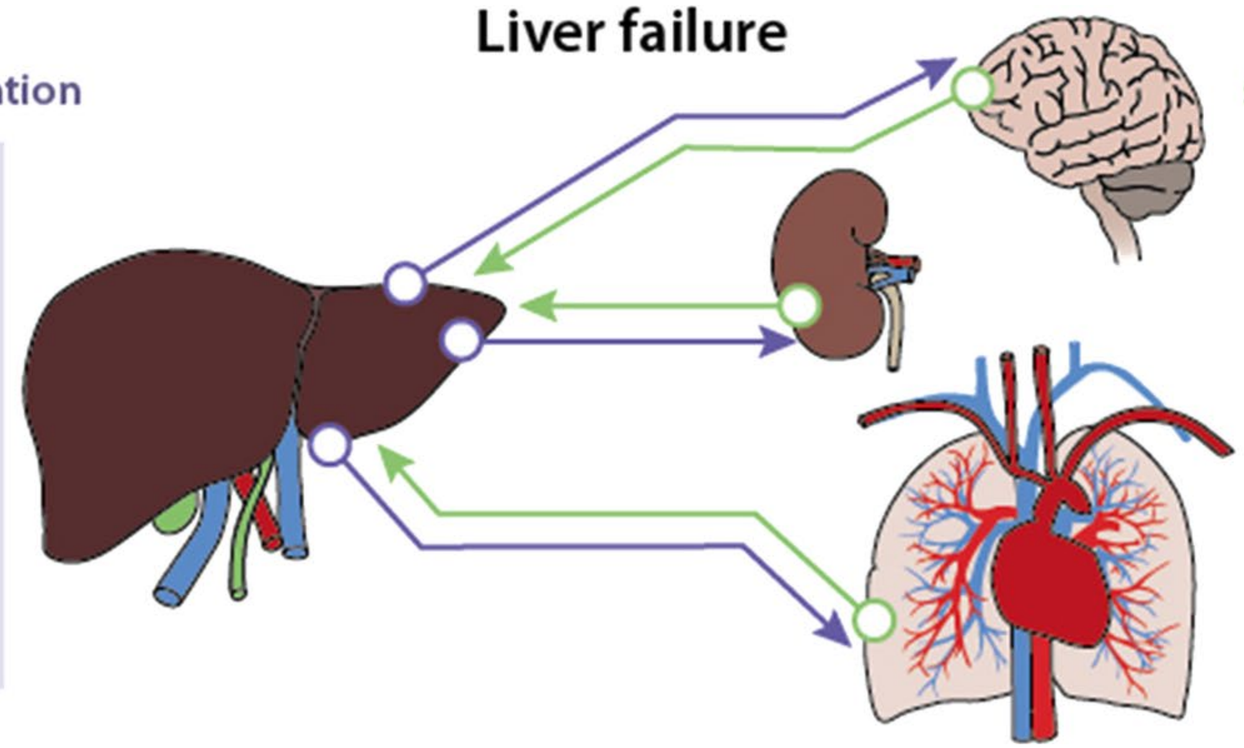
# Nové možnosti v podpůrné terapii jaterního selhání

XXVI. DNY INTENZIVNÍ MEDICÍNY V KROMĚŘÍŽI - 22. - 24. května 2024

**Petr Píza, KARIP IKEM, Praha**

IK+E M INSTITUT KLINICKÉ A EXPERIMENTÁLNÍ MEDICÍNY

# Graphic Abstract




as trigger for clinical deterioration

**Acute Liver Failure (ALF)**
Incidence (ICU) <1%
Mortality 23 - 53%

**Acute-on-Chronic Liver Failure (ACLF)**
Incidence (ICU) 1 - 5%
Mortality 13 - 86%
(depending on ACLF severity)

secondary to extrahepatic insult

**Cholestasis**
Incidence (ICU) 11 - 36%
Mortality 27 - 48%

**Hypoxic Liver Injury (HLI)**
Incidence (ICU) 1 - 18%
Mortality 40 - 60%

Critical care hepatology: definitions, incidence, prognosis and role of liver failure in critically ill patients

Aritz Perez Ruiz de Garibay[1,4], Andreas Kortgen[2], Julia Leonhardt[2], Alexander Zipprich[3] and Michael Bauer[2*]

# Extracorporeal Liver Support system (ECLS)

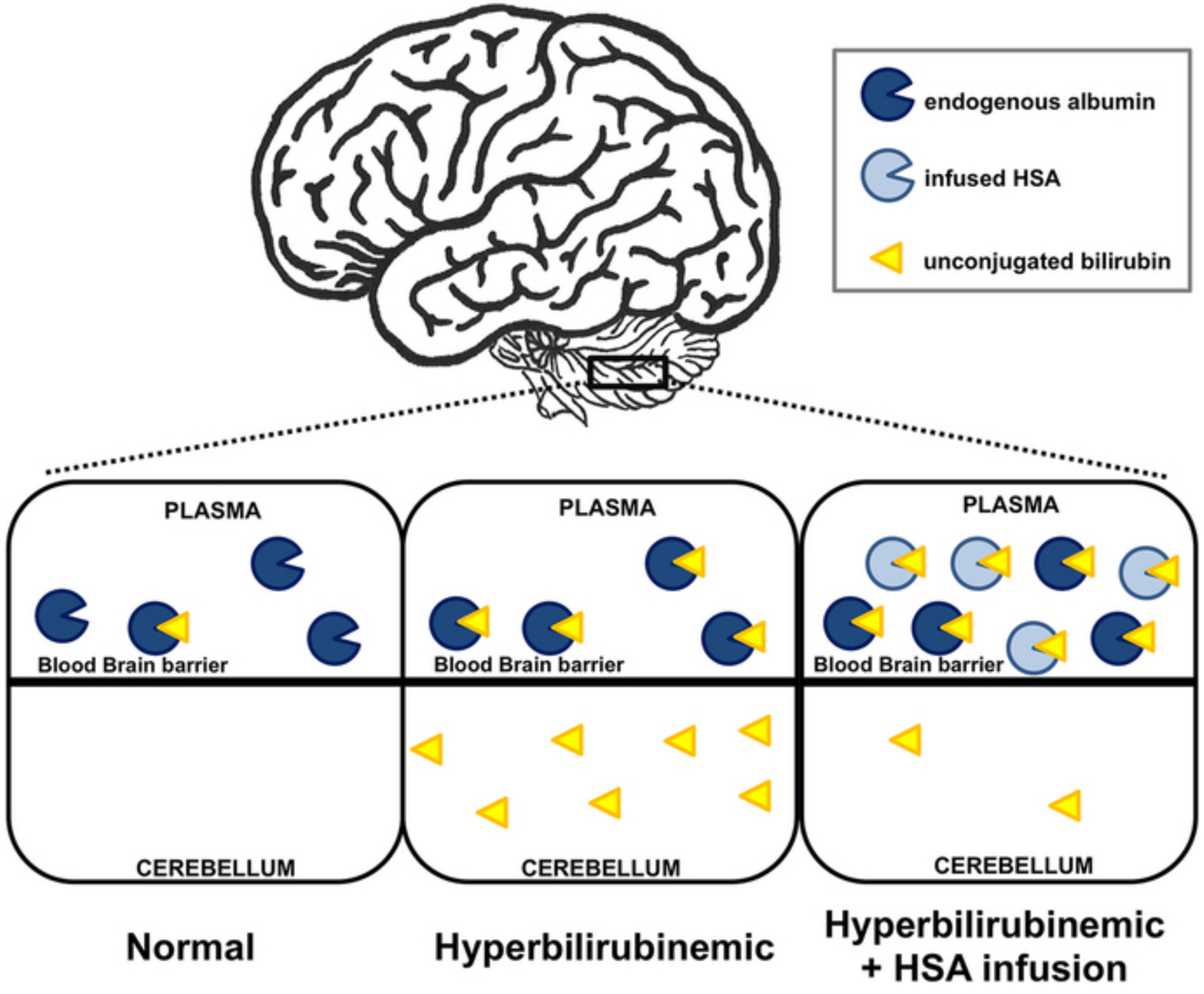
Jaterní dysfunkce = porucha hlavních jaterních funkcí:

**detoxikace, syntéza a regulace**

Změna detoxikační funkce - neschopnost metabolizovat různé molekuly ———> **akumulace** v systémovém oběhu.

Metabolické a biochemické změny postihující především **neurologickou a renální funkci** a případně vedoucí k **sekundární multiorgánové dysfunkci** (MODS)

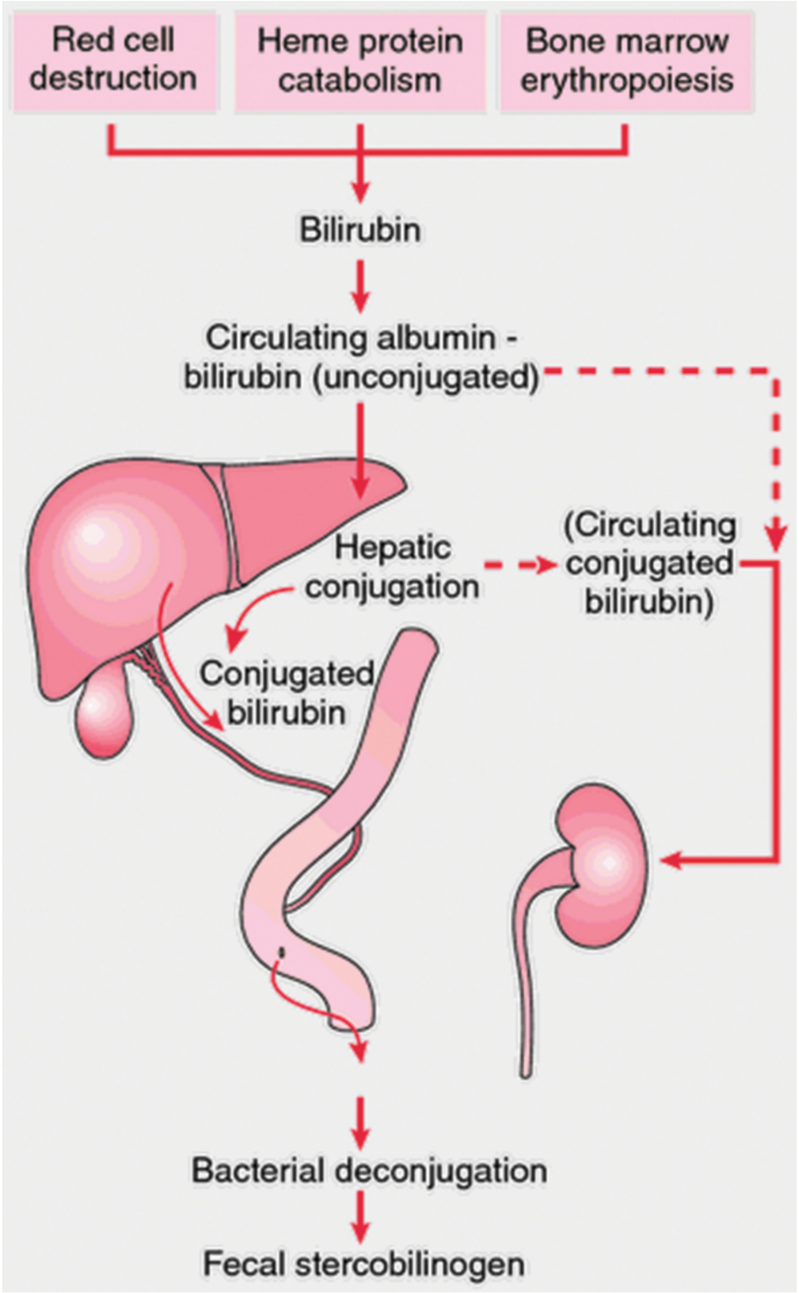
Hromadí se **zánětlivé mediátory a jaterní toxiny** + **ve vodě rozpustné sloučeniny** (např. amoniak), tak **hydrofobní** (např. bilirubin, žlučové kyseliny, hydrofobní aminokyseliny a endogenní benzodiazepiny), vázané proteinů v plazmě (albumin).




Molekula lidského **albuminu** (68 kDa) je schopna vázat dvě molekuly bilirubinu (první je pevněji vázaná než druhá).

Celkový tělesný albumin je asi **280 g**. Každý gram lidského albuminu váže **8,2 mg bilirubinu**.

Při průměrné koncentraci **albuminu 30 g/l** by měla být obě vazebná místa schopna vázat 250 mg bilirubinu/l plazmy, každé, s celkovou vazebnou kapacitou **500 mg/l**




**“Nenavázaný” bilirubin - (406 Da)**

**— —-> omezená rozpustnost v plazmě.**

Transportován do jater v plazmě, pevně vázán na albumin.

