

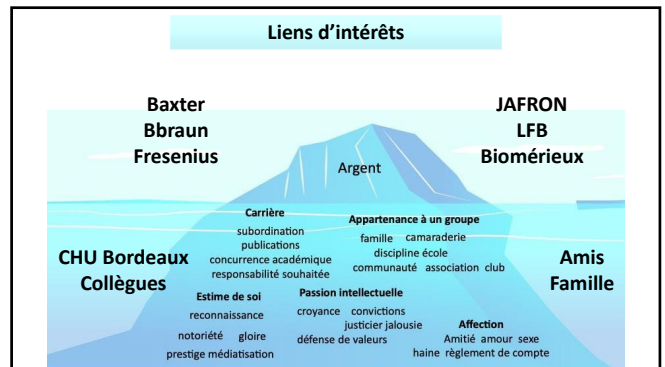


Epuration et sepsis





Pr Olivier JOANNES-BOYAU
Pôle Anesthésie-Réanimation, CHU Bordeaux
Olivier.joannes-boyau@chu-bordeaux.fr





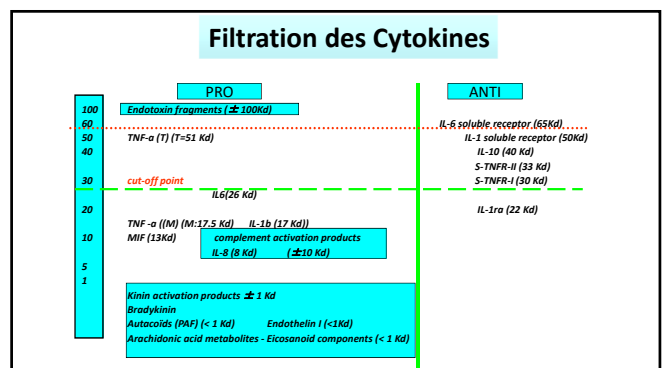
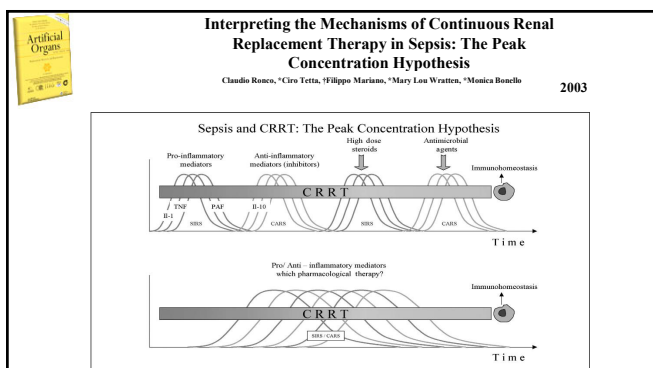
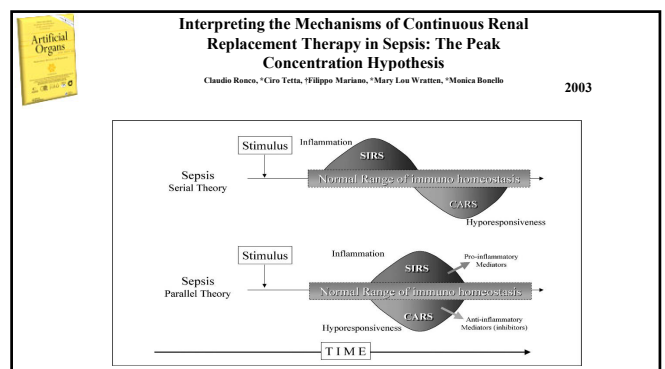
Infusion of ultrafiltrate from endotoxemic pigs depresses myocardial performance in normal pigs

