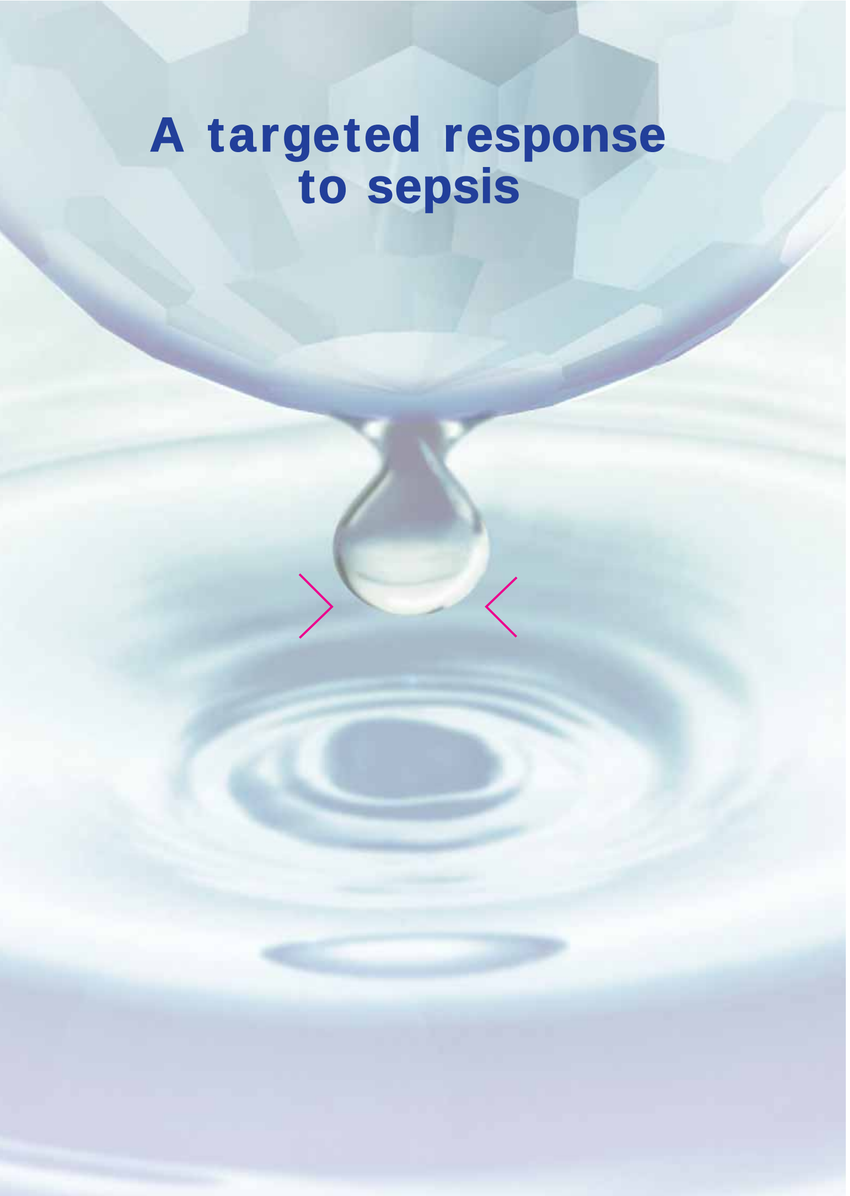

CPFA®

COUPLED PLASMA FILTRATION ADSORPTION

A targeted response to sepsis

RIGHT THERAPIES

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The right therapy way

CPFA®

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The right therapy way

CPFA®

COUPLED PLASMA FILTRATION ADSORPTION

A simple response to complex questions

The Abyle® line provides simple and innovative answers to complex questions. CPFA® is an extracorporeal therapy that was developed and patented by Bellco for the treatment of sepsis. Lynda® (Bellco acute machine) is the technologic response suited to the treatments of multi organ dysfunction.