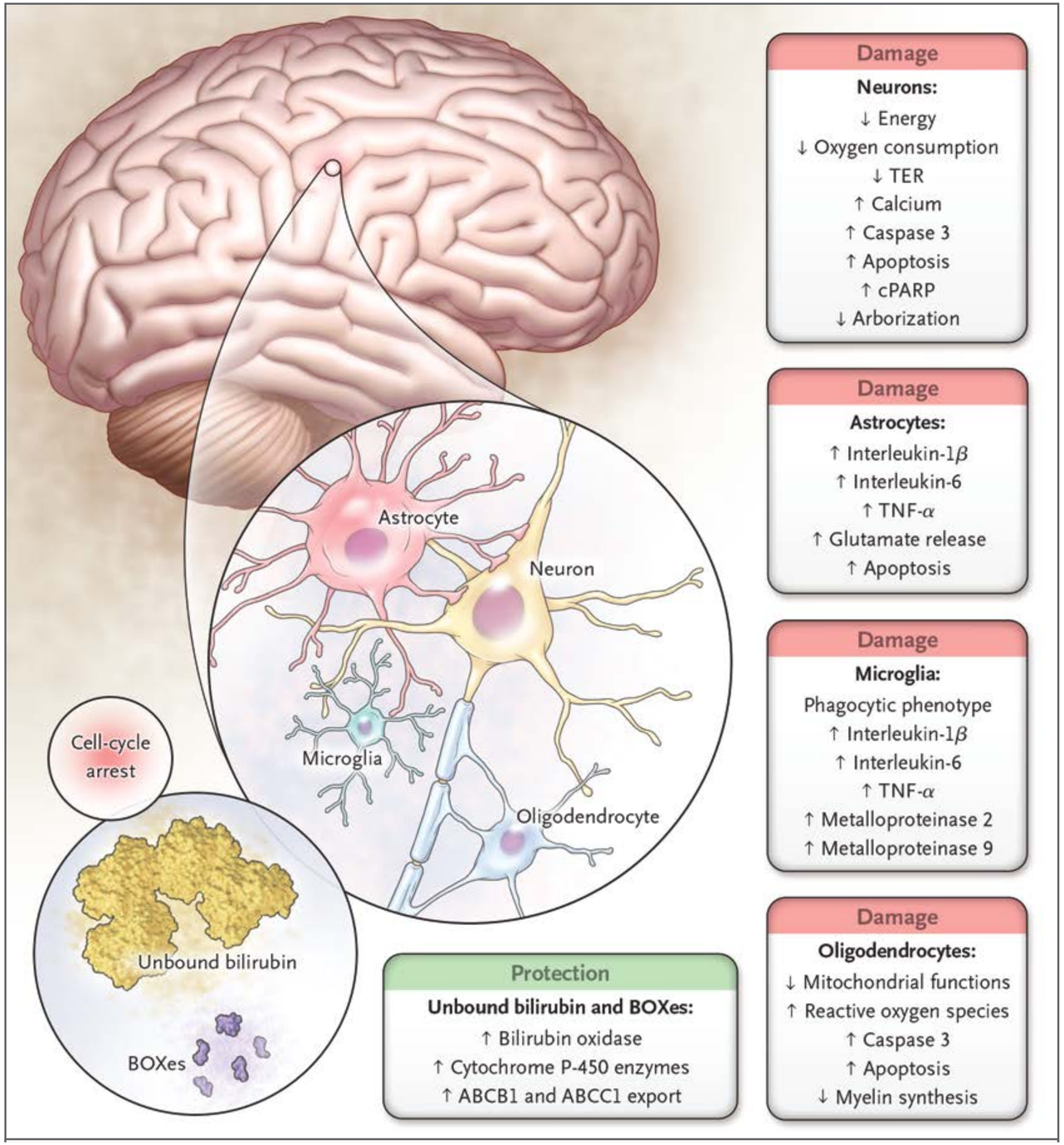
Vazba na albumin **omezuje jeho migraci z vaskulárního prostoru a jeho glomerulární filtraci,** čímž **zabraňuje jeho precipitaci a ukládání ve tkáních**.

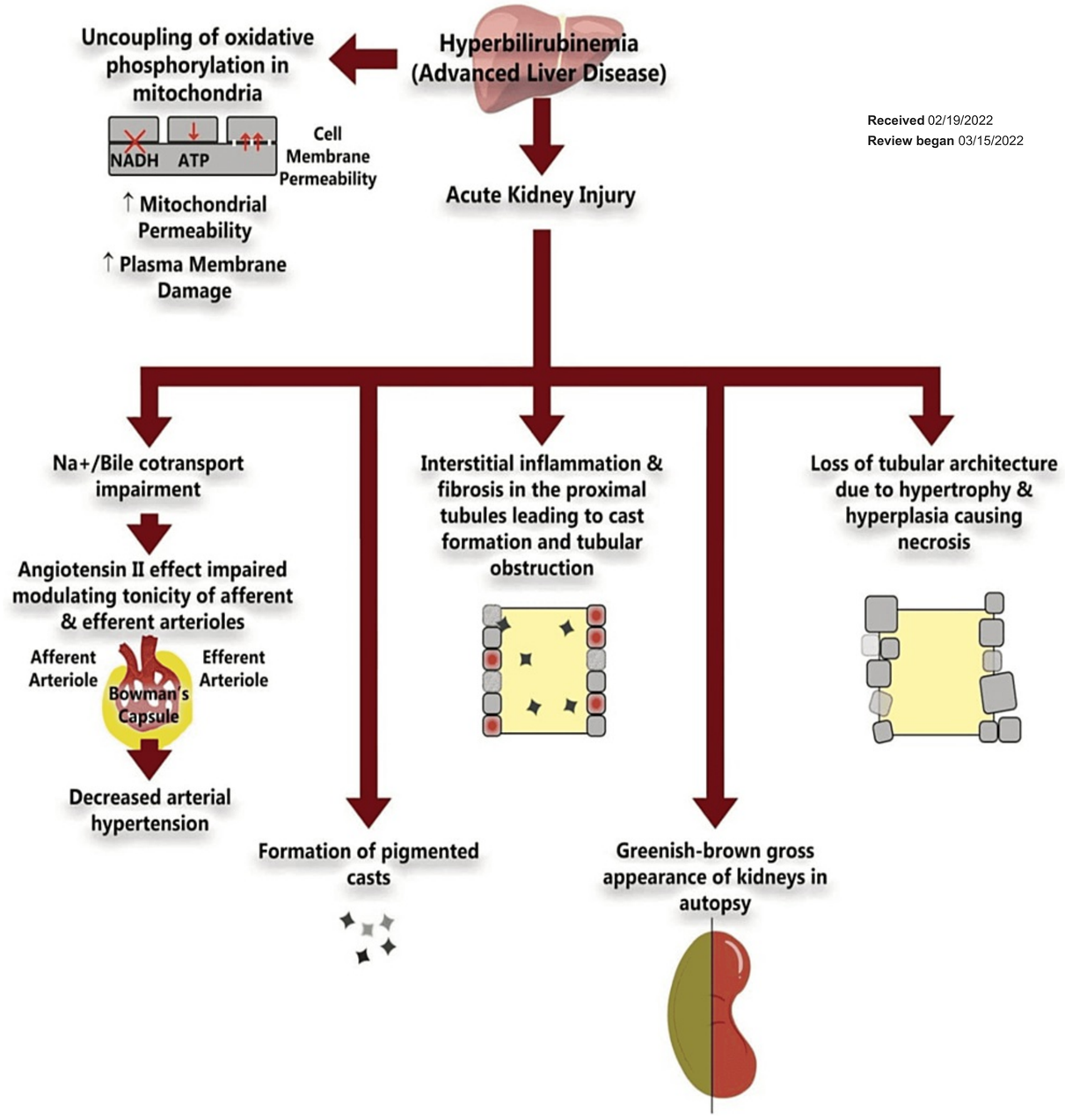
**VOLNÁ FRAKCE :**

Z těchto důvodů **nelze bilirubin, žlučové kyseliny a další toxiny vázané na albumin odstranit konvenční hemodialýzou nebo hemofiltrací.**

Nevázaný bil. je **neurotoxický** díky své schopnosti **procházet hematoencefalickou bariérou** a vázat se na mozkovou tkáň **(bazální ganglia, mozkový kmen)**

**Cytotoxicita** ——-> na CNS - **poškozují astrocyty a neurony oxidativním stresem a apoptózou** ——> narušení transportu neurotransmiterů ——-> **jaterní encefalopatie** (HE)






**Received** 02/19/2022
**Review began** 03/15/2022

# Bile Cast Nephropathy: A Comprehensive Review

Manoj R. Somagutta [1, 2], Molly S. Jain [3, 2], Maria Kezia Lourdes Pormento [4, 2], Siva K. Pendyala [1, 2], Narayana Reddy Bathula [1, 2], Nagendrababu Jarapala [5, 2], Ashwini Mahadevaiah [6, 2], Nayana Sasidharan [7, 2], Mohamed A. Gad [8, 2], Greta Mahmutaj [9, 2], Namrata Hange [10, 2]

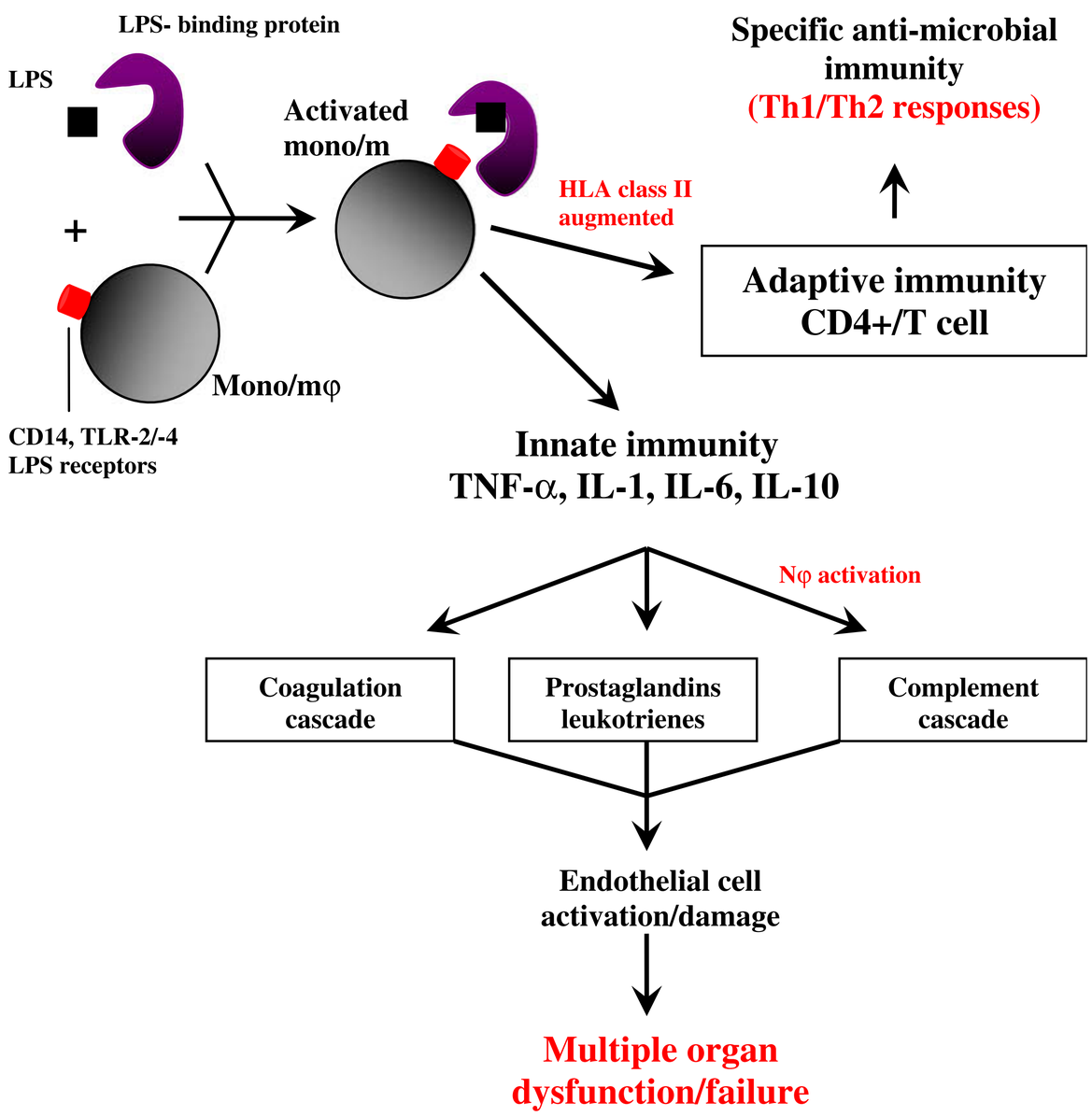
**AKI** - spouštěcí faktory = **systémový zánět, vazokonstrikce ledvin s portální hypertenzí, bakteriální infekce nebo cholestatická nefróza**.