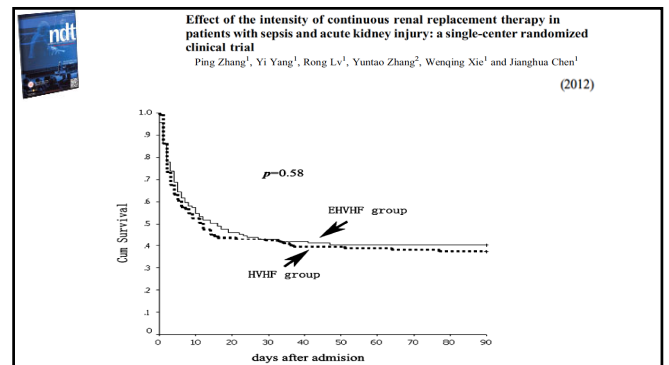
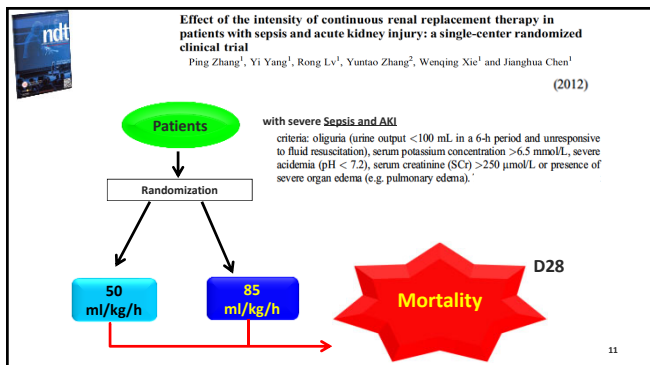
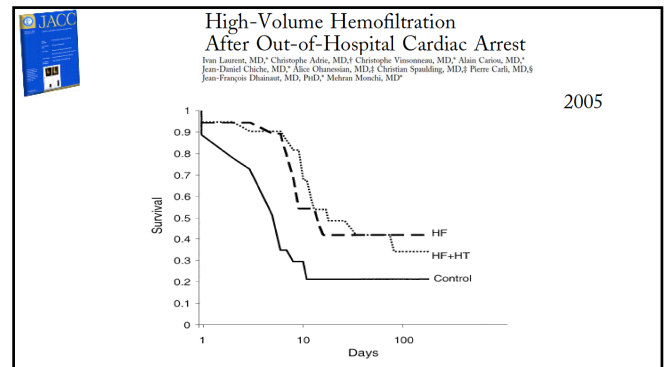
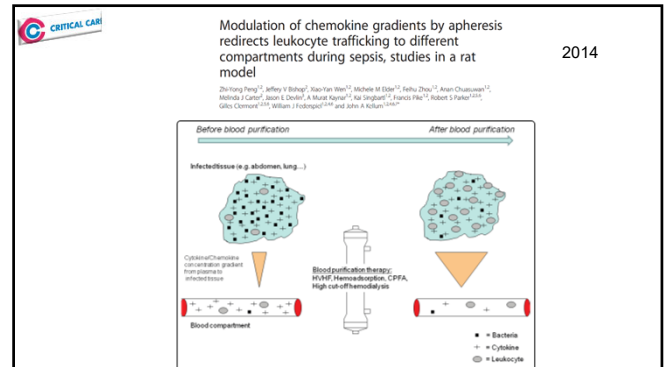
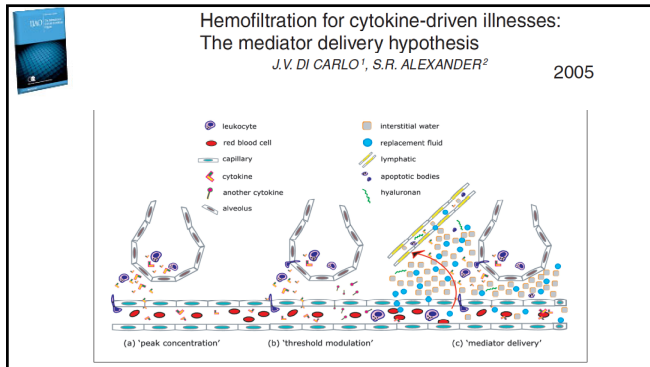
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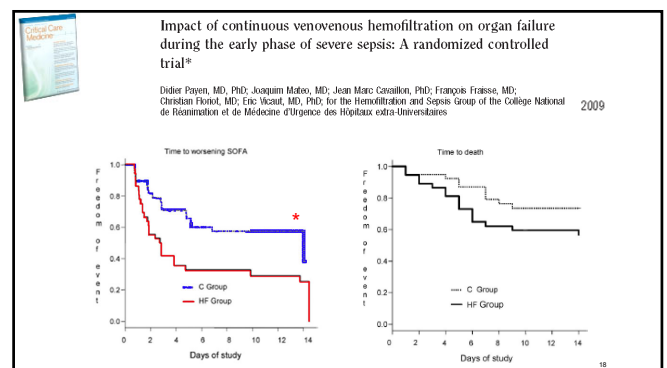
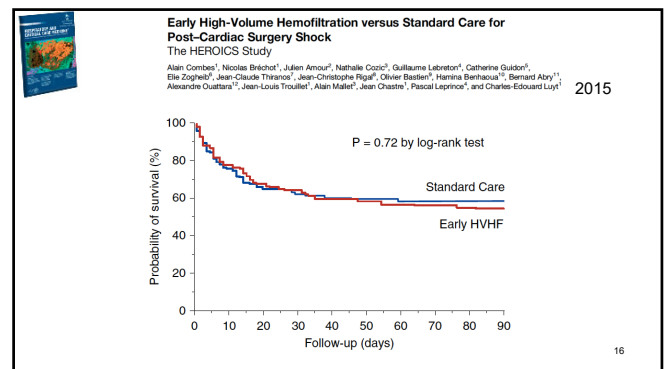
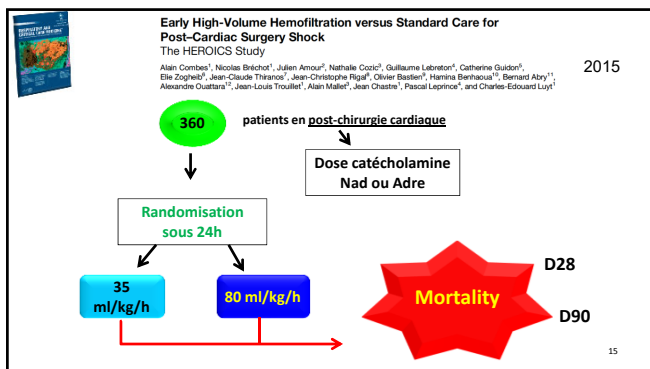
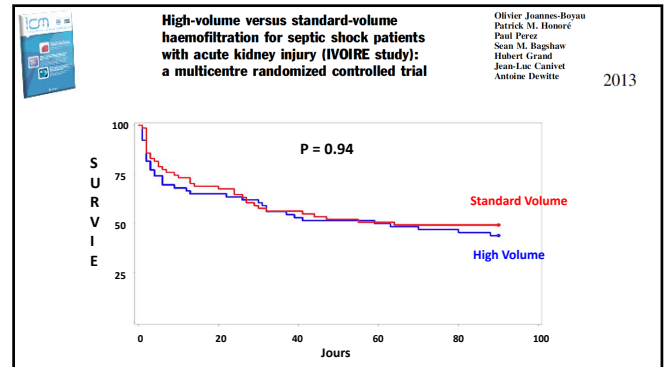
