Effective Removal of Cytokines Using Polyacrylonitrile PAN (AN69®) Membranes Compared to PS and PMMA Membranes During the Initiation of Hemodialysis

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APCNXTSN 2025

Introduction

History of Polyacrylonitrile (PAN) membrane

PAN (AN69) membrane

Cuprophan ®
1965

1968
Hollow fiber dialyzer (USA)

Polyacrylonitrile (PAN) membrane (developed)
1969

1972年

1975年
Regenerated cellulose membrane (Germany)
on market

PMMA membrane
(on market)
1977年

1983年
PS membrane
(Germany)
on market

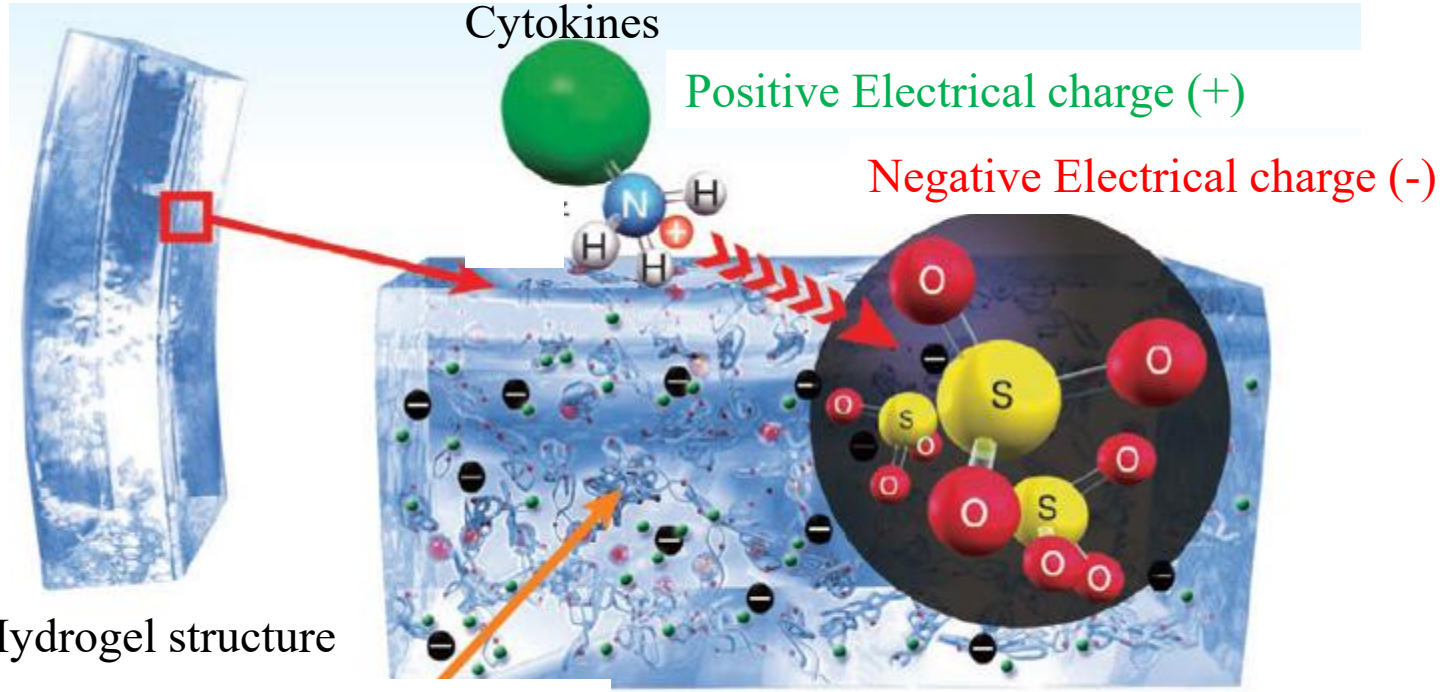
Polyacrylonitrile (PAN) membrane on market

Target: larger molecular-weight uremic toxins

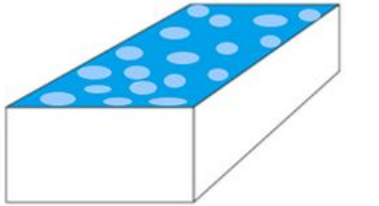
Different type of Synthetic membrane

Synthetic polymer membrane	Removal flux	Biocompatibility
Polysulfone (PS)	High flux (β2MG) Higher ALB leakage	
Polyethersulfone (PES)	High flux (β2MG) Low ALB leakage	Lower complement activation Lower PLT fluctuation
polyester polymer alloy membrane (PEPA)	High flux (β2MG) Low ALB leakage	
Polymethyl methacrylate (PMMA)		β2-MG absorption Cytokine removal
Polyacrylonitrile (PAN)	Low amino acid leakage Low ALB leakage	Cytokine removal Lower WBC fluctuation Lower complement activation
Ethylene-vinyl alcohol copolymer (EVAL)		Anti coagulation Lower WBC fluctuation

PAN membrane :

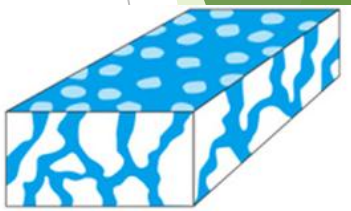


Surface capacity



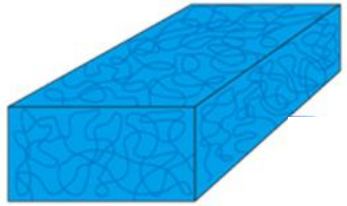
PS membrane

Surface & tunnel capacity



PMMA membrane

Abundant capacity



PAN membrane

https://www.baxterpro.jp/products/crrt/sepxiris

- High biocompatibility
- Bulk adsorption capacity (cytokine / mediator)