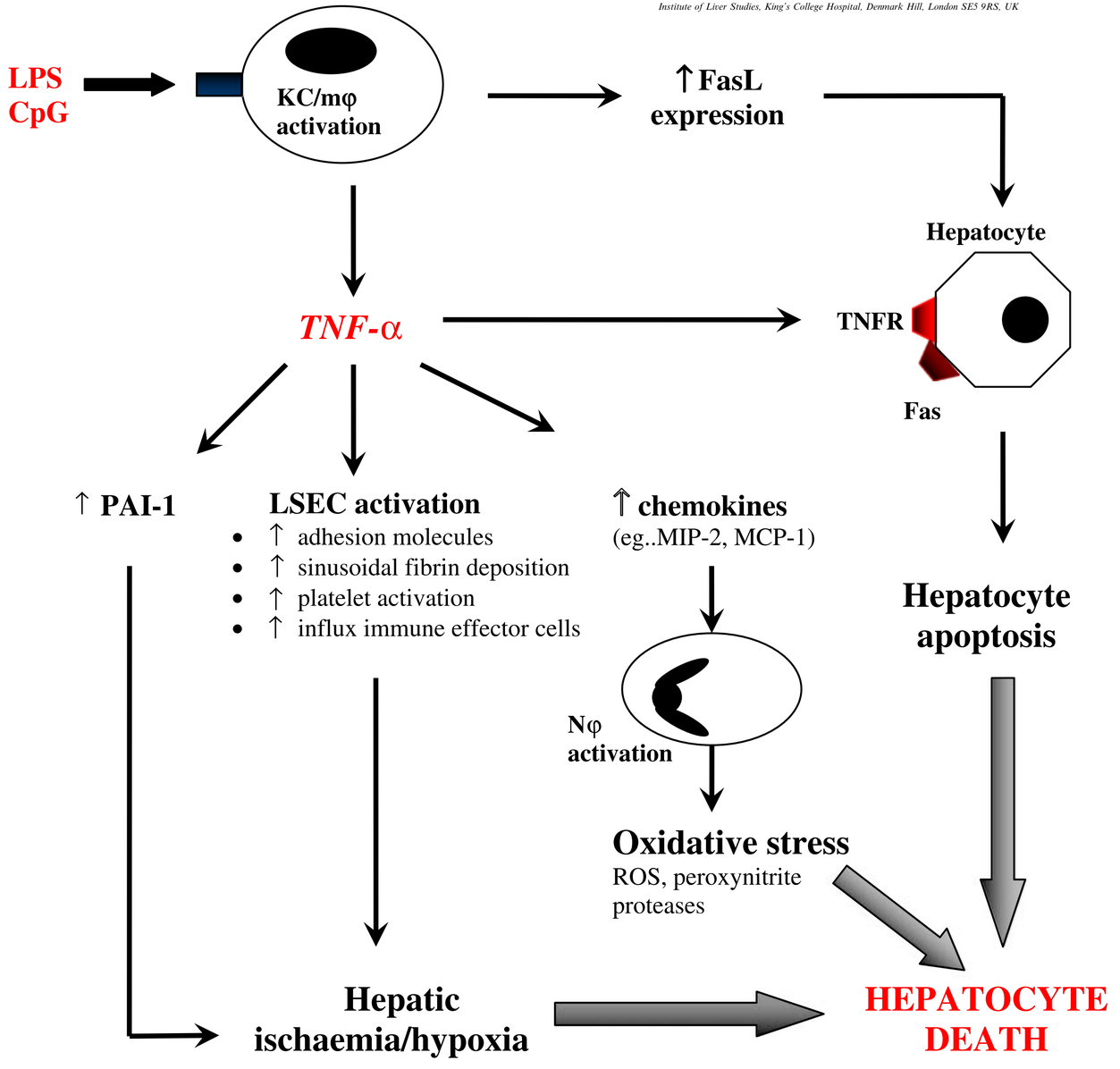
Zvýšení plazmatických koncentrací žlučových kyselin a bilirubinu —→ **nefrotoxické vlastnosti akumulace intraduktálního a intracelulárního bilirubinu** (odstranění játry je velmi pomalé).

The importance of immune dysfunction in determining outcome in acute liver failure☆

Charalambos Gustav Antoniades*, Philip A. Berry, Julia A. Wendon+, Diego Vergani+

*Institute of Liver Studies, King's College Hospital, Denmark Hill, London SE5 9RS, UK*



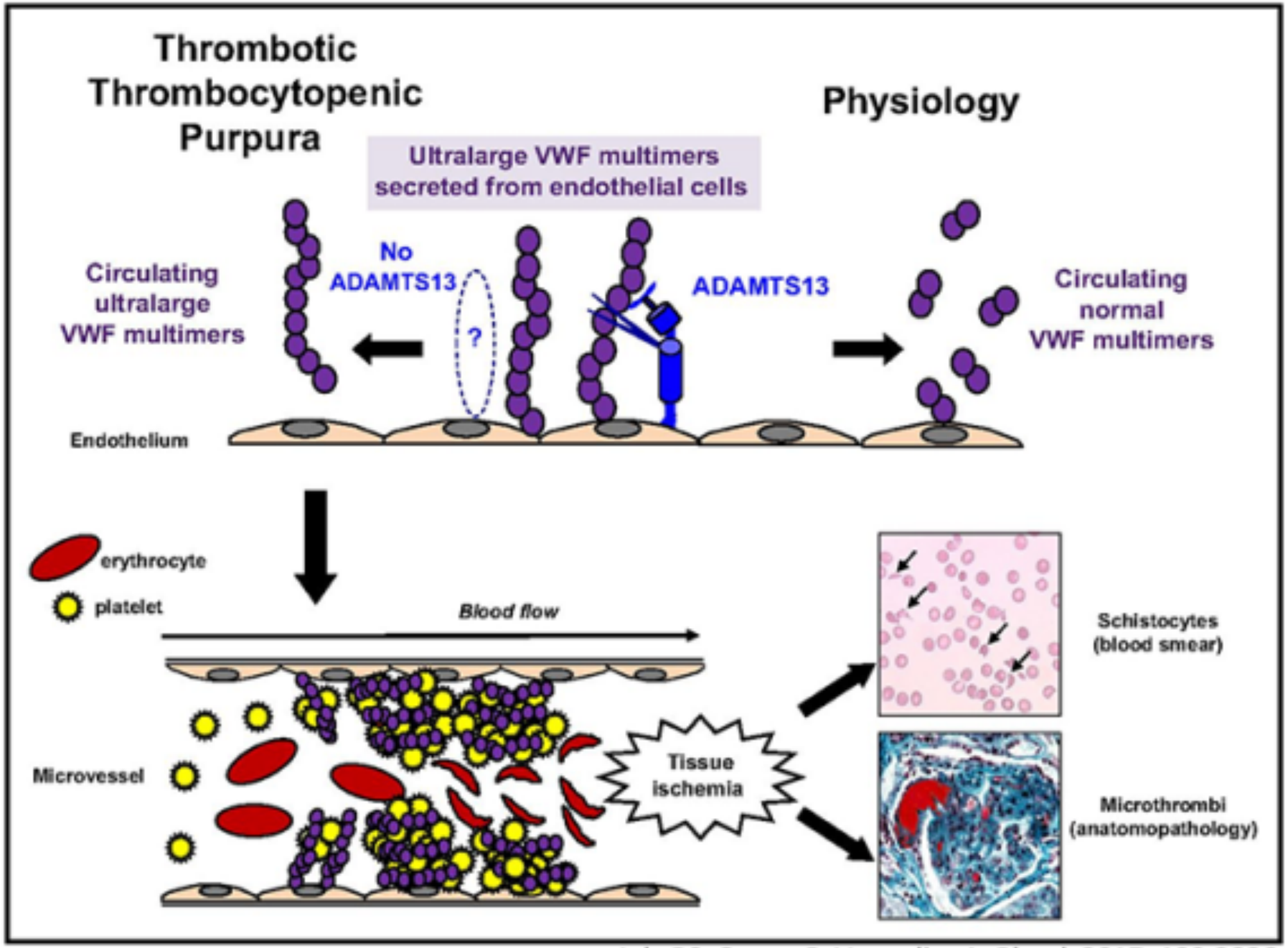
# Hemostasis in Liver Disease

| Increased risk of bleeding | Increased risk of clotting |
|---|---|
| ↓ FII | ↑FVIII |
| ↓ FVII | ↑ vWF |
| ↓ FIX | ↑ fibrinogen |
| ↓ FX | |
| ↓ FXI | ↓ Protein C |
| Dysfibrinogen | ↓ Protein S |
| ↓Platelets | ↓ antithrombin III |
| Qualitative platelet defects | |

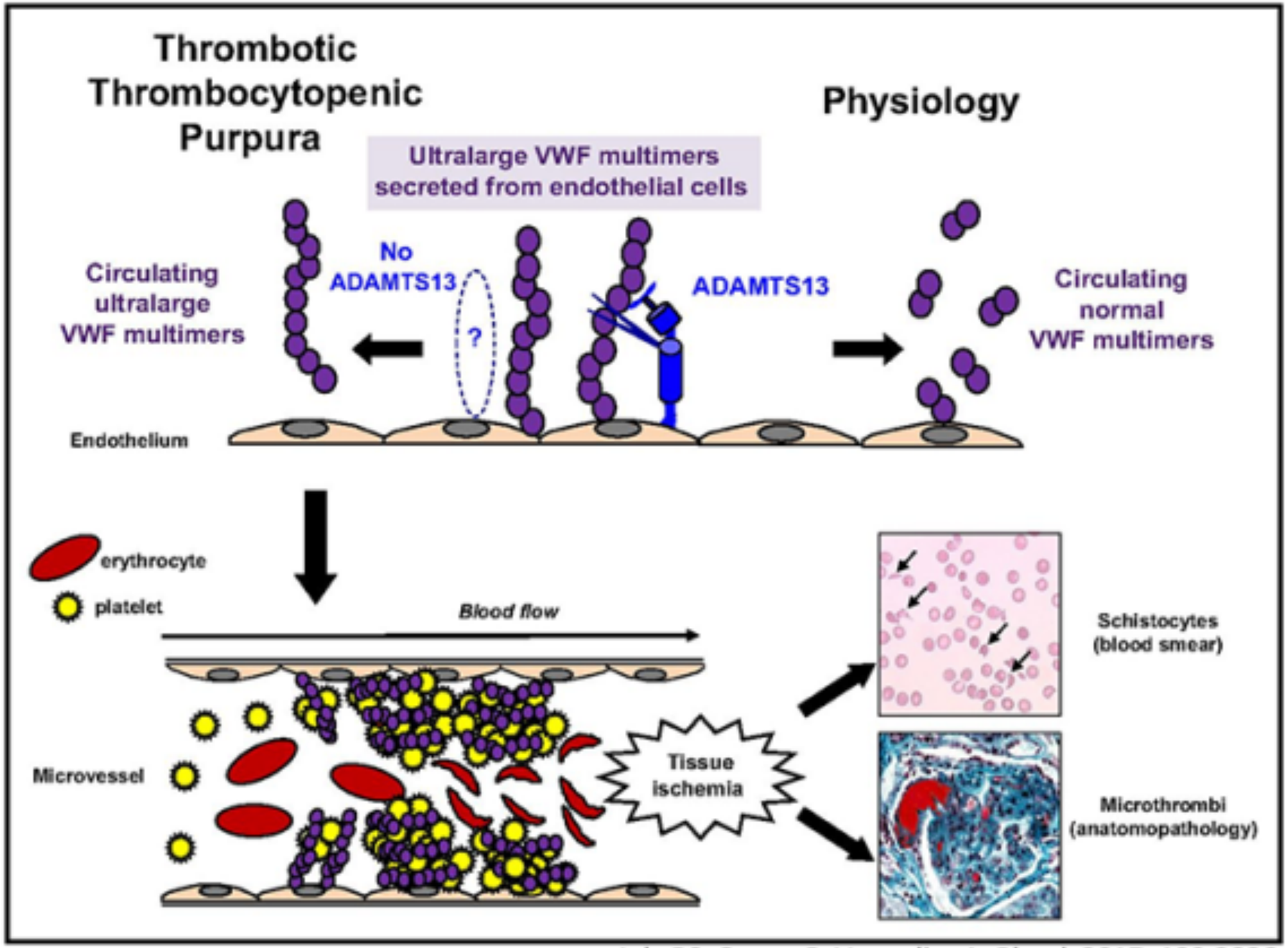
***Altered levels with unknown associated risk of bleeding or clotting***