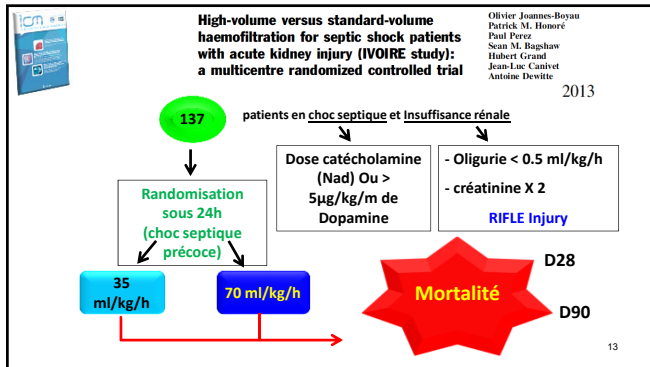
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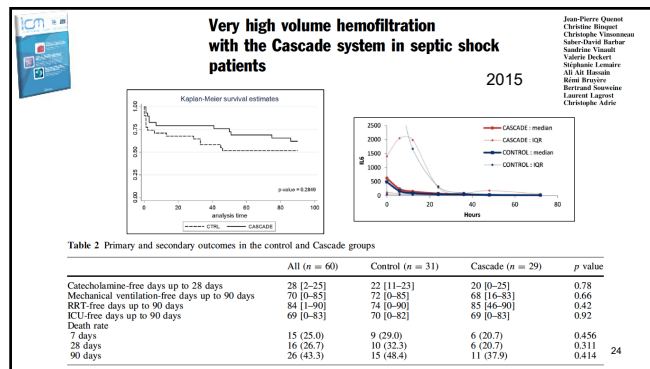
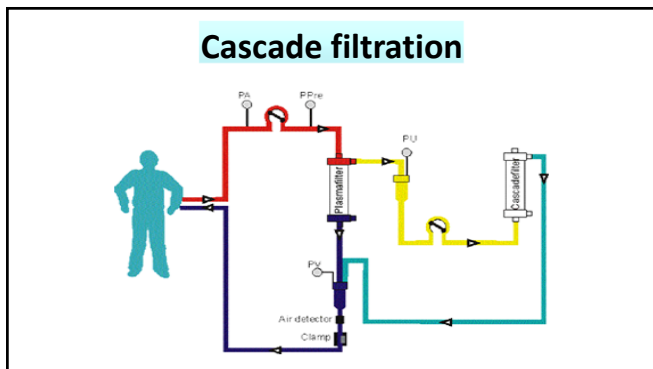
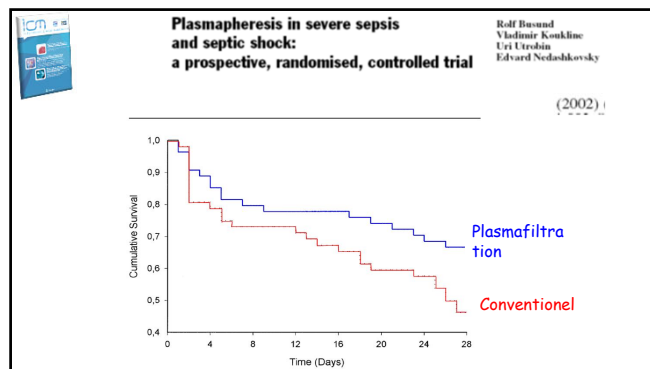
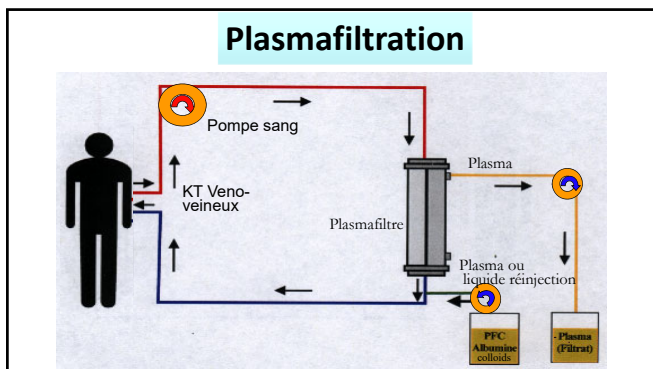
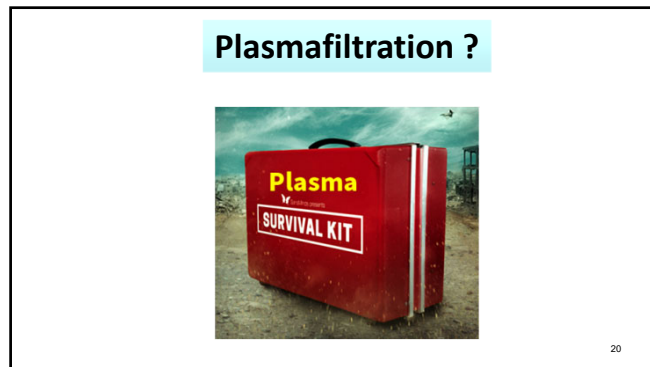
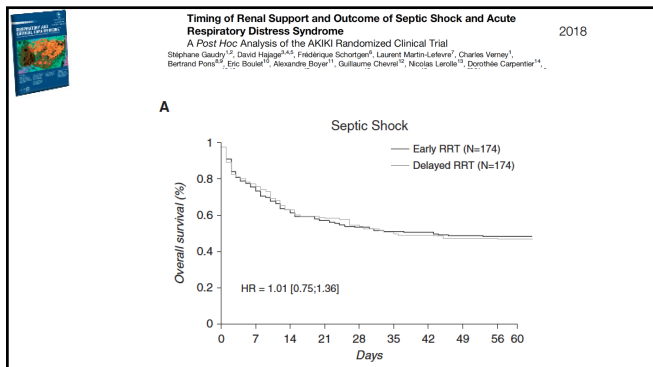
Control: Normal pig (blue line) → No effect (Pas d'effet).