PAN membrane evidences for maintenance HD patients

Improve

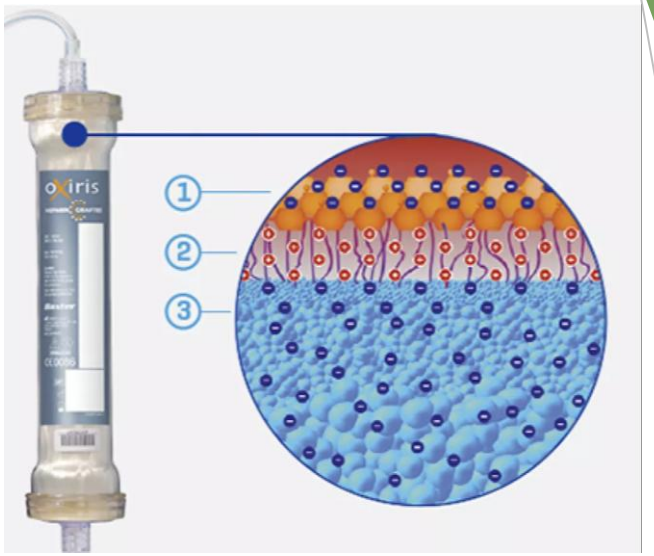
- Malnutrition & Appetite loss
- Chronic inflammation
- Erythropoietin resistance
- Ischemia in Atherosclerosis and peripheral arterial disease

J Clin Med . 2023 Jan 31;12(3):1123.

Emergency and Critical Care

- The modified PAN membrane (oXiris®)
  enables adsorption of cytokines and endotoxins

- PMMA and PAN membrane improve
  life expectancy (3 times longer)



Intervention	Implementation of SSCG					CAH-CHDF	
						PMMA-CHDF	AN69ST-CHDF
Author	Shapiro [13]	Shorr [14]	Ferrer [15]	Castellanos-Ortega [16]	Opal [12]	Nakada [5]	Shiga
Country	US	US	Spain	Spain	International (ACCESS trial)	Japan	Japan
Year of publication	2006	2007	2008	2010	2013	2008	2012
Number of cases	116	60	1,465	384	1,304	43	34
Age, years	68.0±16.0	61.4±20.0	62.1±16.3	64.5±15.1	65.4±15.0	63.5±13.3	67.1±12.1
APACHE II score	22.6±8.8	23.3±9.6	21.3±7.8	23.2±7.8	27.2±4.5	29.4±8.4	32.7±9.8
Predicted survival, %	57.6	54.0	61.1	54.0	39.5	32.8	20.3
Observed 28-day survival, %	79.7	70.0	68.9	62.5	71.9	79.1	73.5
Observed/predicted survival ratio	1.38	1.29	1.13	1.16	1.82	2.41	3.62

Data are given as number or mean ± SD.

https://pro.vantive.com/oxiris-set

Blood Purif . 2014;38(3-4):211-8.

Cytokine ranges

Pathophysiological conditions	IL-6 (pg/ml)	TNFα (pg/ml)
Septic shock	4,000～20,000	10～50
Trauma injury	200～1000	10～50
CKD stage 4-5	4.39 (3.19-8.25)	2.26 (1.69-2.86)
Healthy individuals	1.06 (0.70-1.83)	0.86 (0.68-1.10)

Renal Replacement Therapy (2025) 11:7
Inflamm Res . 2022 Jun;71(5-6):591-602.

Clinical question:

Malnutrition and inflammation in maintenance HD patients

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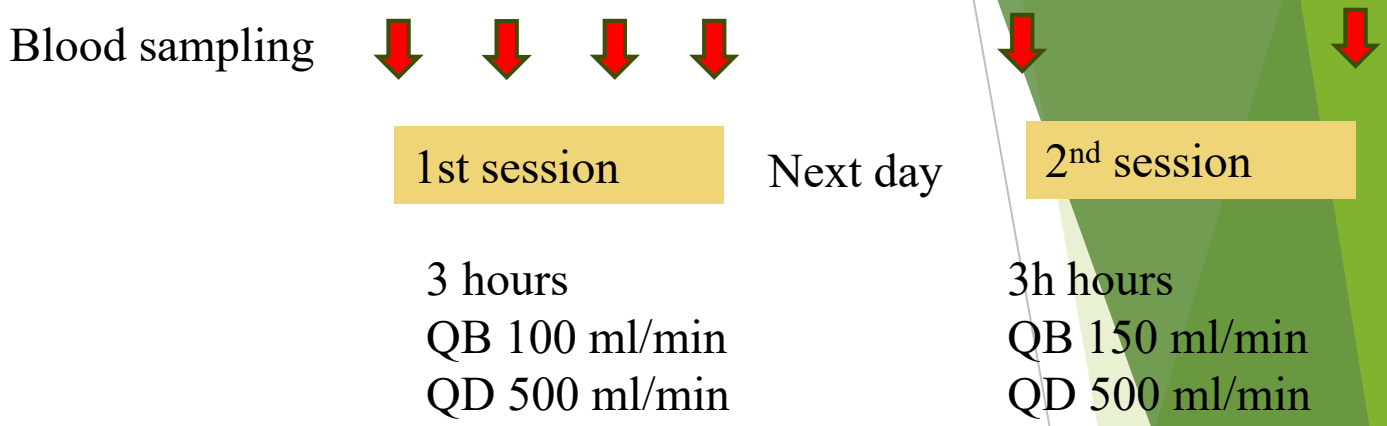
Emergency and critical patients

Can PAN and PMMA membrane effectively remove cytokine?

PURPOSE

To compare the biocompatibility of three membrane types (PAN, PMMA, and PS) in patients undergoing initiation of maintenance hemodialysis without acute illness.