d-dimer, TAFI, PAI-1, TF, tPA, TM, IL-11, TNF-α, APC-PCI

TMA

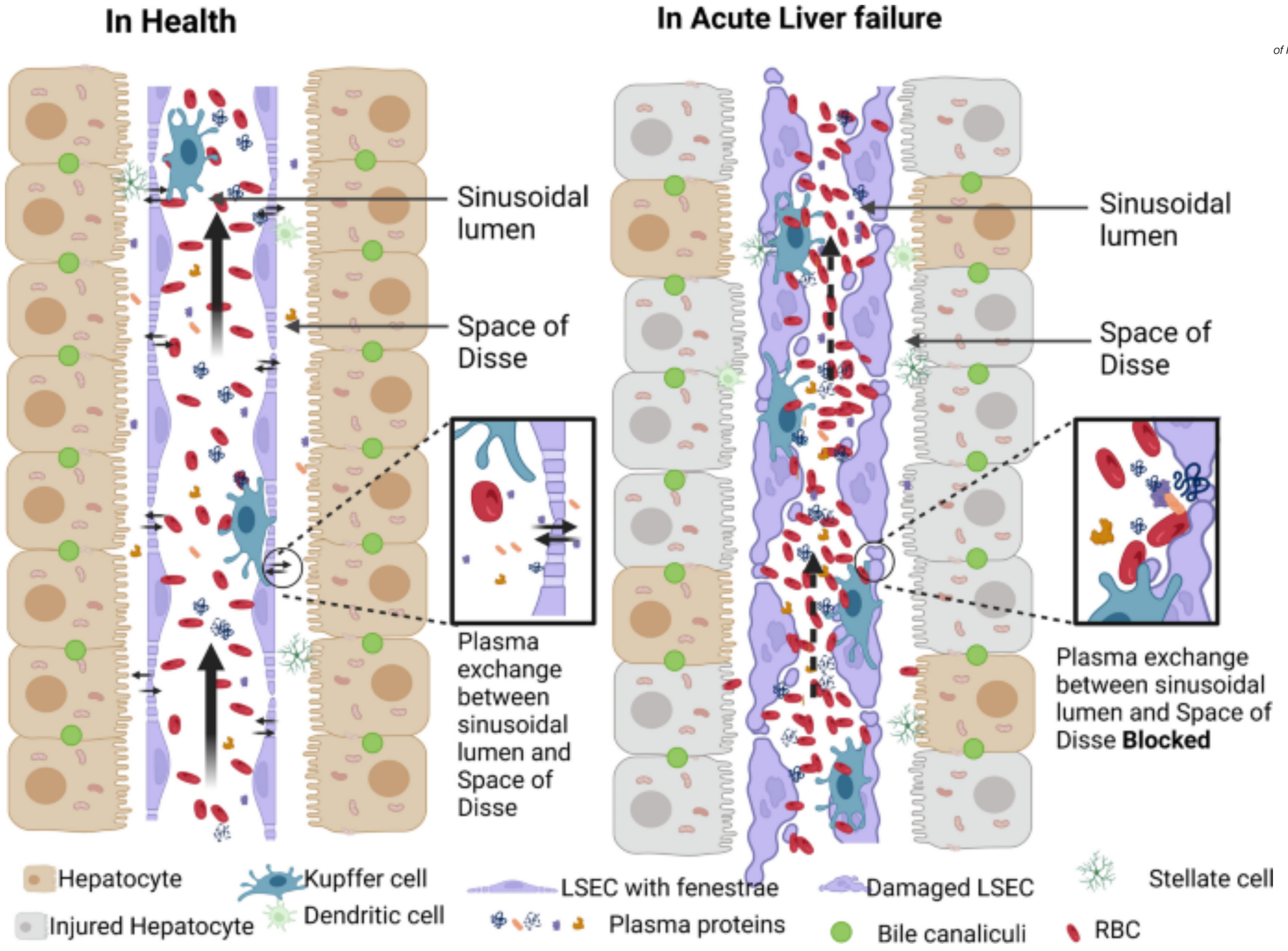



Joly BS, Coppo P, Veyradier A. Blood 2017; 129:2836




Joly BS, Coppo P, Veyradier A. Blood 2017; 129:2836

# “TRAFFIC JAM IN LIVER SINUSOIDS” HYPOTHESIS




**Growing Evidence for Survival Benefit with Plasma Exchange to Treat Liver Failure**


Ashish Goel , Uday Zachariah, Dolly Daniel, Chundamannil E. Eapen

*of Hepatology and Transfusion Medicine and Immunohaematology, Christian Medical College, Vellore, Tamil Nadu, India*


**Extra-corporeal non-liver transplant therapies for acute liver failure: Focus on plasma exchange and continuous renal replacement therapy**


Narrative review | Published: 26 March 2024


Ucpávání zánětlivými buňkami a zbytky v jaterních sinusoidech („dopravní zácpa“) a může způsobit **funkční akutní sinusoidní obstrukci,** která zase snižuje **perfuzi** v jaterní mikrocirkulaci a způsobí **selhání jater**.

# Indikace

Těžké akutní poškození jater definuje syndrom charakterizovaný markery poškození jater **(zvýšené sérové transaminázy) a zhoršenou funkcí jater (ikterus a INR > 1,5),** které obvykle předchází klinické encefalopatii (úroveň důkazu II-2, stupeň doporučení 1).

Pacienti s **akutní prezentací chronické autoimunitní hepatitidy, Wilsonovou chorobou a Budd-Chiariho syndromem** jsou považováni za pacienty s ALF, **pokud se u nich rozvine jaterní encefalopatie**, navzdory přítomnosti již existujícího onemocnění jater v kontextu příslušných abnormalit v krvi jater. testy a koagulační profil (úroveň důkazu II-2, stupeň doporučení 1)

**Klinický výskyt jaterní encefalopatie je pro diagnózu ALF zásadní, ale mentální změny mohou být zpočátku jemné a intenzivní screening při prvních známkách jaterní encefalopatie je povinný (nutný)** (úroveň důkazu II-2, stupeň doporučení 1).

# EASL Clinical Practical Guidelines on the management of acute (fulminant) liver failure☆

European Association for the Study of the Liver*

reference pacientů na ICU:

| **Paracetamol and hyperacute aetiologies** |
|---|
| Arterial pH <7.30 or $HCO_3$ <18 |
| INR >3.0 day 2 or >4.0 thereafter |
| Oliguria and/or elevated creatinine |
| Altered level of consciousness |
| Hypoglycaemia |
| Elevated lactate unresponsive to fluid resuscitation |

| **Non-paracetamol** |
|---|
| pH <7.30 or $HCO_3$ <18 |
| INR >1.8 |
| Oliguria/renal failure or Na <130 mmol/L |
| Encephalopathy, hypoglycaemia or metabolic acidosis |
| Bilirubin >300 μmol/L (17.6 mg/dl) |
| Shrinking liver size |

**Risk criteria for referral of patients with acute hepatitis**[10]

- - Patients with a prothrombin index from 30% to 50% and any of the following conditions:
  - Children < 15 years of age.
  - Adults > 40 with suspected aetiology with poor prognosis for spontaneous survival (e.g. liver injury caused by drugs, Wilson's disease, cryptogenic).
  - Fever >38 °C.
  - Immediate post-operative period.
  - Pregnancy.
  - Comorbidities: diabetes mellitus, HIV infection, previous cancer, malaria, severe acute kidney injury, metabolic acidosis.
  - Plasma bilirubin > 250 μmol/l (14 mg/dl).
- - Patients with a prothrombin index below 30%:
  - Any patient (particularly if >40 or suspected aetiology with poor prognosis).

Once the diagnosis of ALF is established, i.e. after they develop HE, regardless of the suspected aetiology, the patient should be moved to an ICU in a centre capable of performing ELT.

**Management of acute liver failure. Clinical guideline from the Catalan Society of Digestology**☆

Àngels Escorsell[a,b,c,*], José Castellote[b,c,d], Jordi Sánchez-Delgado[c,e,f], Ramon Charco[c,f,g], Gonzalo Crespo[b,c,h], Javier Fernández[a,b,c,i]

Včasné postoupení pacienta s těžkou akutní hepatitidou do centra s programem transplantace jater před nástupem HE znamená, že hodnocení může začít s potenciálním zařazením na WL (**stupeň evidence III, stupeň doporučení 1**)

**Doporučení na specializované centrum** je zásadní v případech ALF s subakutním průběhem, s ohledem na vysoký výskyt souvisejících komplikací (**stupeň důkazů III, stupeň doporučení 1**)

# DPMAS Prescription Tips Card

## 1. INDICATIONS (PATIENT SELECTION AND ENDOTYPE)

1） **Acute/Acute-on-chronic Liver Failure:**

TBiL≥ 85.5μmol/L; or daily increased ≥17.1μmol/L; PTA≤50%, or INR≥1.51

2） **Cholestatic Liver Disease & Severe Hyperbilirubinemia:**

Exceptional Obstructive Jaundice. If the bilirubin level remains high with the general treatment, it is recommended to start artificial liver therapy.

3） **Pre & Post Liver Transplant:**

Patients who are waiting for a liver source before surgery, with rejection after liver transplantation, or in the non-functional phase of the transplanted liver.

- MELD < 30:DPMAS/DPMAS+LPE/DPMAS+PE;
- 30 < MELD≤40:PE+DPMAS
- MELD≥40: Liver Transplant

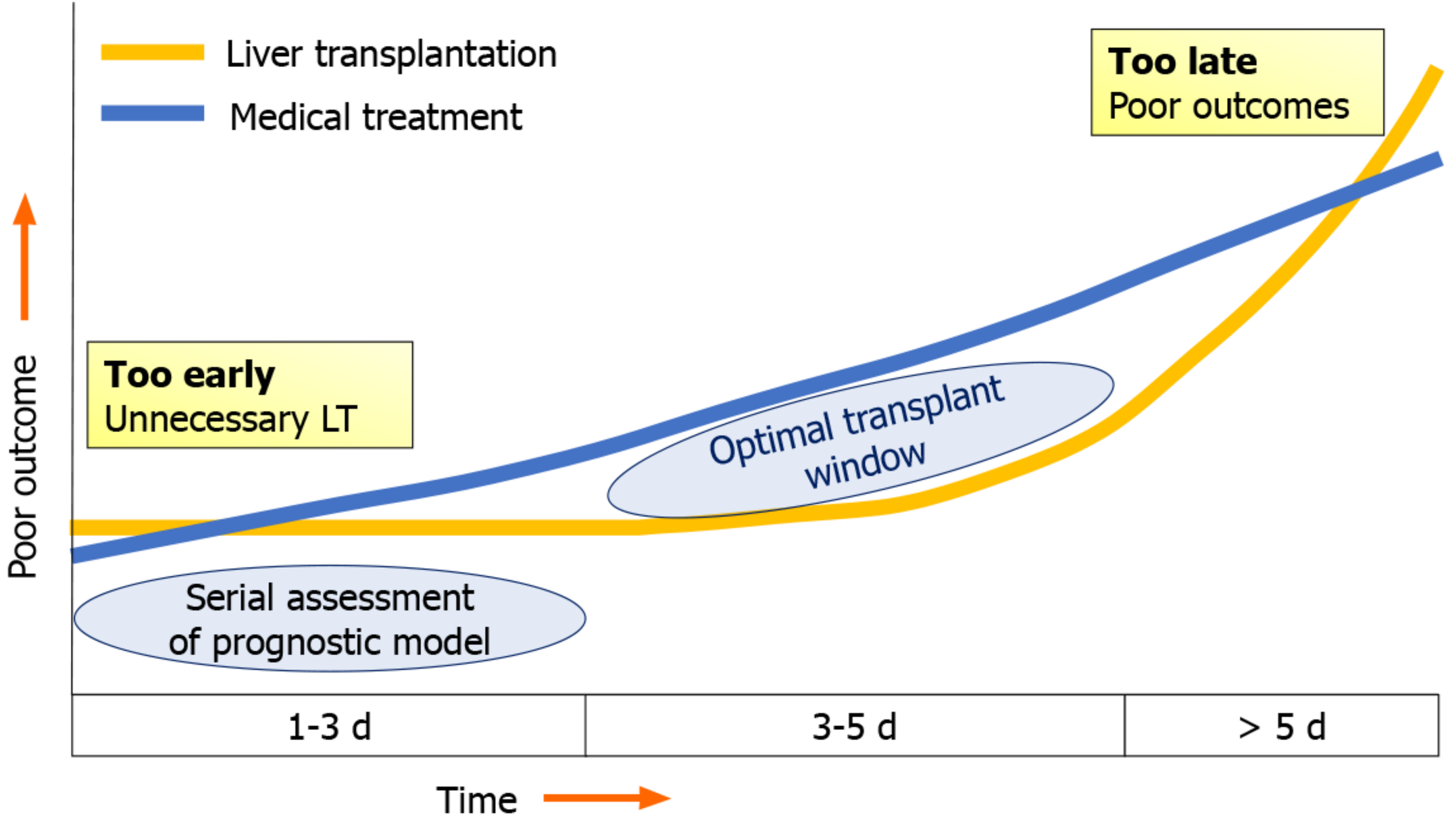
**4）Liver Failure combined with Hepatic Encephalopathy：**