Ultrafiltrate: Endotoxemic pig (red line) → Sepsis like (↓ SVRi, ↓ CO).





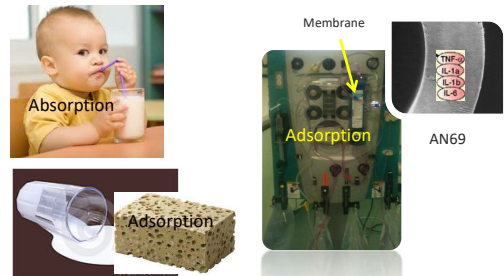




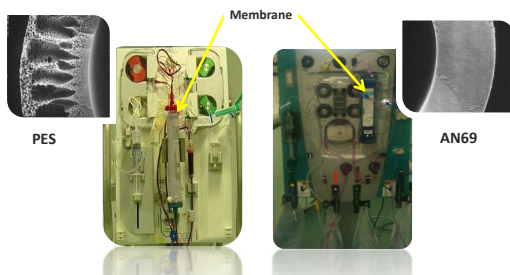
Adsorption



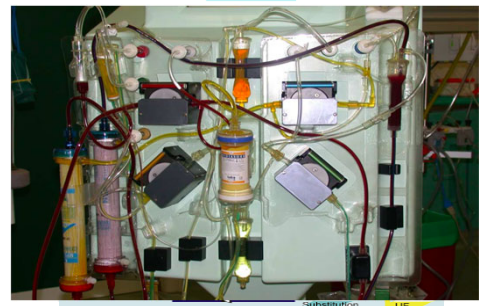
Adsorption ou Absorption ?



Adsorption



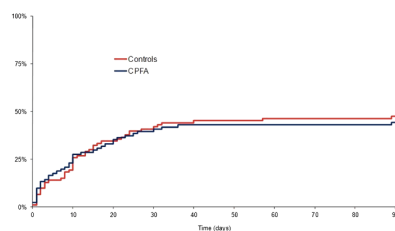
CPFA



Efficacy of coupled plasma filtration adsorption (CPFA) in patients with septic shock: A multicenter randomised controlled clinical trial

Sergio Livigni,¹ Guido Bertolini,² Carlotta Rossi,² Fiorenza Ferrari,¹ Michele Giardino,² Marco Pozzato,² Giuseppe Remuzzi,² GIVITI: I