Methods

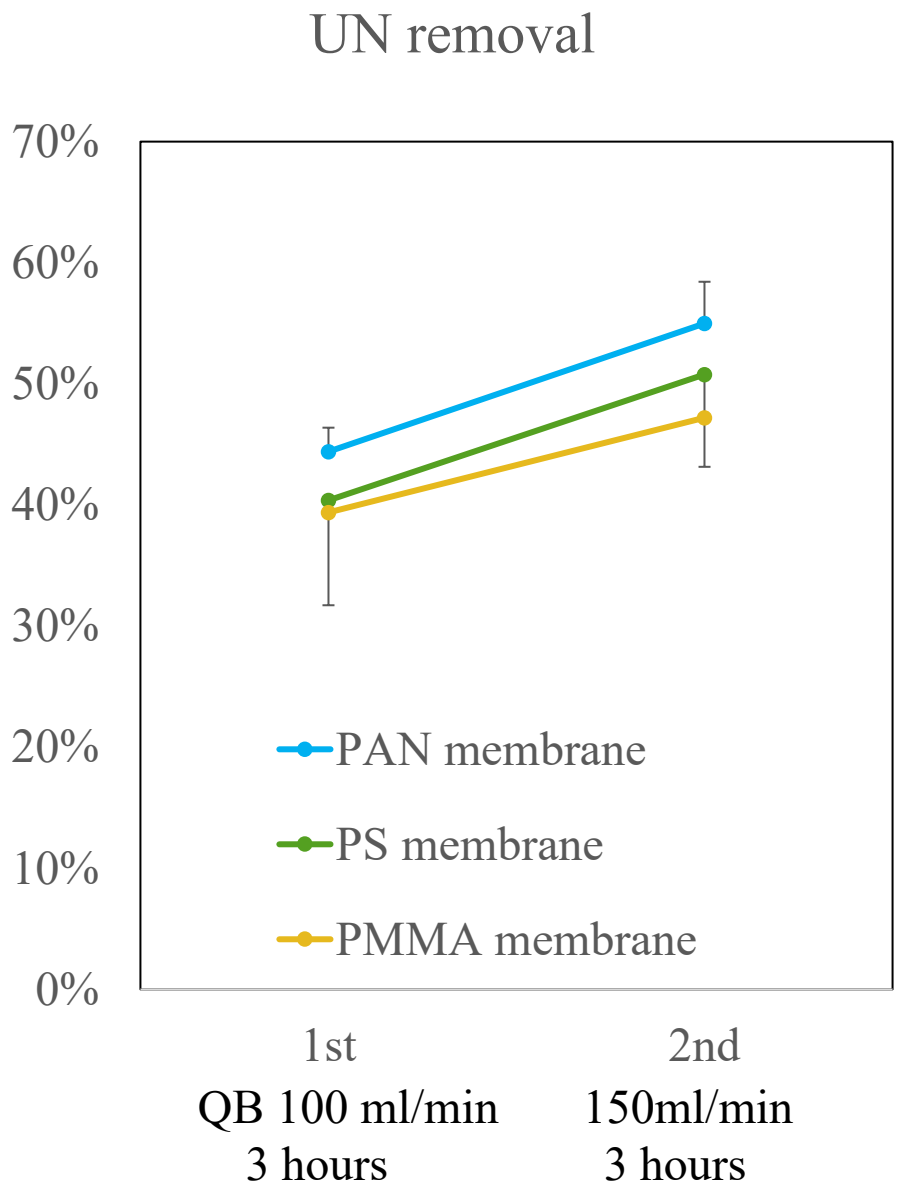


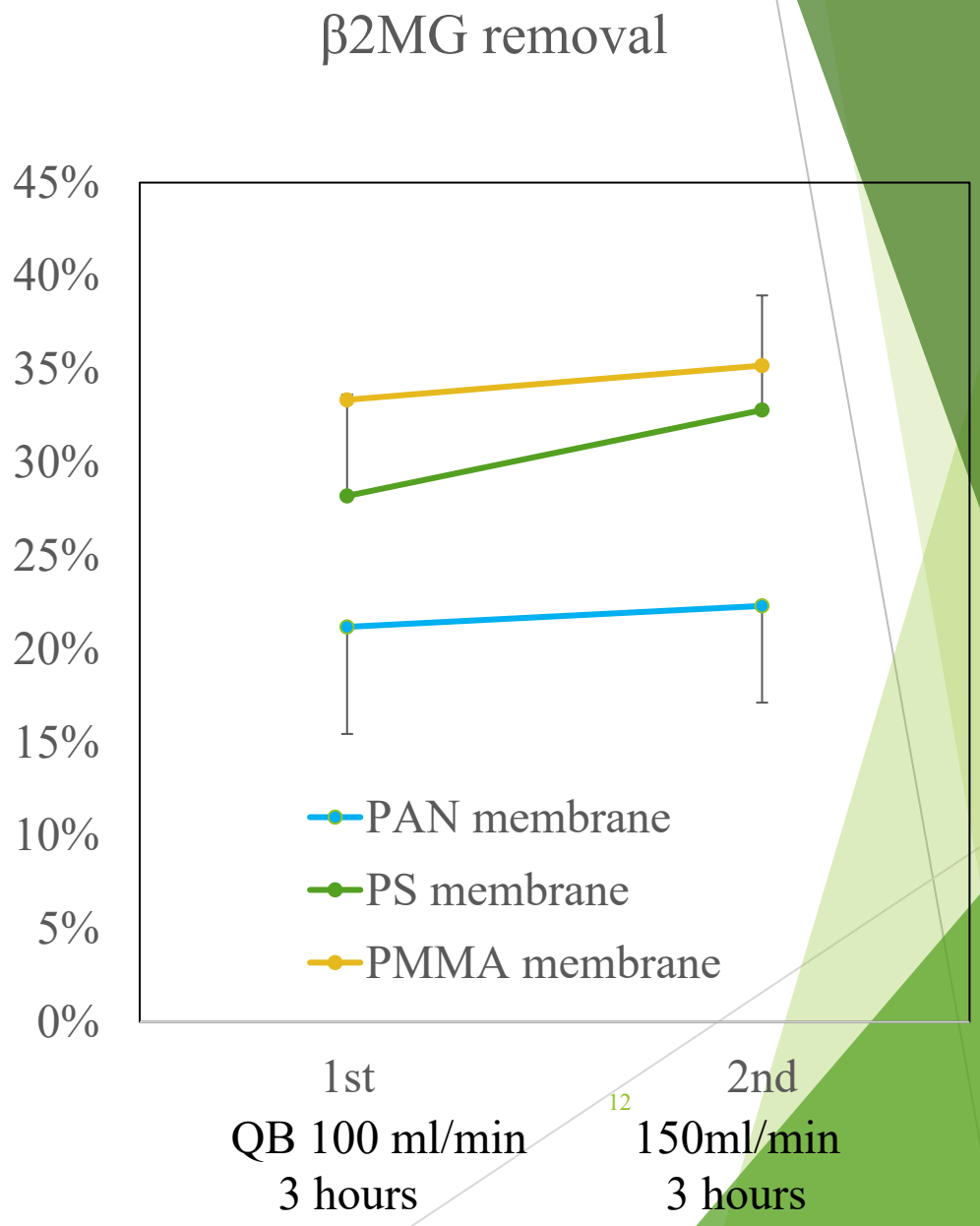
Planned HD introduction cases