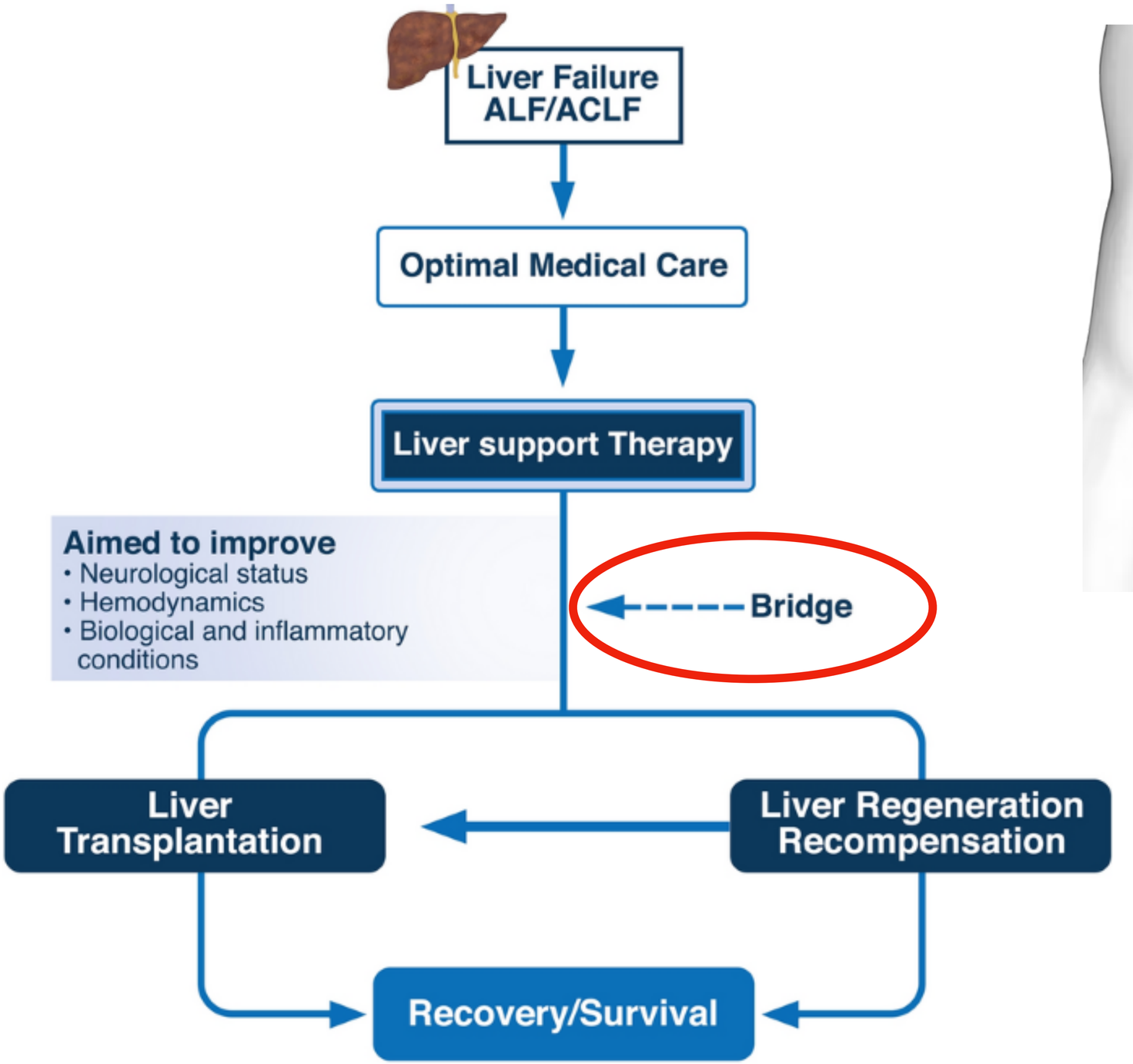
DPMAS/HA+CRRT/HDF/PDF/LPE/PE

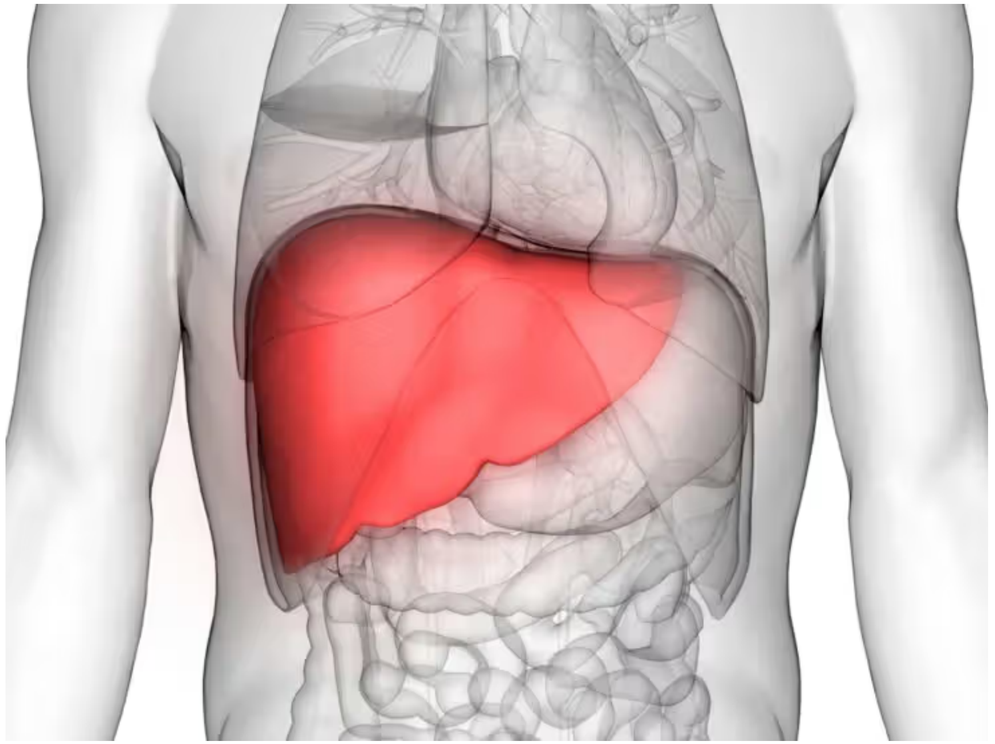
**5）Sepsis or MODS with Severe Liver Injury：**

HA/DPMAS+CRRT/HDF/PDF， reference biomarkers:

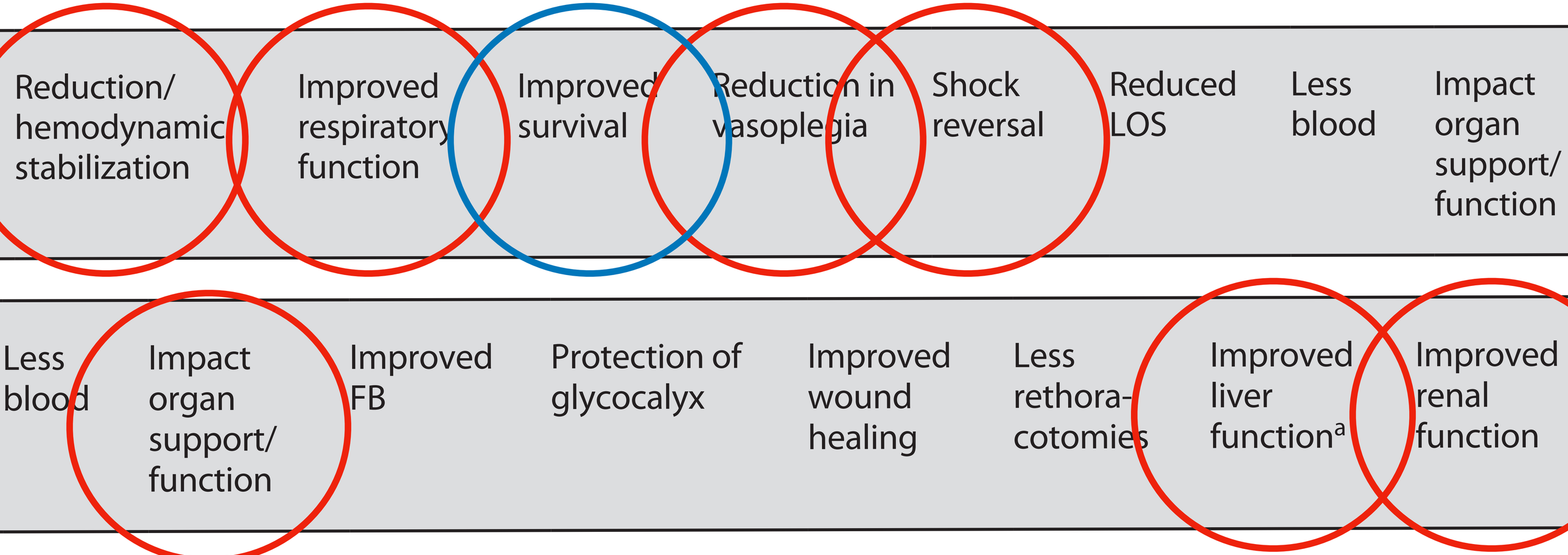
Serum inflammatory mediator (e.g., IL-6) concentrations are five times more than normal value or increase at more than double the daily rate， IL-6 > 500pg/ml, TNF-a > 100pg/ml, Bilirubin > 171umol/L.


Liver transplantation
Medical treatment
Too late
Poor outcomes
Too early
Unnecessary LT
Optimal transplant window
Serial assessment of prognostic model
Poor outcome
1-3 d
3-5 d
> 5 d
Time


Liver Failure
ALF/ACLF
Optimal Medical Care
Liver support Therapy
Aimed to improve
• Neurological status
• Hemodynamics
• Biological and inflammatory conditions
Bridge
Liver Transplantation
Liver Regeneration Recompensation
Recovery/Survival



# Hodnocení efektivity



# Přístrojová podpora jaterního selhání

(co je a není na trhu dostupné aneb Prometheus už není a nebude)

**Table 6.2. Toxic Substances Accumulating in the Blood Due to Hepatic Failure**

| Protein-Bound Substances | Water-Soluble Substances |
|---|---|
| Bilirubin, un/conjugated | Ammonia |
| Bile acids | Gamma aminobutyric acid |
| Short-chain fatty acids | Aromatic amino acid[#] |
| Benzodiazepenes | Cytokines[#] |
| Mercaptans | Creatinine |
| Nitric oxide | |
| Indoyxlsulfate | |
| Copper | |
| Protoporphyrin | |
| Endotoxin | |

[#] Represents different classification in different documents (Hughes, 2002; Mitzer *et al.*, 2009)