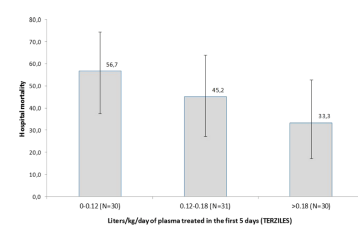
2014

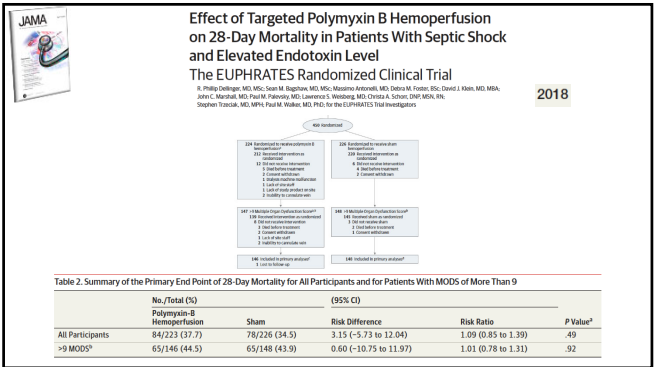
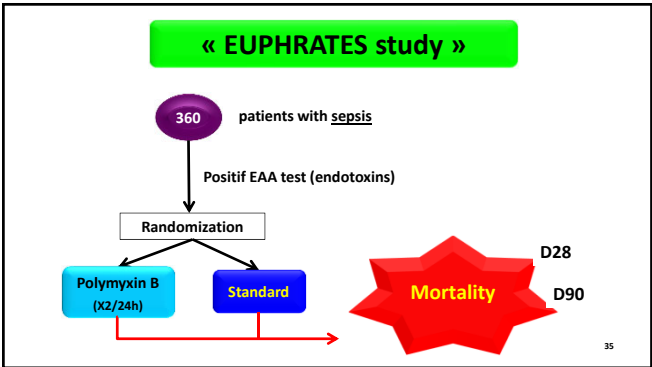
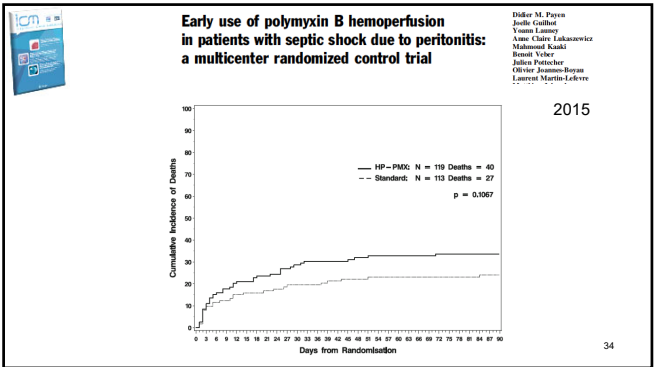
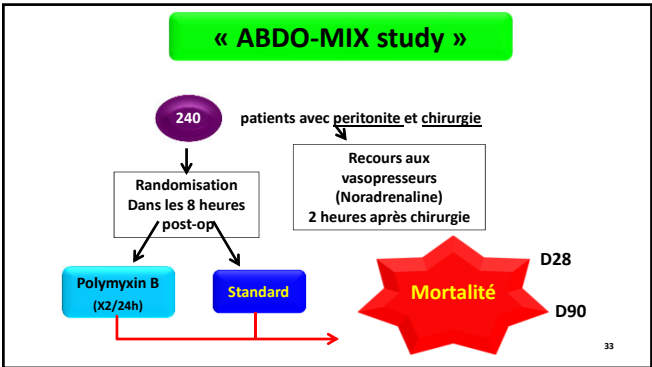
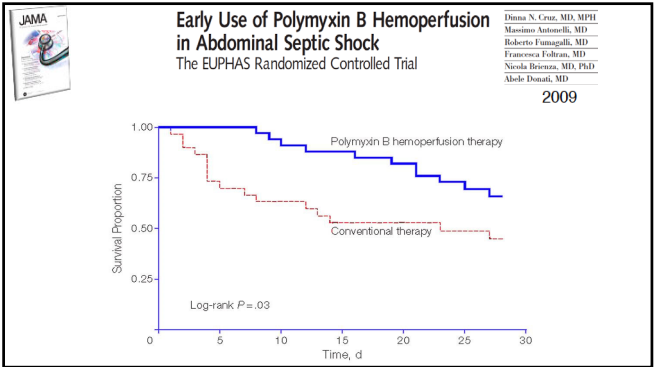
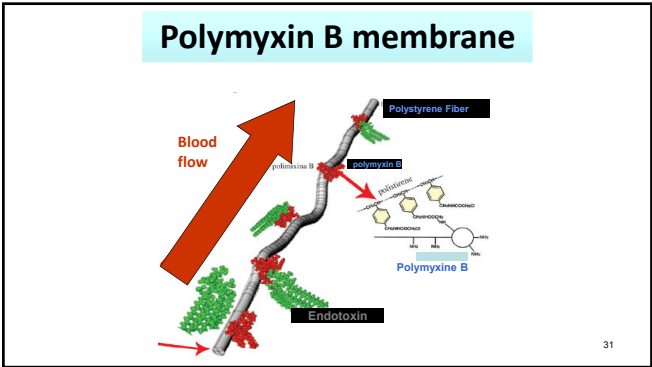


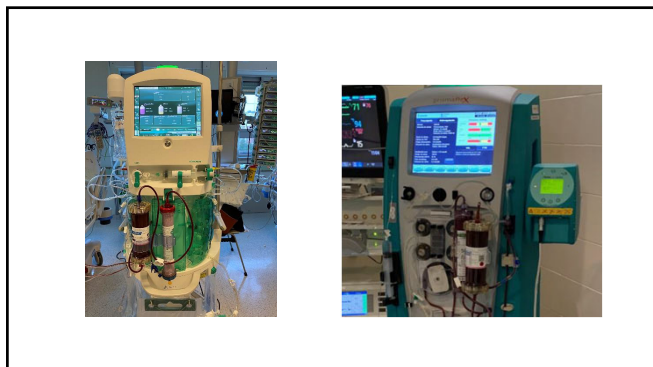
Efficacy of coupled plasma filtration adsorption (CPFA) in patients with septic shock: A multicenter randomised controlled clinical trial

Sergio Livigni,¹ Guido Bertolini,² Carlotta Rossi,² Fiorenza Ferrari,¹ Michele Giardino,² Marco Pozzato,² Giuseppe Remuzzi,² GIVITI: I