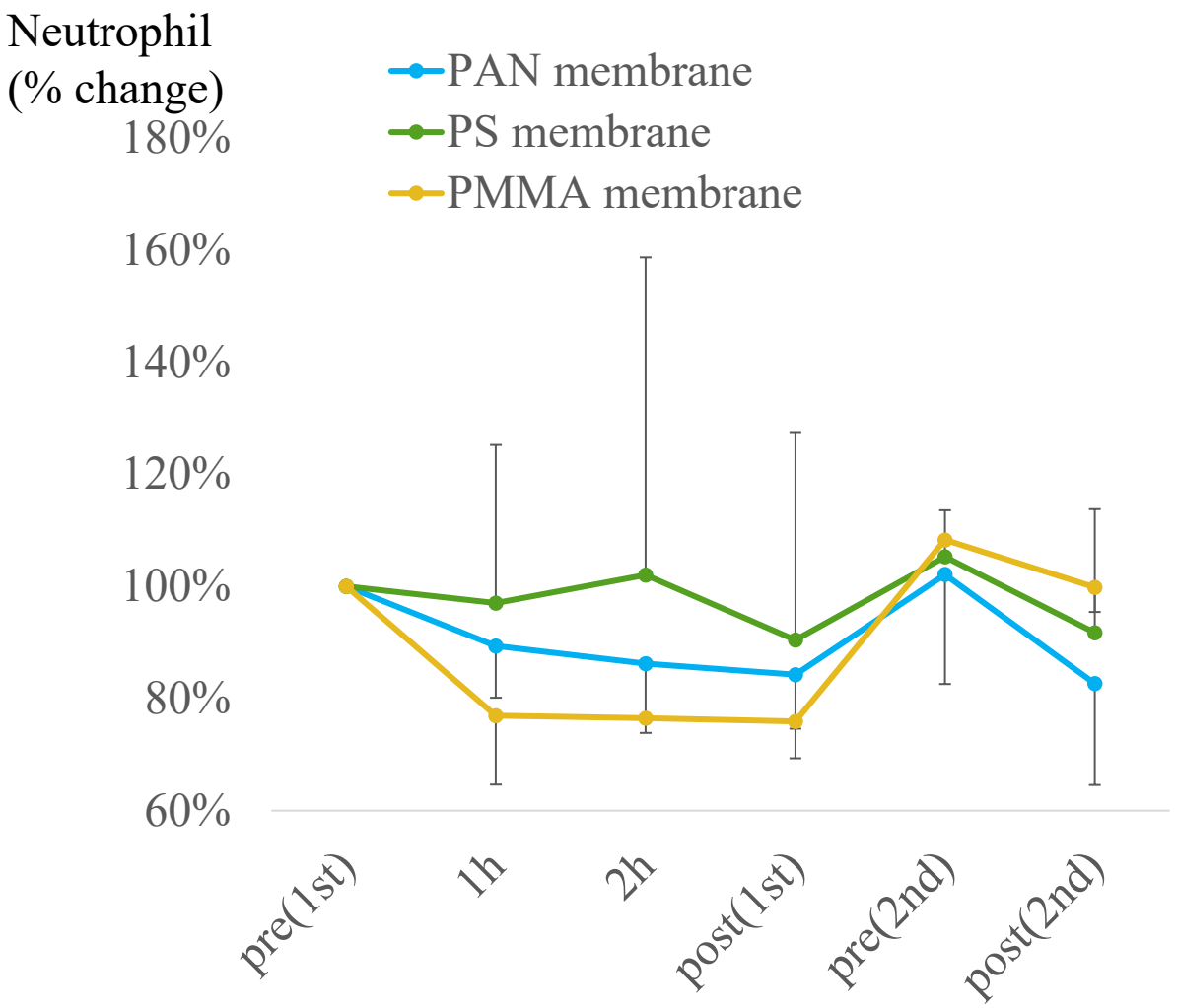
- PAN membrane (H12-2800: 1.0 ㎡)
- PS membrane (FX-100: 1.0㎡)
- PMMA membrane (NF-1.0H: 1.0㎡)