**HD, CRRT**
**SLED**

***

**TPE, PLAX**

**Hemadsorpce**

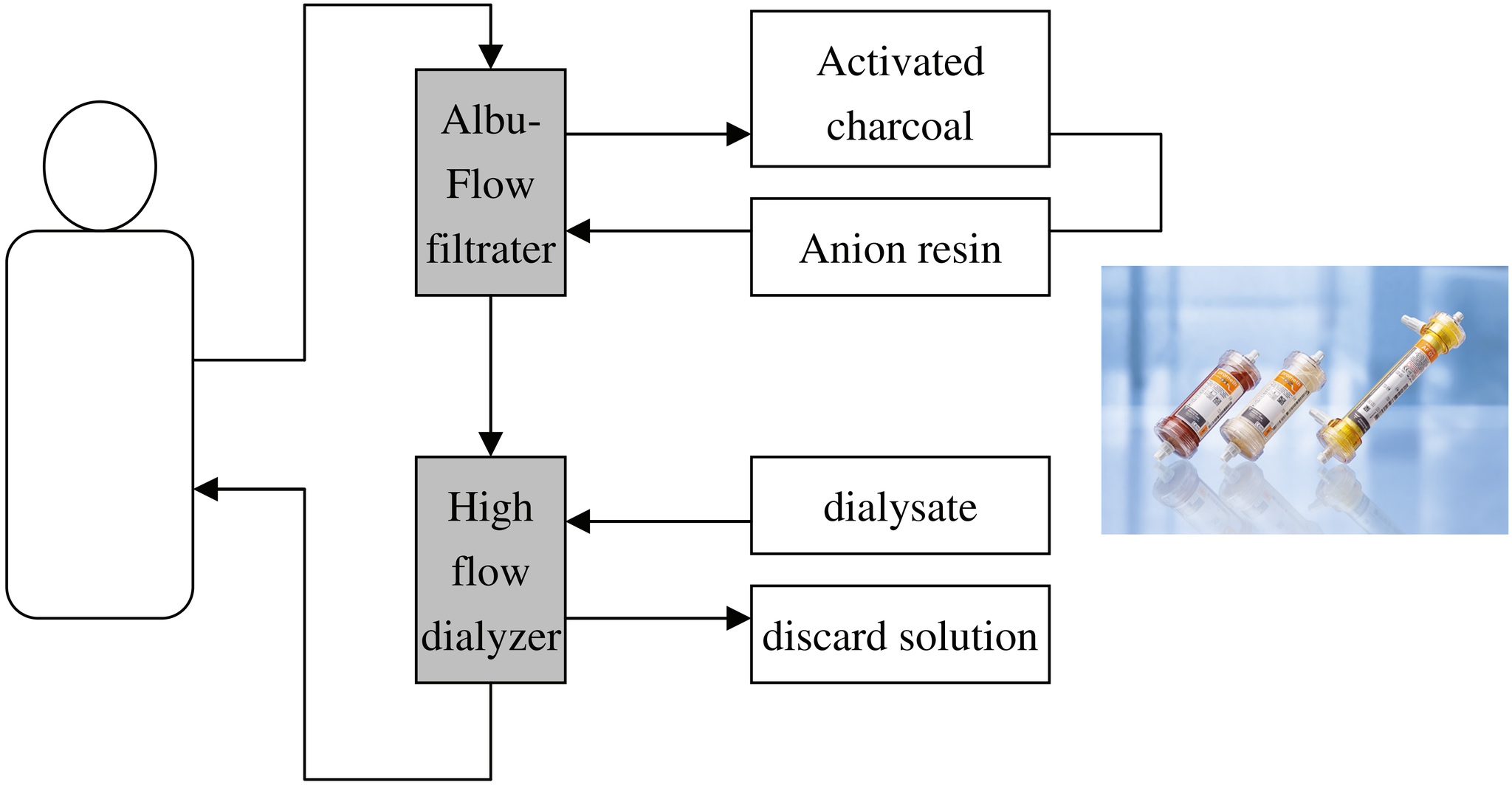



**Fig. 6.6.** Circulation pattern diagram of Prometheus.

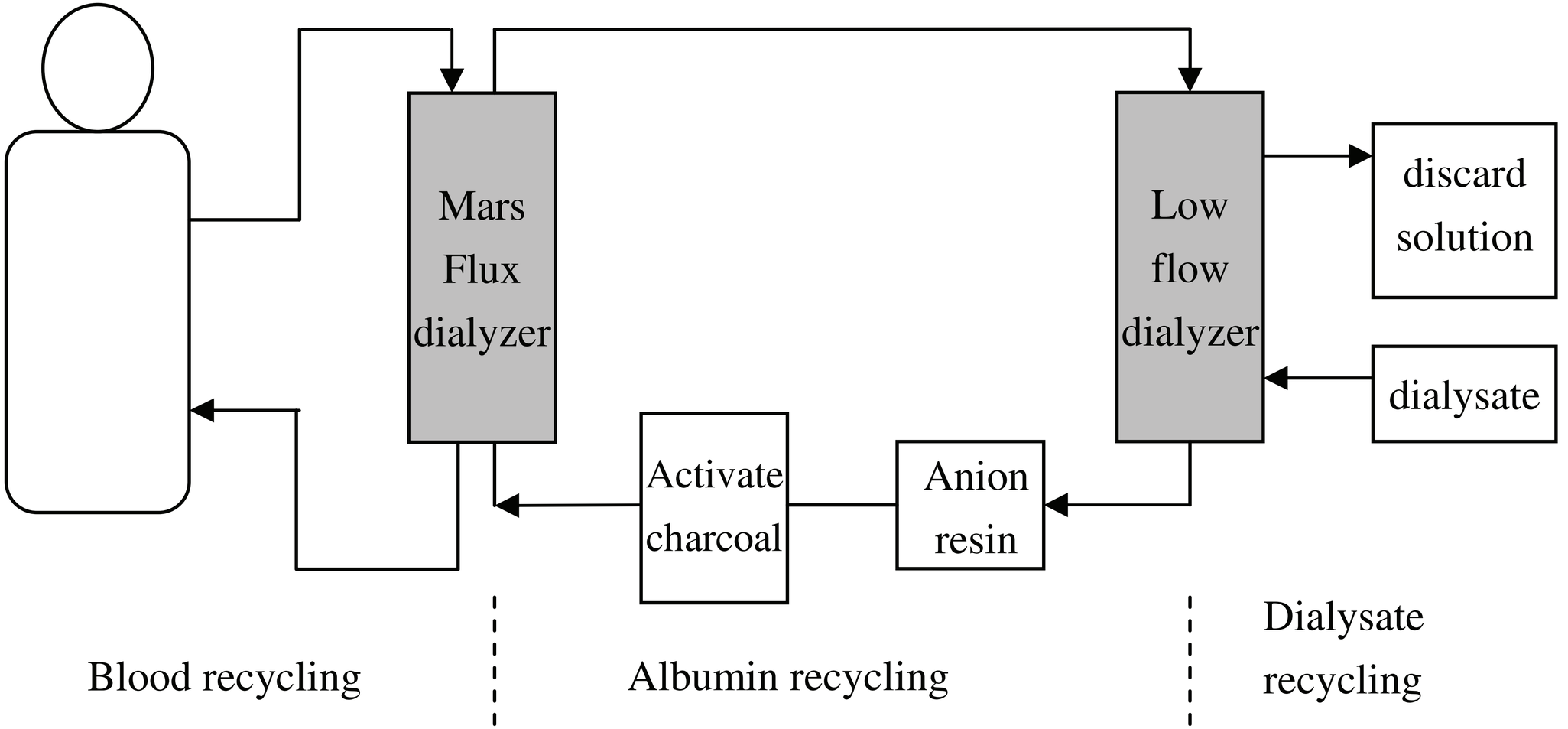
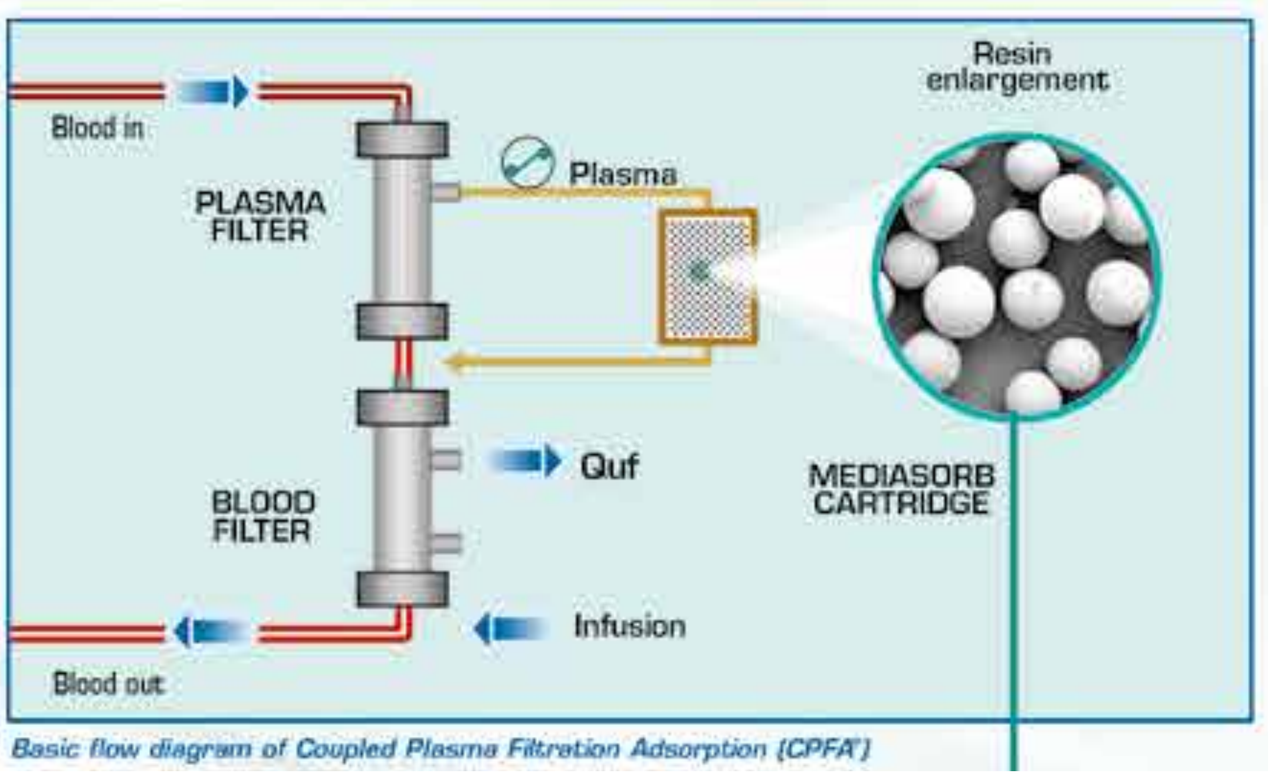



**Fig. 6.4.** Circulation pattern diagram of MARS system.

# CPFA®

COUPLED PLASMA FILTRATION ADSORPTION




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

## 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

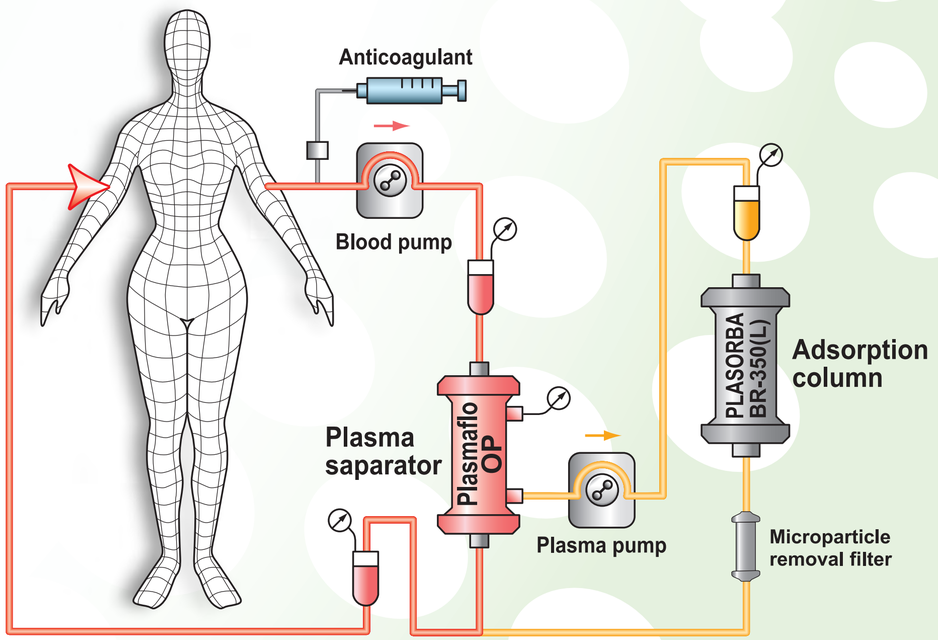
- CPFA® increases mean arterial pressure while reducing vasopressor requirements
- Applicable for both severe sepsis and septic shock
- Improves cardiac and respiratory parameters


# PLASORBA

PLASORBA™ BR-350 (L)
Plasma Perfusion Column

Selective adsorption of bilirubin and bile acid from plasma for efficient liver support