2014







From AN69 to AN69 Oxiris

Honore PM, Joannes-Boyau et al. ASAIO 2013

Fig. 1. Chemical formula for AN69 copolymer, consisting of acrylonitrile and sodium methallylsulfonate.

$$\left[\text{CH}_2 - \underset{\text{CN}}{\text{CH}} \right]_x \left[\text{CH}_2 - \underset{\text{CH}_2 - \text{SO}_3\text{Na}}{\text{CH}} \right]_y$$

Modified Surface

AN69 → AN69ST → OXIRIS

OXIRIS: Heparin, Polyethyleneimine, Polyacrylonitrile methylol sulfonate

High-volume haemofiltration with a new haemofiltration membrane having enhanced adsorption properties in septic pigs

Thomas Rimmel^{1,2,3}, Abdoulasser Assadi², Mathilde Cattaneo⁴, Olivier Deschamps^{2,3}, Corine Lambert⁴, Emmanuel Boscchi^{1,3}, Joëlle Goudali^{4,5}, Jérôme Etienne^{2,3}, Dominique Chassard^{1,3}, Guillaume Riteau^{4,5} and Bernard Allouche^{2,3,5}

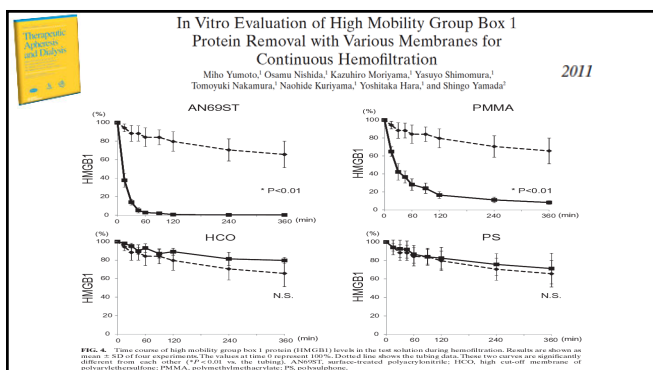
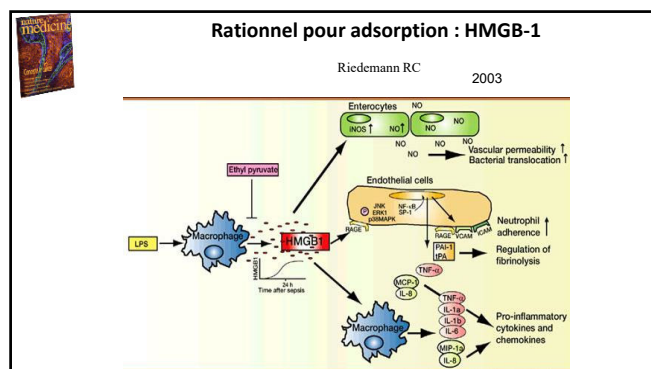
Table 3. Mean ± SD haemodynamic and biochemical parameters after a 6-h HVHF session, at T6

	AN69 mb (n = 10)	Treated mb (n = 10)	P-value
HR (beats/min)	138 ± 20	148 ± 16	0.23
MAP (mmHg)	64 ± 6	59 ± 8	0.13
SRAP (mmHg)	39 ± 9	36 ± 8	0.029
MPAP (mmHg)	34 ± 8	24 ± 7	0.008
PCWP (mmHg)	12 ± 3	11 ± 4	0.53
CO (l/min)	6.9 ± 4.8	5.5 ± 2.8	0.44
SAR (dyn/cm ²)	672 ± 205	797 ± 346	0.34
PVR (dyn/cm ²)	325 ± 186	234 ± 148	0.24
Epinephrine (mg)	3.27 ± 3.02	2.11 ± 1.05	0.27
Cryoprecipitate (ml)	7587 ± 1456	5937 ± 1588	0.026
Hydroxyethylstarch (ml)	1912 ± 538	1437 ± 320	0.027
pH	7.10 ± 0.07	7.20 ± 0.11	0.026
Lactate (mmol/l)	14.11 ± 3.36	9.61 ± 4.47	0.02

Table 4. Mean ± SD serum endotoxin levels (EU/ml)

	AN69 mb (n = 10)	Treated mb (n = 10)
T0	3.98 ± 3.31	4.26 ± 7.68
T1	11.07 ± 10.64	1.91 ± 1.19*
T6	2.96 ± 2.75	2.26 ± 2.39

D'après T. Rimmelé



CRRT 2013

CONTINUOUS RENAL REPLACEMENT TREATMENT (CRRT) COMBINED WITH ENDOTOXINS REMOVAL IN SEPTIC PATIENTS: A PILOT STUDY

Patrice Carclet¹, Angèle Lapeere², Fabienne Monnet³, Nicolas Kervadec⁴, Frédéric Combes⁵, Francis Turrel⁶, Mounir Faleu⁷

AIM

We tested a recently developed CRRT membrane having enhanced adsorption capability on endotoxins (okarisTM, Gambro Industries, Meyzieu - France). This membrane is a AN 69TM based membrane, surface treated with a polyethyleneimine (PEI) and grafted with heparin (8000 U/g) to perform a combined treatment of CRRT and selective adsorption of endotoxins and cytokines in patients with acute kidney injury caused by severe sepsis or septic shock (see Figure 1).