Today,sepsis still remains as one of the principle causes of acute patient mortality.
It is characterized by the presence of infectious microorganisms (bacteria virus or fungal) and the presence of systemic inflammation. Approximately 25% of sepsis patients develop severe sepsis (associated with multiorgan dysfunction). Sepsis is associated with approx. 210000 deaths in the USA, 140000 in Europe.

CPFA® has achieved international recognition as an effective therapy able to remove mediators involved in the inflammatory cascade, restore cellular function, improve hemodynamics – all with the aim of reversing the downward spiral of severe sepsis and septic shock.

Vast removal of mediators

- CPFA® removes a wide range of cytokines, chemokines and inflammatory mediators
- Plasma filter allows greater removal of higher molecular weight mediators than traditional hemofilters used for intermittent or continuous renal replacement therapies
- High performance resin permits fast and extensive adsorption of mediators while allowing reinfusion of albumin and amino acids
- Removal of cytokines produced during both gram positive and gram negative infections

Restoration of immune response

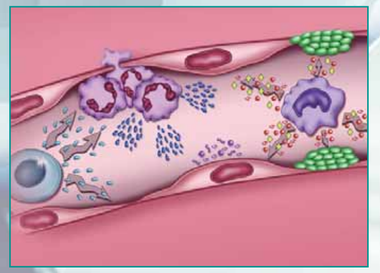
- CPFA® removes both pro- and anti-inflammatory mediators; both associated with increased morbidity and mortality in septic patients
- Previous studies have shown restoration of cellular immune responsiveness after 10 hours of CPFA® treatment

Improved hemodynamics

- CPFA® increases mean arterial pressure while reducing vasopressor requirements
- Applicable for both severe sepsis and septic shock
- Improves cardiac and respiratory parameters

Sepsis snapshot

Reaction to sepsis is an extremely complex process that involves the activation of inflammatory, coagulation and complement cascades as well as production of pro- and anti-inflammatory cytokines. The non-linear complexity is largely determined by the interplay of the cells involved in the systemic response. These include: monocytes, lymphocytes, neutrophils, dendritic cells, platelets and endothelial cells.

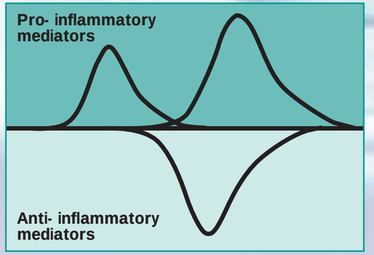


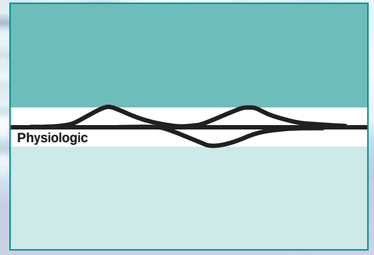
Why CPFA®?

The aim of CPFA® is to remove the excess circulating mediators in order to re-establish homeostasis and restore a more physiologic immune response.

It is advisable to start the treatment as soon as possible to avoid further amplification of the inflammatory response.

CPFA® offers the advantage of working with plasma and an adsorbent cartridge. In this way, the adsorbent cartridge can remove a wide array of inflammatory mediators (cytokines, chemokines, as well as pro-inflammatory and immunosuppressive mediators)

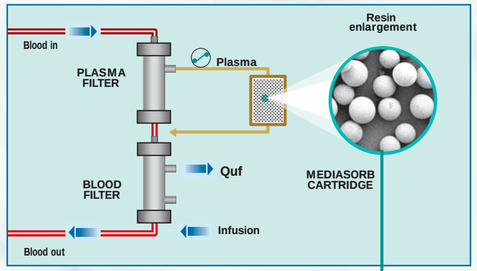




Vast removal of mediators

Mediators that can be removed with the cartridge:

- Interleukin 1-β
- Interleukin 5
- Interleukin 6
- Interleukin 7
- Interleukin 8
- Interleukin 10
- Interleukin 12p70
- Interleukin 16
- Interleukin 18
- Macrophage inflammatory protein-a (MIP-α)
- Macrophage inflammatory protein-b (MIP-β)
- Tumor necrosis factor--a TNF-α
- Monocyte chemotactic protein (MCP-1)
- RANTES
- Epithelial neutrophil activating peptide 78 (ENA-78)