## Circuit Diagram




## Specifications

| | | | |
|---|---|---|---|
| Adsorption Column | Adsorbent | Material | Styrene divinylbenzene copolymer |
| | | Volume | 350mL |
| | Priming Volume | | 130mL |
| | Container | Material | Polypropylene |
| | Weight | | 600g |
| | Sterilization | | Moist heat |
| Microparticle Removal Filter | Filter | Material | Polyethylene (coated with ethylene-vinylalcohol copolymer) |
| | | Area | 0.07m$^2$ |
| | Container | Material | Polyvinyl chloride |
| | Priming Volume | | 30mL |
| | Sterilization | | Ethylene oxide |

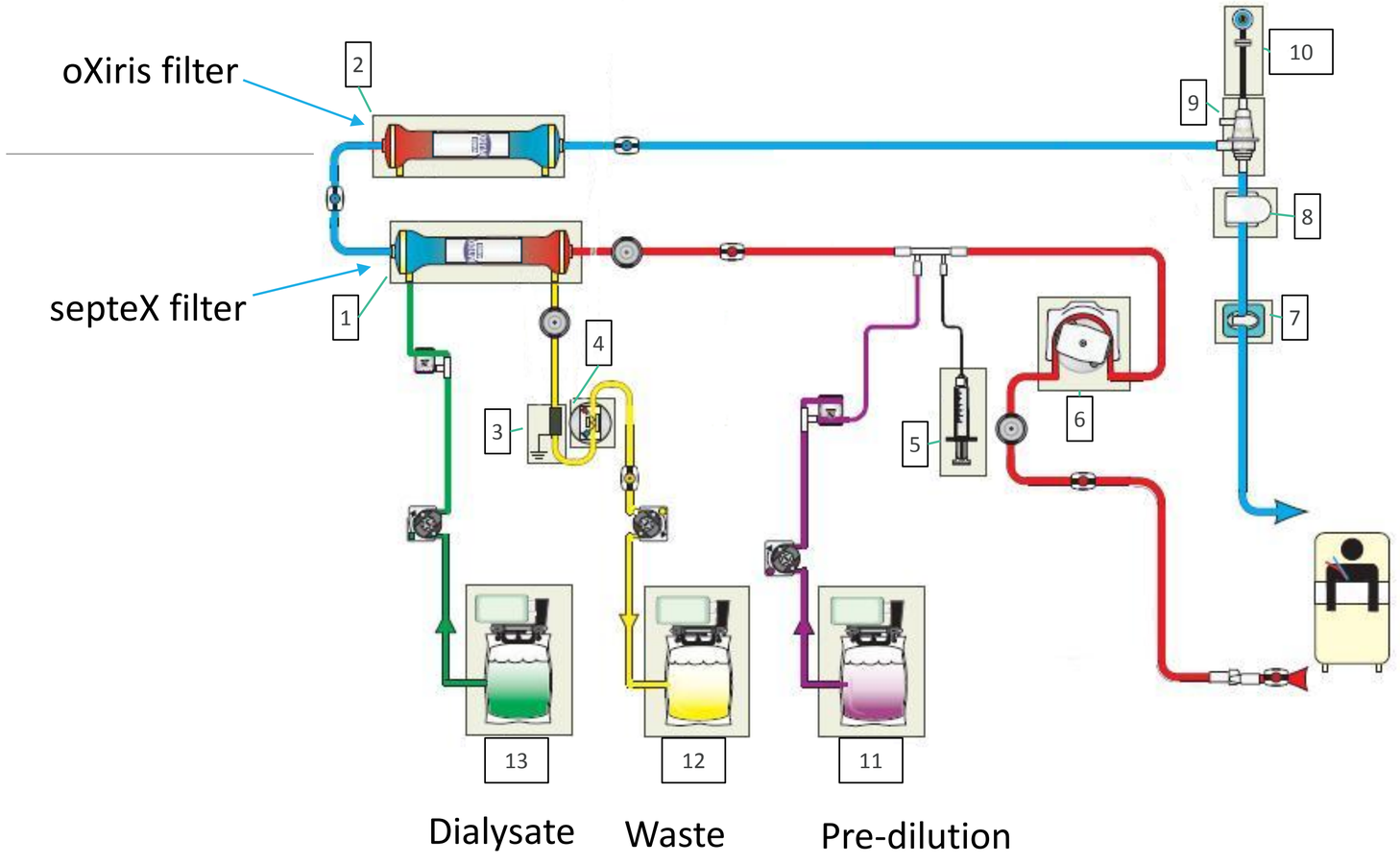
ALIVER

**ALIVER Consortium** - nové „zařízení na dialýzu jater“, DIALIVE.
(i) **albumin**, cirkulující protein zapojený do detoxikace, má nevratně sníženou funkci v ACLF
(ii) **endotoxémie** (hromadění endotoxinů v krvi) přispívá ke zvýšenému riziku infekce při selhání jater.
Prostřednictvím tohoto projektu, testování a implementace přístroje DIALIVE, se snažíme dát naději kriticky nemocným pacientům s akutním chronickým selháním jater. Testovaný systém nemá být náhradním orgánem pro játra, ale novou terapií **chronických jaterních onemocnění.**
DIALIVE zahrnuje odstranění a nahrazení albuminu a odstranění endotoxinu.
**Cíl: snížit endotoxémii, zlepšit albumin a imunitní funkce**
**Prodloužit přežití**

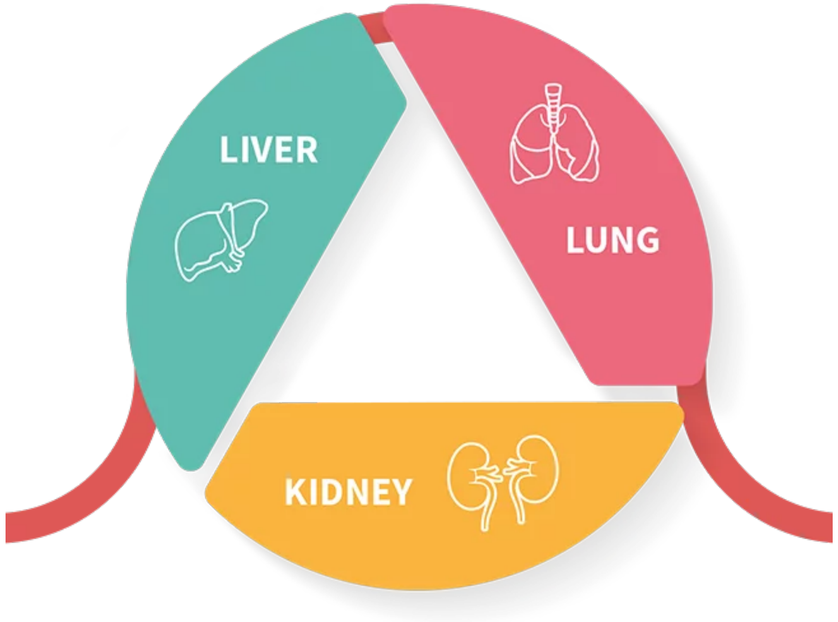
# Randomized, controlled clinical trial of the DIALIVE liver dialysis device versus standard of care in patients with acute-on- chronic liver failure

Journal of Hepatology **2023.** vol. ■ | 1–14

**Výsledky:** Mezi skupinami nebyly signifikantní rozdíly v 28denní mortalitě. Významné snížení závažnosti endotoxémie a zlepšení funkce albuminu bylo pozorováno ve skupině DIALIVE, což se promítlo do významného **snížení orgánového selhání CLIF-C** (Chronic Liver Failure consortium) (p = 0,018) a skóre CLIF-C ACLF ( p = 0,042) v den 10. Biomarkery systémového zánětu, jako je **IL-8** (p = 0,006), **buněčná smrt** [cytokeratin-18: M30 (p = 0,005) a M65 (p = 0,029)], **endoteliální funkce** [asymetrický dimethylarginin (p = 0,002)] a, **ligandy pro Toll-like receptor 4** (p = 0,030) a **inflammasom** (p = 0,002) se významně zlepšily ve skupině DIALIVE. Závěry: Tyto údaje naznačují, že DIALIVE se zdá být bezpečný a pozitivně ovlivňuje prognostické skóre a patofyziologicky relevantní biomarkery u pacientů s ACLF. K dalšímu potvrzení jeho bezpečnosti a účinnosti jsou zaručeny větší, přiměřeně účinné studie.



ADVITOS
Bridging Life



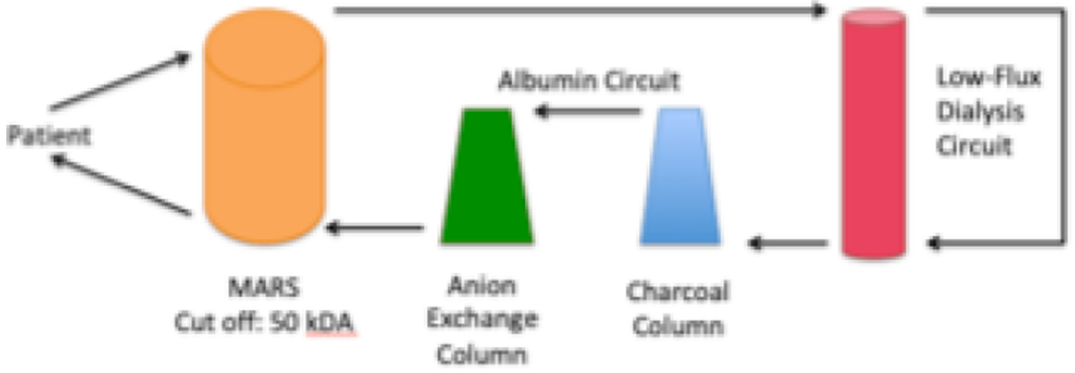

**4-in-1-zařízení: Současná podpora pro všechny detoxikační orgány**

Podpora jater: odstranění jaterních toxinů

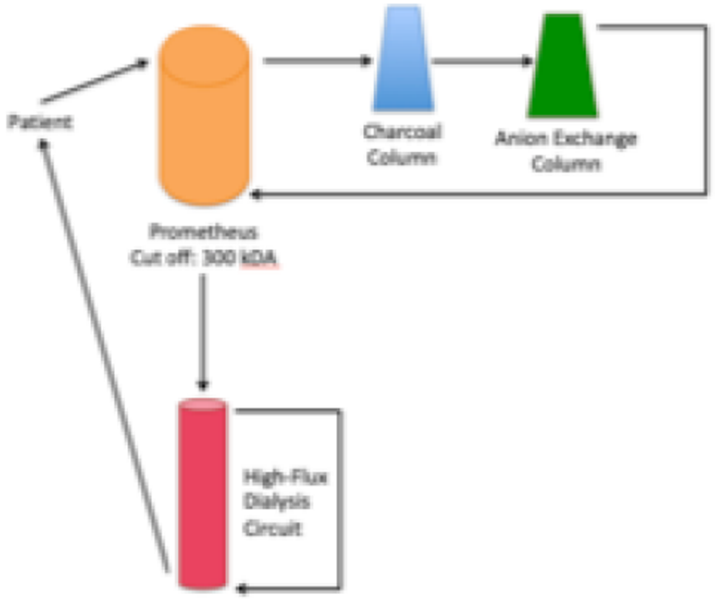
Podpora plic: extracorporeal CO2 odstranění v nízko invazivních nastaveních

Podpora ledvin: odstranění vody rozpustné a také proteinové nefrotoxiny

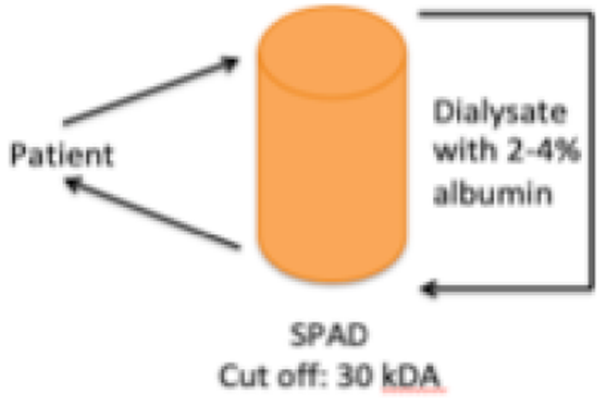
Řízení pH krve: Stabilizace rovnováhy kyselé báze přímým odstraněním kyseliny, což má za následek korekci acidózy



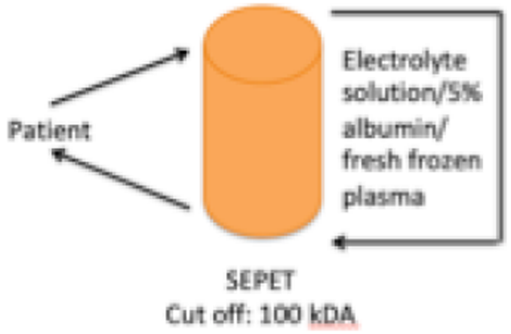

MARS




Prometheus




SPAD




SEPET

REVIEW ARTICLE

# Artificial liver support systems

Radhika Tandon* and Saied Froghi*,†

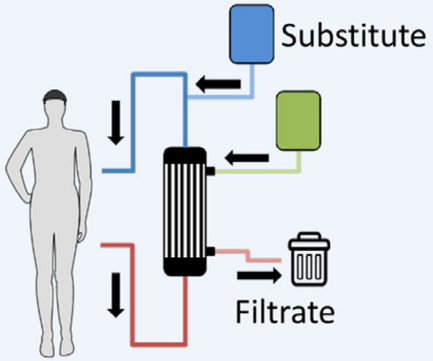
*Guys Campus, King's College London, and †Department of HPB and Liver Tra

*Review*

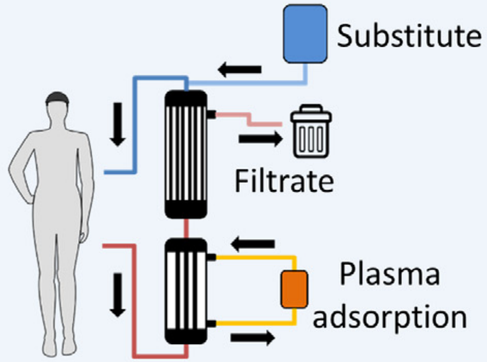
# Septic Hyperinflammation—Is There a Role for Extracorporeal Blood Purification Techniques?

