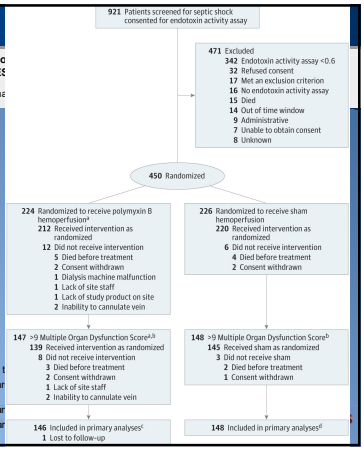

Figure Legend:

Patient Recruitment, Randomization, and Flow of t…

[b]Protocol adjusted following interim analysis to enr… Dysfunction Score of more than 9.

[c]Primary analyses also included all participants ran…

[d]Primary analyses also included all participants ran…

JAMA Network

From: **Effect of Targeted Polymyxin B Hemoperfusion on 28-Day Mortality in Patients With Septic Shock and Elevated Endotoxin Level: The EUPHRATES Randomized Clinical Trial**

JAMA. 2018;320(14):1455-1463. doi:10.1001/jama.2018.14618

Table 2. Summary of the Primary End Point of 28-Day Mortality for All Participants and for Patients With MODS of More Than 9

	No./Total (%)		(95% CI)		
	Polymyxin-B Hemoperfusion	Sham	Risk Difference	Risk Ratio	*P* Value[a]
All Participants	84/223 (37.7)	78/226 (34.5)	3.15 (−5.73 to 12.04)	1.09 (0.85 to 1.39)	.49
>9 MODS[b]	65/146 (44.5)	65/148 (43.9)	0.60 (−10.75 to 11.97)	1.01 (0.78 to 1.31)	.92

[a] *P* values were calculated by χ^2 and were unadjusted.

[b] Multiple Organ Dysfunction Score (MODS)–measure of altered organ function in acutely ill patients using 6 organ systems with weighted scores (0, normal; 4, severe) of each organ system (MODS range, 0-24). A higher score is associated greater burden of organ dysfunction. A MODS of 9 to 12 points has a hospital mortality of approximately 50%. Prior to the protocol amendment, the MODS score was calculated at baseline (time of randomization to the initiation of the study treatment). After the amendment, MODS of more than 9 was included at the time of screening, prior to randomization.

Table Title:

Summary of the Primary End Point of 28-Day Mortality for All Participants and for Patients With MODS of More Than 9-P values were calculated by χ^2 and were unadjusted.

[b] Multiple Organ Dysfunction Score (MODS)–measure of altered organ function in acutely ill patients using 6 organ systems with weighted scores (0, normal; 4, severe) of each organ system (MODS range, 0-24). A higher score is associated greater burden of organ dysfunction. A MODS of 9 to 12 points has a hospital mortality of approximately 50%. Prior to the protocol amendment, the MODS score was calculated at baseline (time of randomization to the initiation of the study treatment). After the amendment, MODS of more than 9 was included at the time of screening, prior to randomization.

Research

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effect of Targeted Polymyxin B Hemoperfusion on 28-Day Mortality in Patients With Septic Shock and Elevated Endotoxin Level

The EUPHRATES Randomized Clinical Trial

R. Phillip Dellinger, MD, MSc; Sean M. Bagshaw, MD, MSc; Massimo Antonelli, MD; Debra M. Foster, BSc; David J. Klein, MD, MBA; John C. Marshall, MD; Paul M. Palevsky, MD; Lawrence S. Weisberg, MD; Christa A. Schorr, DNP, MSN, RN; Stephen Trzeciak, MD, MPH; Paul M. Walker, MD, PhD; for the EUPHRATES Trial Investigators

CONCLUSIONS AND RELEVANCE Among patients with septic shock and high endotoxin activity, polymyxin B hemoperfusion treatment plus conventional medical therapy compared with sham treatment plus conventional medical therapy did not reduce mortality at 28 days.

TRIAL REGISTRATION ClinicalTrials.gov Identifier: NCT01046669

Intensive Care Med (2008) 34:1638–1645
DOI 10.1007/s00134-008-1124-6

ORIGINAL

OpenAccess

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Polymyxin-B hemoperfusion inactivates circulating proapoptotic factors

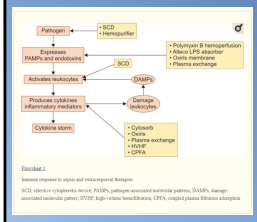
Extracorporeal therapy with PMX-B reduces the proapoptotic activity of the plasma of septic patients on cultured renal cells. These data confirm the role of apoptosis in the development of sepsis related ARF.

University of Virginia School of Medicine

Therapeutic Apheresis Academy

Extracorporeal Therapy in Sepsis 2020

Govil & Kumar Indian J Crit Care Med. 2020 Apr; 24(Suppl 3): S117–S121.



Significant progress has been made ……but till date no conclusive evidence has emerged to support a routine use of any of these modalities as an adjunct to standard sepsis care.

Govil & Kumar
April 2020

University of Virginia School of Medicine

Therapeutic Apheresis Academy

Post Hoc Analysis: Not there yet but…..

Intensive Care Med (2018) 44:2205–2212
https://doi.org/10.1007/s00134-018-5463-7

ORIGINAL

CrossMark

Polymyxin B hemoperfusion in endotoxemic septic shock patients without extreme endotoxemia: a post hoc analysis of the EUPHRATES trial

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