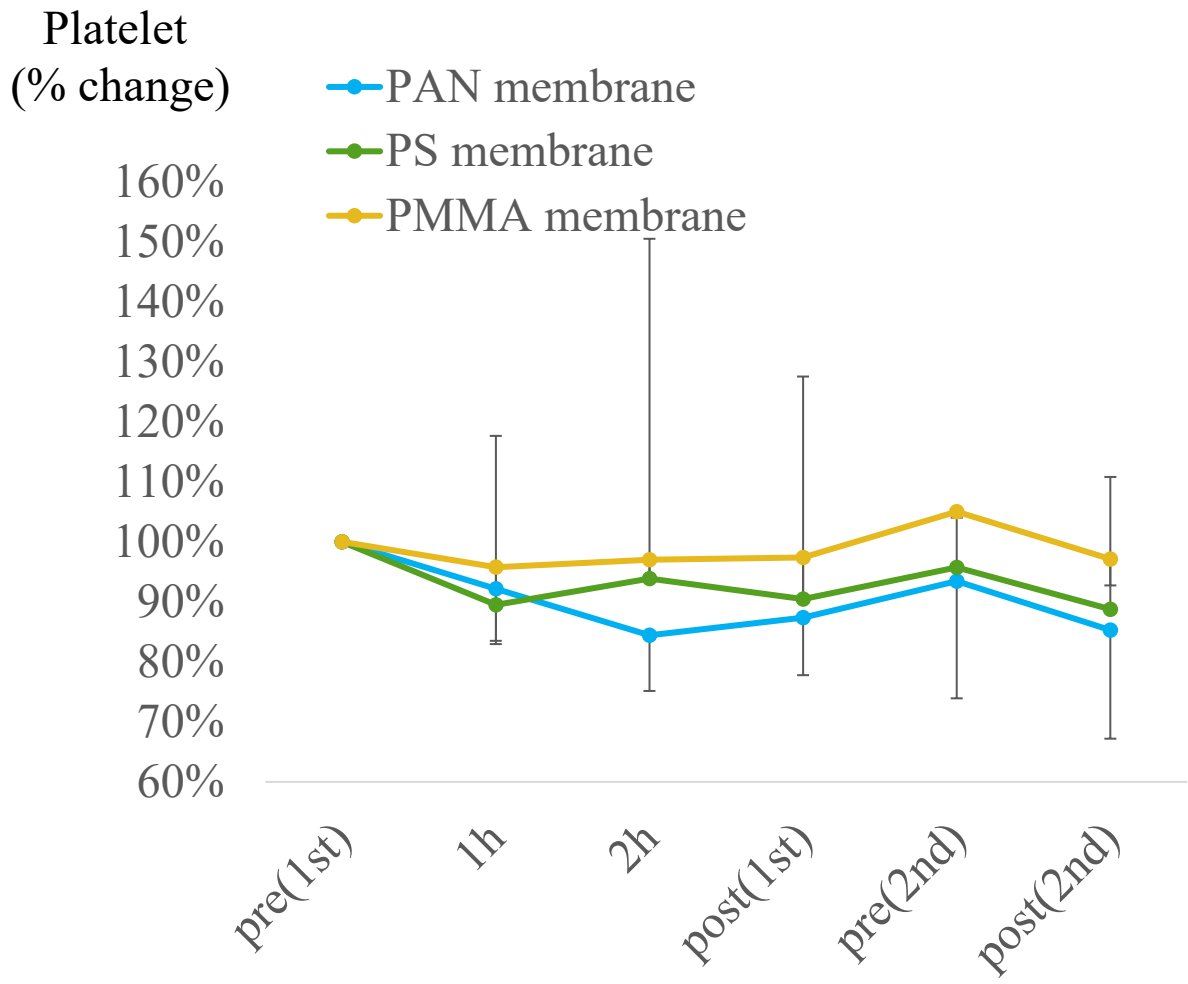
RESULTS

UN / β2MG removal



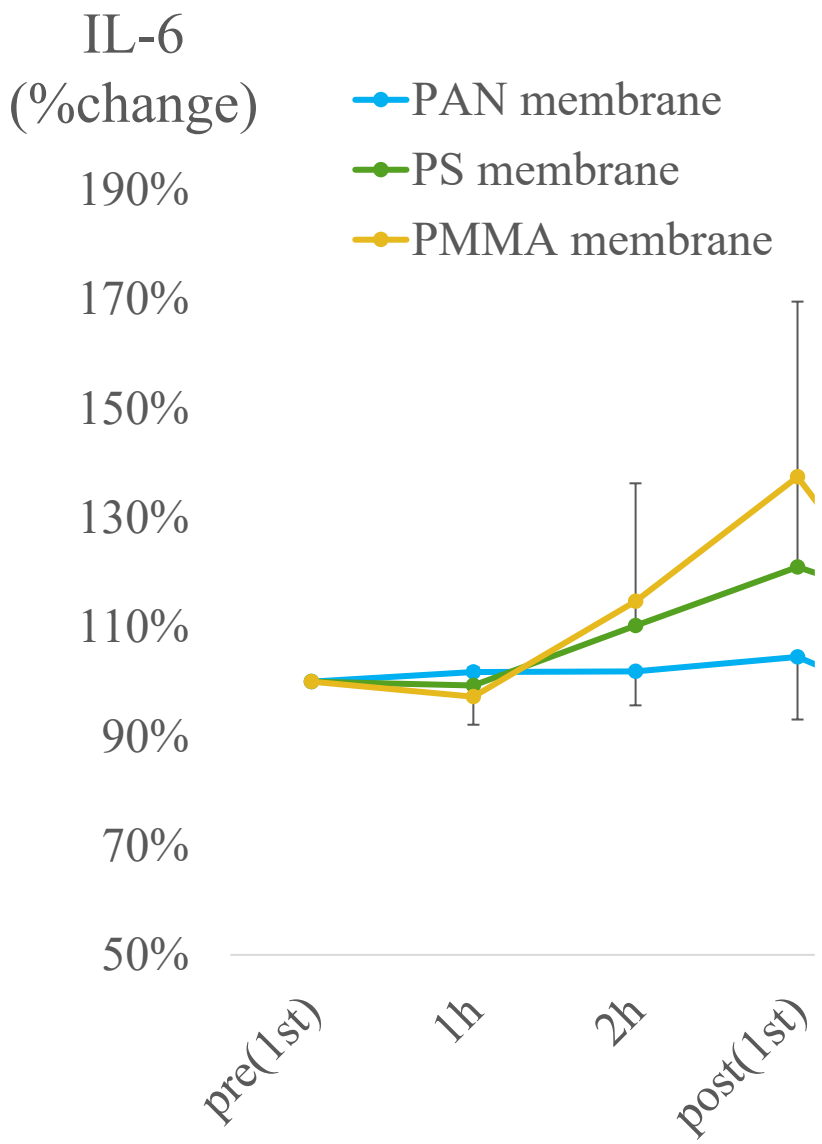


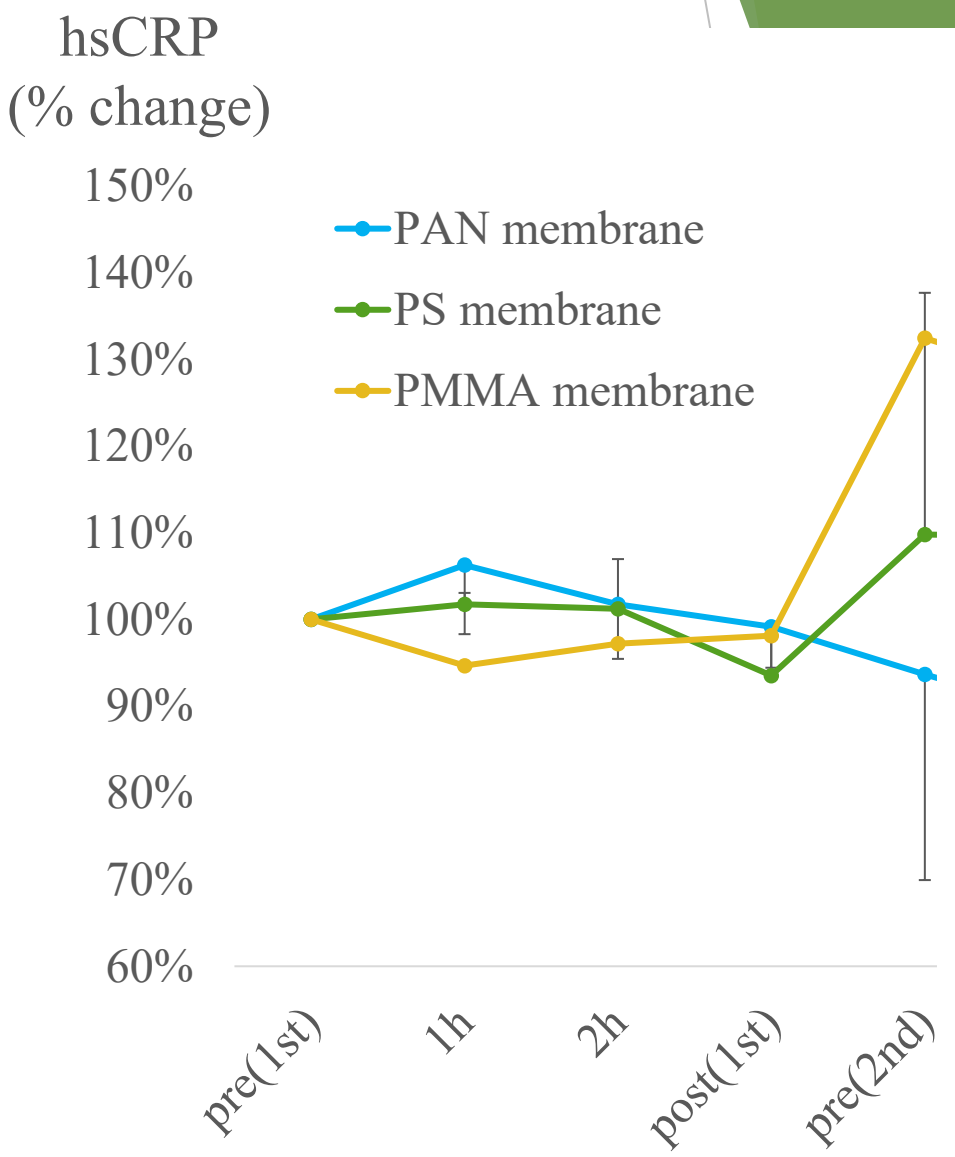