RESULTS

34 patients (Age = 65.1 ± 10 years, Weight = 74.5 ± 13 kg, 8 F / 26 M) received CRRT with use of 1.350 L okarisTM cells per patient for average treatment time of 79.2 ± 25 hours. Relevant improvements in terms of haemodynamic stability and renal function were found comparing before and after okarisTM treatment. In particular, an increase of mean arterial pressure and urine output combined with decrease of SOFA scores and norepinephrine dose were found (see Table 1). These results were associated to a relevant decrease of inflammatory markers such as interleukin 6 (IL6) and procalcitonin (PCT) that decrease from 37450.1 to 4657 (p<0.01) pg/ml and from 76889 to 12115 (p<0.01) ng/ml respectively. Mortality rate at 28 days of 23% (10/44) and a good renal function recovery (15/23 patients + 1 ESRD) were found.

Table 1 - Changes in SOFA, mean arterial pressure (MAP), urine output and norepinephrine dose in patients treated with okarisTM (mean ± SD).

	PRE	POST	T-TEST
SOFA	18.6 ± 5.0	12.4 ± 5.0	0.001
MAP (mmHg)	12.9 ± 2.8	13.2 ± 2.7	0.001
Urine output (ml/kg/h)	0.18 ± 0.17	0.31 ± 0.11	0.001
Norepinephrine dose (μg/kg/min)	0.40 ± 0.30	0.20 ± 0.10	0.001

CONCLUSION

In our experience, the use of this new filter was associated with haemodynamic improvements combined with positive trends of SOFA score and norepinephrine requirements. Moreover, good renal recovery and a survival rate higher than the SOFA predicted one resulted in this population (29% vs 40%). Although this study has many limitations such as lack of endotoxins levels assessment and no randomization analysis, we believe that it will represent a promising result to start further investigations related to the sepsis mediators adsorption combined with AKI treatment by using this newly developed membrane.

P063 - A643 - Continuous renal replacement therapy with the adsorbent membrane oXiris in septic patients: a clinical experience.
 F. Turani, F. Candidi, R. Barchetta, E. Grilli, A. Belli, E. Papi, A. Di Marzo, M. Falco
 AUGELIA HOSPITAL/EUROPEAN HOSPITAL, Anesthesiology Intensive Care, R, Italy

Introduction: Renal failure is an important complication of sepsis and CRRT with adsorbing membranes may be useful in this clinical setting (1). The aims of the study in septic / septic shock patients is to evaluate 1 - the safety of a new hemofilter membrane oXiris with adsorbing properties and anti endotoxin activity 2 - the renal and hemodynamic response 3 - the changes of endotoxin and pro - inflammatory molecules.

Methods: 40 septic / septic shock patients with renal failure were enrolled in the study. All patients had preoperative endotoxin > 0.6 level - units (EAA Spectral D.) and were submitted to high volume haemofiltration (50 ml/kg/h - Prismaflex - Gambro) with a new treated membrane heparin coated (oXiris TM - Gambro). At T0 (pretreatment) T1 (24 hours) the main clinical and biochemical data were evaluated. All data are expressed as mean SD . ANOVA TEST one way with Bonferroni correction was used to evaluate the data changes . P < 0.05 was considered significant.

Results: At table 1 are shown the main results of this study.

Conclusions: In septic / septic shock patients with renal failure CRRT with a new treated membrane heparin coated (oXiris TM - Gambro) is clinically feasible - has a positive effect on renal function and hemodynamic. An adsorbing effect on pro - inflammatory mediators may have a role in these results. These data and the trend toward a decrease of endotoxin during the treatment warrant further investigation.

References:
 1. Raimondo T et al. Nephrol Dial Transplant 2009 ; 24 :421-427.

33rd ISTCCM 2013

Parameters	Units	T0	T1	p
Creatinine	mg/dl	1.34 ± 1	1.18 ± 1	p= 0.05
Diuresis	ml/24 h	1264 ± 76	1573 ± 96	
Nonopreptine	mcg/kg/min	0.17 ± 2	0.06 ± 1	p= 0.05
IL6	pg/ml	572 ± 76	278 ± 37	p= 0.05
Procalcitonine	ng/ml	35 ± 7	15 ± 2	p= 0.05
Endotoxin	LevelU	0.64 ± 0.2	0.49 ± 0.1	

High cut-off membrane

SEPTEX® et EMIC2®

Albumine ?

44

A Double-Blind Randomized Controlled Trial of High Cutoff Versus Standard Hemofiltration in Critically Ill Patients With Acute Kidney Injury
 Rafidh Ann, PhD¹; Leah Peck, GnaCertCeph Care²; John Prowse, MD^{3,4}; Elise Liaw, MD⁵; Glenn M. Eastwood, PhD⁶; Markus Storr, PhD⁵; Hermann Goehl, MSc⁷; Rinaldo Bellomo, MD⁷

2018

Neutrophil count in x10⁹/L

CVR-HCO
CVR-HD

p=0.750

Outcomes	Continuous Venovenous Hemofiltration-High Cutoff (n=18)	Continuous Venovenous Hemofiltration-Standard (n=12)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
ICU mortality	18 (100)	12 (100)	2.17 (0.84-5.58); p=0.109	2.13 (0.89-5.00); p=0.101
Hospital mortality	20 (55.6)	13 (34.2)	2.40 (0.94-6.15); p=0.067	2.49 (0.91-7.06); p=0.112

Futur ?