Basic flow diagram of Coupled Plasma Filtration Adsorption (CPFA®)

The 'heart' of the CPFA® system

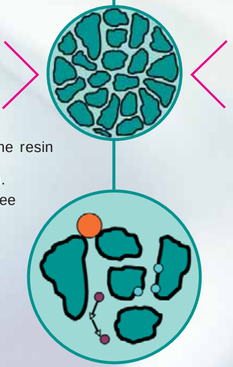
Adsorption efficacy is generally inversely proportional to flow. Working with plasma permits better efficacy and adsorption capacity, due to the slower plasma flow. This allows more contact time with the resin and is associated with less fouling. There is also no risk of cell activation.

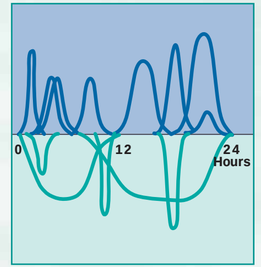
Adsorption is only limited to the degree of mediator affinity with the resin.

The resin used in the sorbent cartridge (synthetic cross-linked styrenic divinylbenzene resin) was chosen based on:

- its adsorption capacity for mediators
- safety profile (no extractable toxins / metals)
- good pressure-flow performance.

It is a reverse phase-type resin that interacts with hydrophobic sites on the molecule, thanks to its physical properties like: sphere dimensions, cross linking, porosity, pore size distribution. The resin is well suited for extracorporeal applications because of its high homogeneity, good pressure-flow performance, and excellent mechanical and chemical stability.





Time factor

Sepsis is a dynamic continually changing processes, that varies depending on the type of pathogen, patient age, presence of co-morbidities, as well as genetic factors.

CPFA® maintains its mediator removal capacity for a long time.

The CPFA® therapy is usually performed for 10 hours and is frequently followed by CVVH for the rest of the day. CPFA® treatments are usually continued for 3-5 days.

Additional material

Bellot G, Bianco N, Tomasini A, et al.
Changes in microvascular blood flow during CPFA.
Anesth Intensive Care 2011; 39:687-89

Caroleo S, Rubino AS, Tropea F, et al.
Coupled plasma filtration adsorption reduces serum bilirubine in a case of acute hypoxic hepatitis secondary to cardiogenic shock.
Int J Artif Organs 2010; 33(10):749-52

Lentini P, Cruz D, Nalesso F, et al.
Coupled Plasma Filtration Adsorption (CPFA) versus emofiltrazione continua con regime intermittente di alti volumi (pHVHF) nel trattamento dello shock settico: uno studio pilota.
G Ital Nefrol 2009; 26 (6): 695-703

ML Wratten - *Therapeutic approaches to reduce systemic inflammation in septic-associated neurologic complications.*
European Journal of Anaesthesiology 2008; 25 (Suppl 42): 1–7

Formica M, Inguaggiato P, Banotti S, Wratten ML - *Coupled plasma filtration adsorption.* Contrib Nephrol. 2007;156:405-10

Mariano F, Tetta C, Stella M, et al.
Regional citrate anticoagulation in critically ill patients treated with plasma filtration and adsorption. Blood Purif 2004; 22:313-9

Ronco C, Brendolan A, D'Intini V, et al.
Coupled plasma filtration adsorption: rationale, technical development and early clinical experience. Blood Purif 2003; 21:409-16

Formica M, Oliveri C, Livigni S, et al.
Hemodynamic response to coupled plasmafiltration-adsorption in human septic shock. Intensive Care Med 2003; 29:703-8

Cesano G, Livigni S, Vallero A, Oliveri C, Borca M, Quarello F, Tetta C, Fonsica M. *Treatment of septic shock with the use of CPFA (associated plasma filtration and adsorption): impact on hemodynamics monitored with PICCO.* G Ital Nefrol 2003; 20(3):258-63

Ronco C, Brendolan A, Lonnemann G, et al.
A pilot study of coupled plasma filtration with adsorption in septic shock. Crit Care Med 2002; 30:1250-5