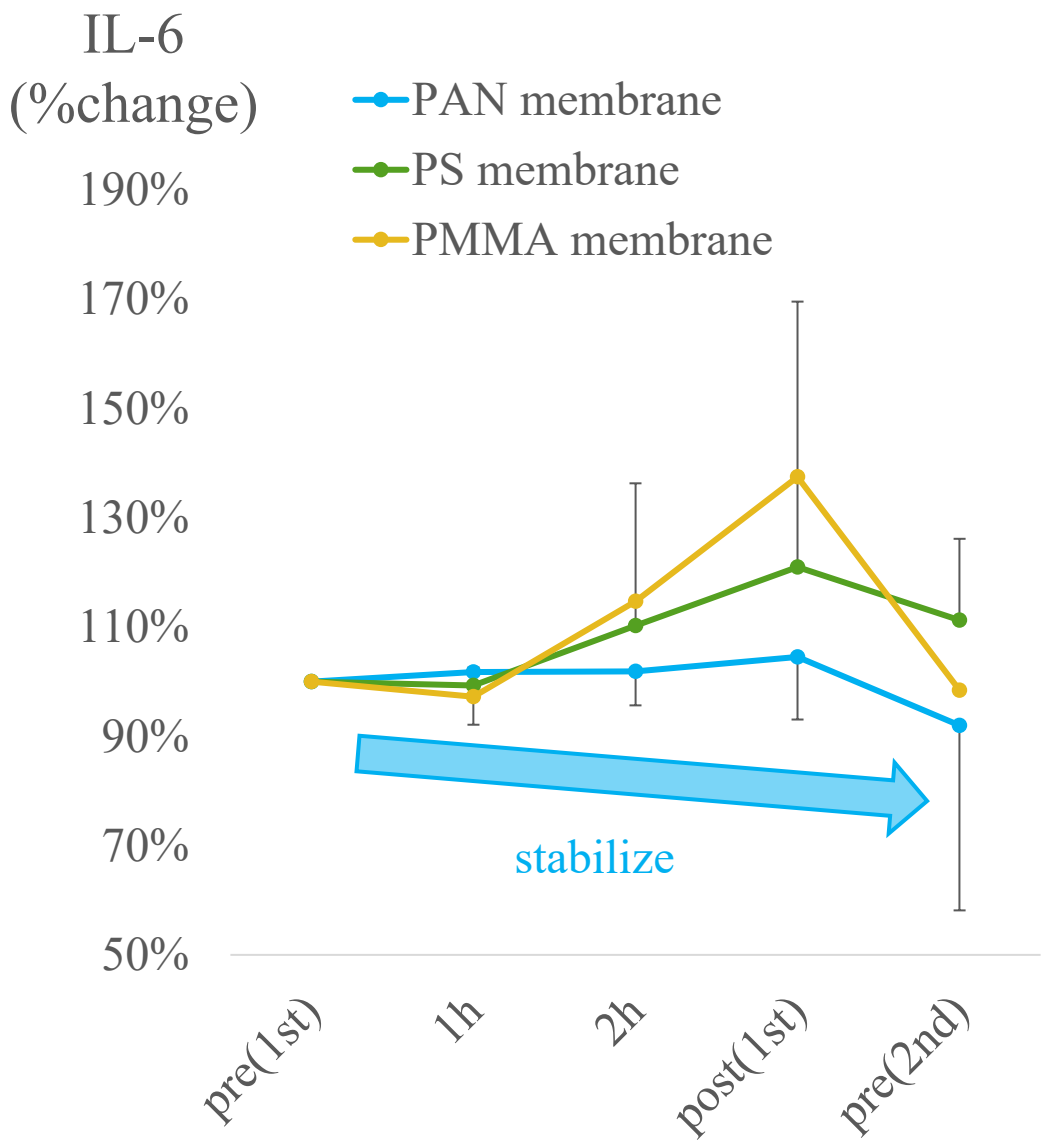
	Neutrophil	Platelet
PAN membrane	Decrease	Decrease
PS membrane	Transient fluctuation	Transient fluctuation
PMMA membrane	Decrease	No change