Hemoabsorption removes tumor necrosis factor, interleukin-6, and interleukin-10, reduces nuclear factor-κB DNA binding, and improves short-term survival in lethal endotoxemia*

John A. Kellum, MD, FCCM; Mingchen Song, MD, PhD; Ramesh Venkataraman, MD

2004

Sham CytoSorb

1 2 3 4

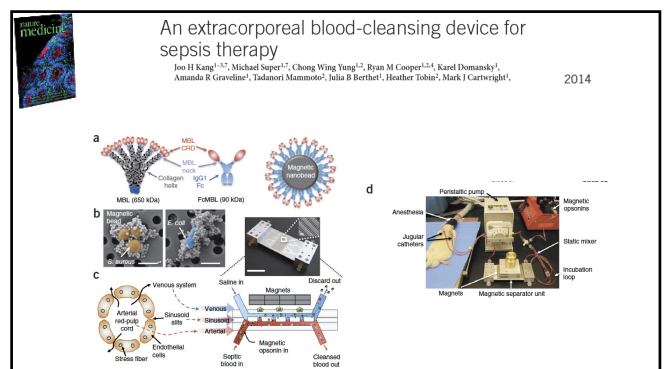
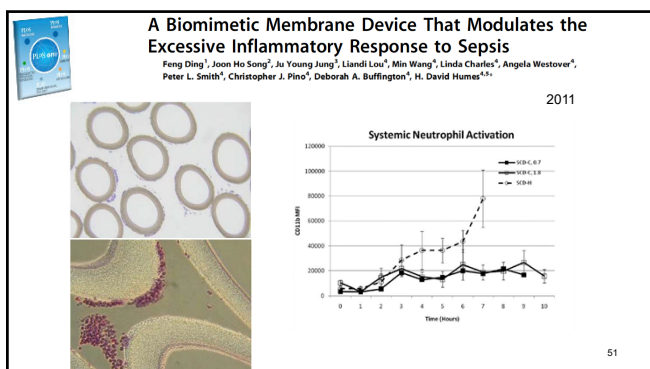
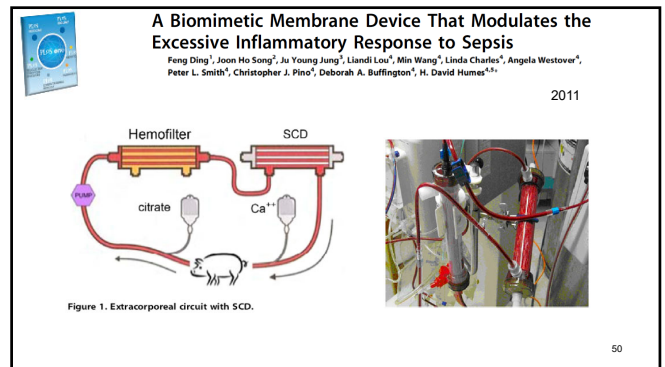
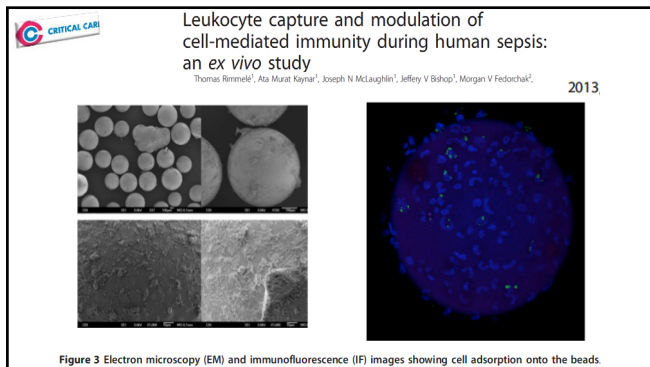
Epuración du NFκB du tissu hépatique

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Blood Purification With CytoSorb in Critically Ill Patients: Single-Center Preliminary Experience
 *Maria Grazia Calabrò, *Daniela Febres, *Gina Recca, *Rosalba Lembo, *Evgeny Fominitsky, *Anna Mara Scandroglio, *Alberto Zangrillo, and *Federico Pappalardo

2018

Values	Peak during treatment	End of treatment	P value
Total bilirubin (mg/dL)	11.6 ± 9.2	6.8 ± 5.1	0.005
Lactate (mmol/L)	12.1 ± 8.7	2.9 ± 2.5	<0.001
CPK (U/L)	2416 (670-8615)	281 (44-2769)	<0.001
LDH (U/L)	1230 (860-3157)	787 (536-1148)	<0.001



Conclusion

- Des théories physiopathologiques prometteuses
- Des études animales et humaines encourageantes
- MAIS aucun RCT montrant un réel bénéfice
- Très coûteux et techniquement compliqué
- Nouveaux essais attendus et nécessaires

L'utilisation de ces techniques en dehors de la recherche n'est pas recommandée