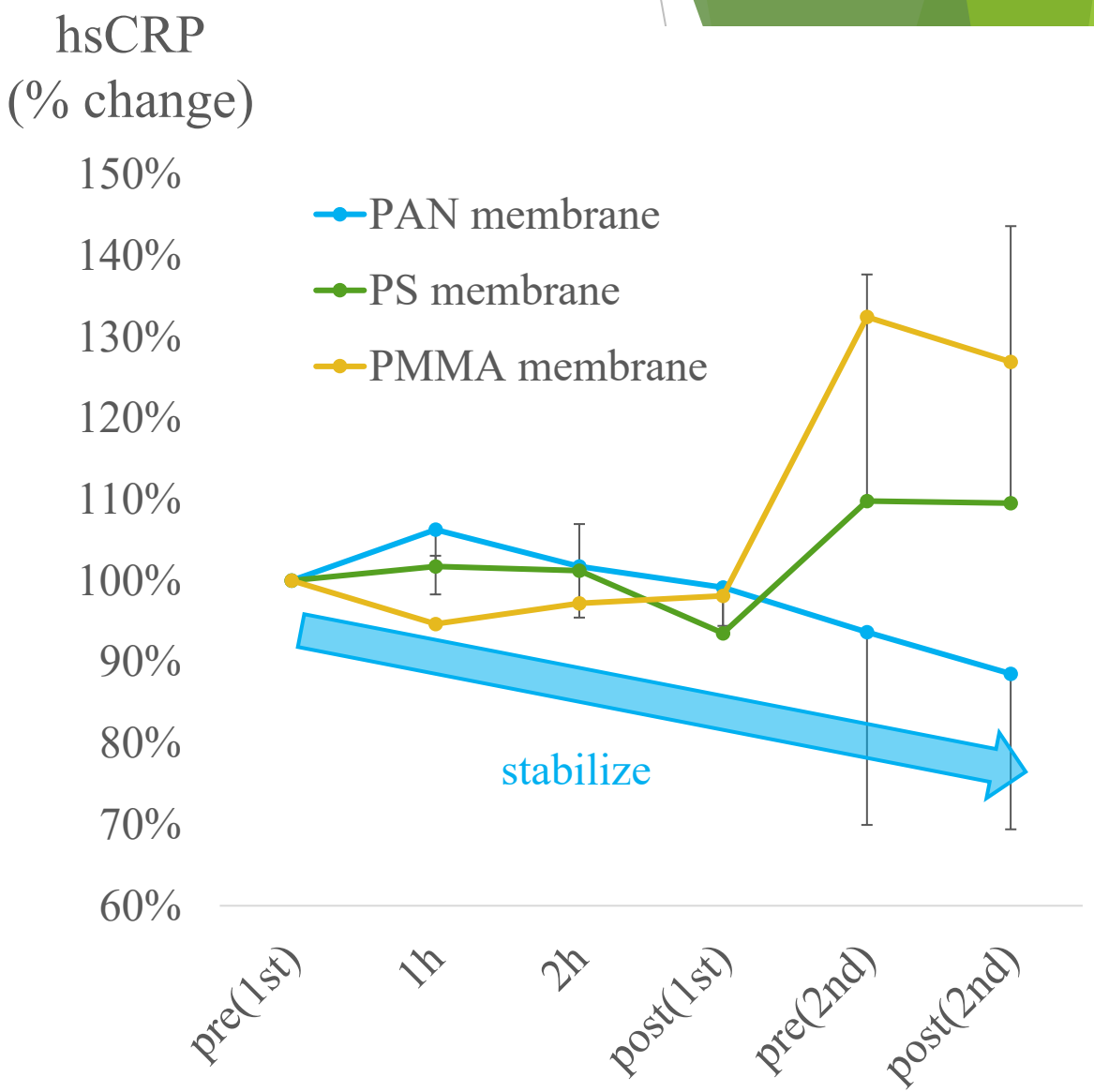
Inflammation markers





Inter dialytic change on IL-6 and hsCRP



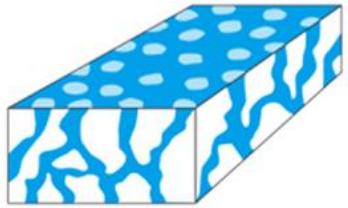


Discussion

What is the difference between PMMA and PAN?

	Cytokine removal	Adsorption mechanism	Capacity
PS membrane	Filtration		Low
PMMA membrane	Adsorption	Hydrophobic binding (Conc. dependent)	High
PAN membrane	Adsorption & Filtration (Release to dialysate)	Electric charge (Conc. Independent)	High ～unlimited

PMMA membrane



Hydrophobic binding

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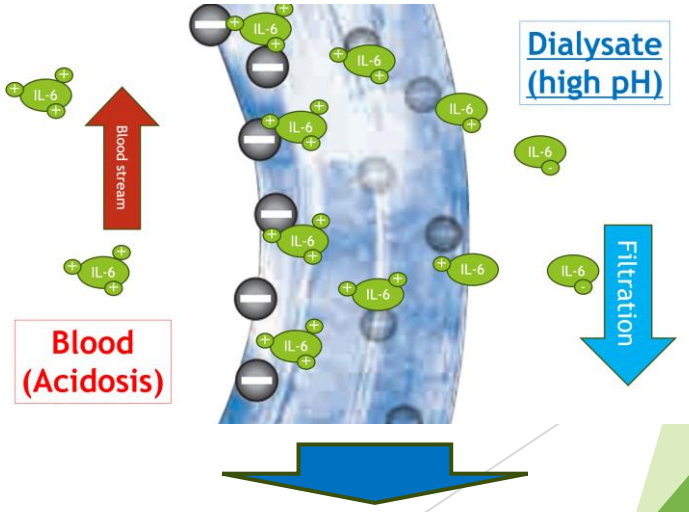
Concentration dependent

PAN membrane

pH dependent bind and release



superior stabilization of mediators

CONCLUSION

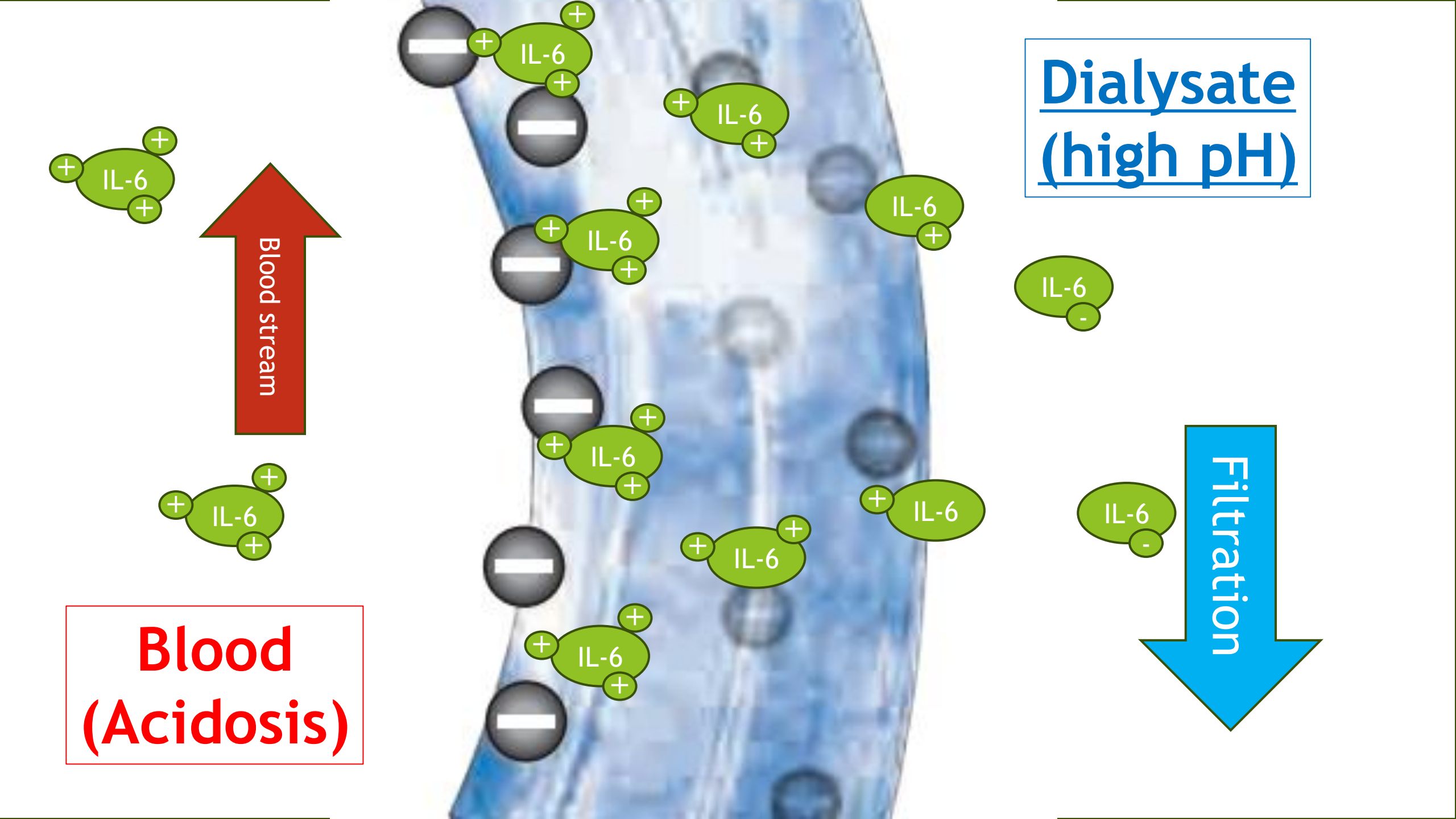
PAN(AN69®) membrane demonstrated

- effective removal of cytokines (CKD range)
- stabilized inflammatory mediators

Introduction: Polyethyleneimine-treated polyacrylonitrile (AN69ST) and polymethyl methacrylate (PMMA) membranes have been reported to exhibit superior cytokine clearance in septic conditions. In patients with chronic kidney disease (CKD), cytokine levels gradually increase with disease progression, contributing significantly to inflammation, malnutrition, cardiovascular disease, and poor prognosis. Although cytokine levels are elevated in end-stage renal disease (ESRD), they remain substantially lower than those observed in septic shock. This study aimed to evaluate whether three different dialysis membranes—AN69, PMMA, and polysulfone (PS) can effectively remove cytokines that are only mildly elevated, close to normal physiological levels. Methods: We conducted a prospective, randomized controlled study in patients scheduled to initiate maintenance hemodialysis without any acute or inflammatory comorbidities. Patients were randomly assigned in a 1:1:1 ratio to receive hemodialysis using one of the three membrane types: AN69, PMMA, or PS. The primary outcomes were changes in plasma interleukin6 (IL-6) and high-sensitivity C-reactive protein (hsCRP) levels before and after dialysis.

Results: In the AN69, PS, and PMMA groups, the average ages were 61.5 ± 15.5, 66.3 ± 13.3, and 65.3 ± 12.3 years, respectively. Neutrophil counts in the AN69 and PMMA groups decreased during the first hemodialysis (HD) session (AN69 13.4%, PMMA 23.6%, and PS 3.5% reduction). In the AN69 group, IL-6 levels did not increase during HD (2.7 ± 9.1%), whereas they increased in the PS and PMMA groups (PS 10.2 ± 26.0%, PMMA 16.5 ± 30.0%). Additionally, hs-CRP decreased at the second session in the AN69 group; however, hs-CRP increased in the PS and PMMA groups (PS 9.5%, PMMA 26.9%).

Conclusion: The AN69 membrane demonstrated superior removal of mildly elevated cytokines during the early phase of hemodialysis initiation, leading to a decrease in subsequent Keywords : Polyacrylonitrile, AN69, hemodialysis


Dialysate
(high pH)
Blood stream
Filtration
Blood
(Acidosis)
IL-6