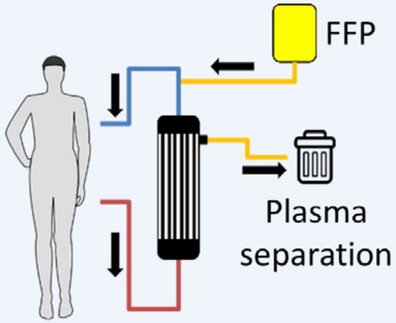
Dominik Jarczak, Stefan Kluge and Axel Nierhaus *

## Extracorporeal Blood Purification Techniques



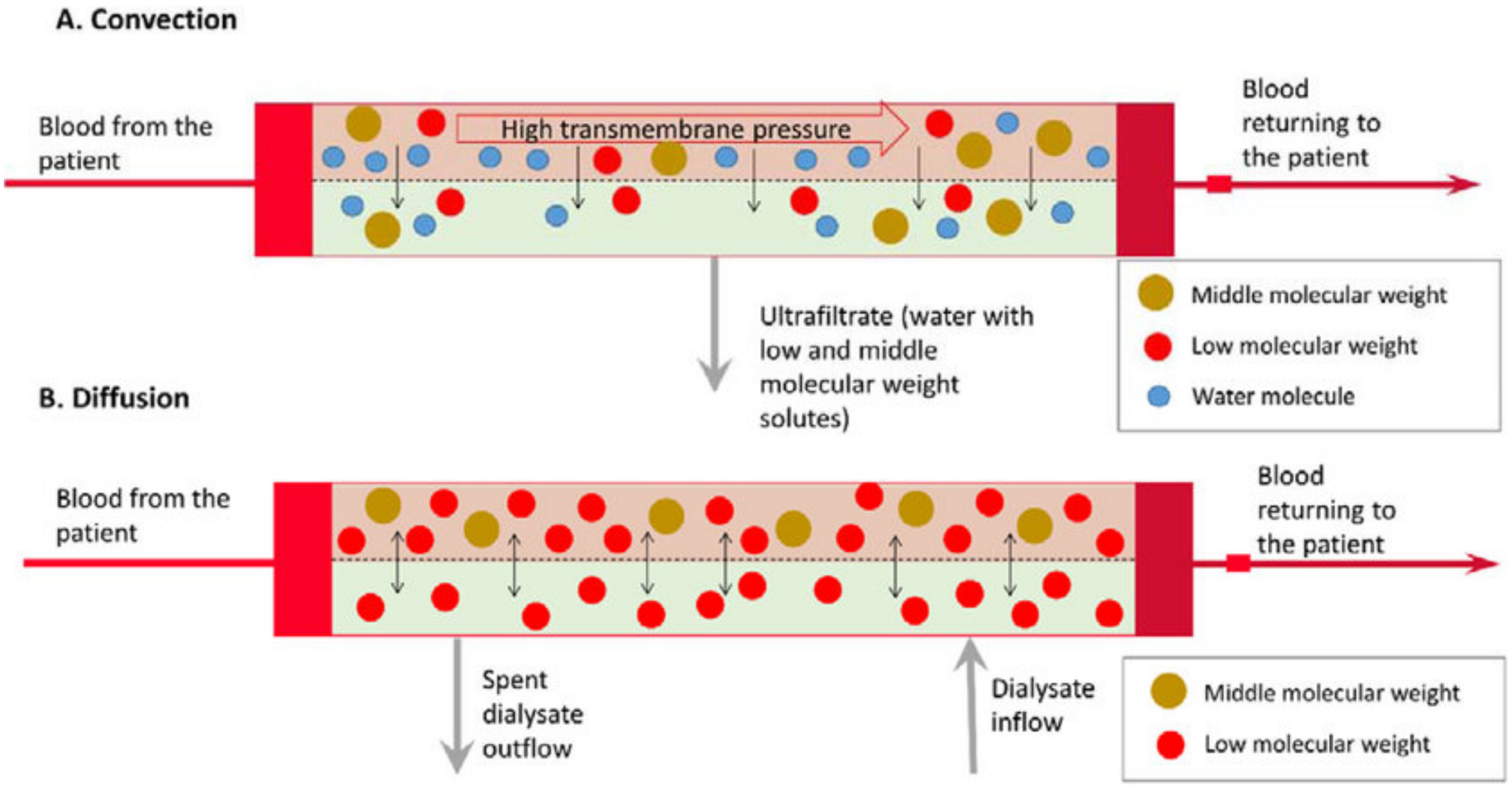





| Convection Therapies | Adsorption Therapies | Combination Therapies | Other Therapies |
|---|---|---|---|
| High Cut-Off Membranes (HCO) | Specific Adsorption<br>Polymyxin B (PMX)<br>LPS Adsorber | Combined filtration and Adsorption (e.g. oXiris®) | Plasma Exchange |
| High Volume Hemofiltration (HVHF) | Unspecific Adsorption<br>Hemoadsorption (e.g. CytoSorb®) | Coupled Plasma Filtration Adsorption (CPFA) | |

# RRT - CRRT

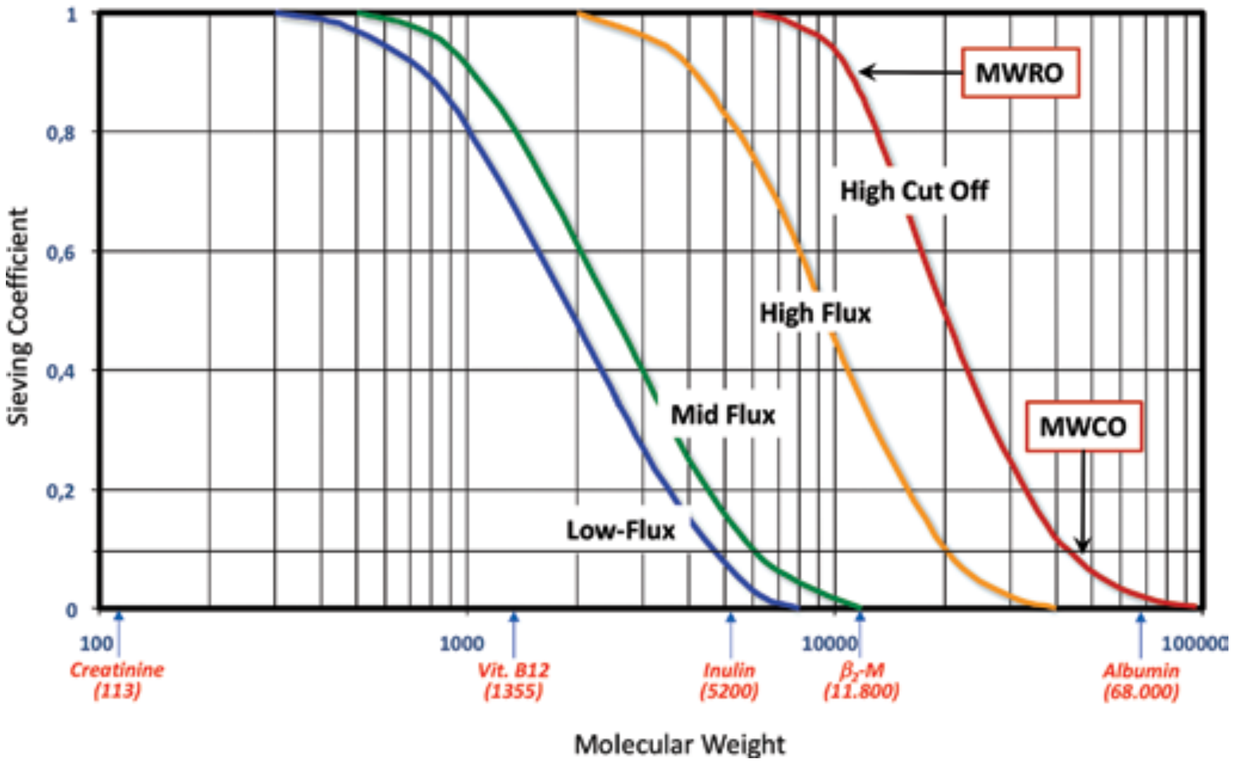



**Omezení pro odstranění cytokinů v důsledku propustnosti membrány.**

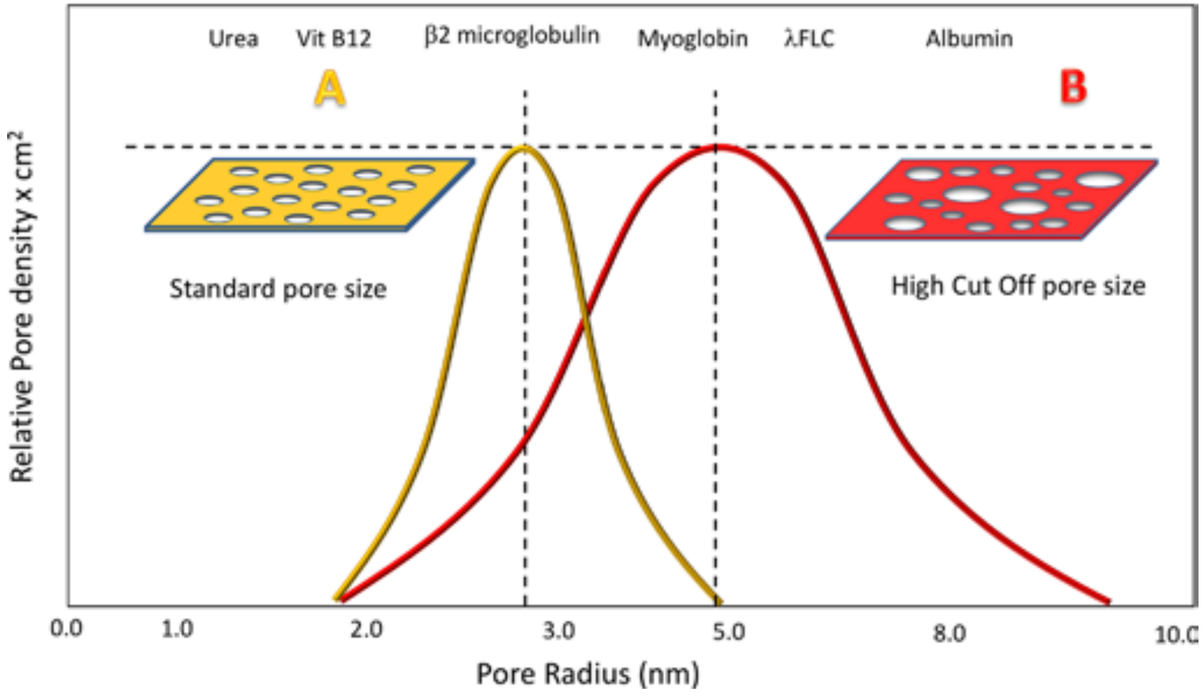
**High cut-off membranes in acute kidney injury and continuous renal replacement therapy**

Zaccaria Ricci[1], Stefano Romagnoli[2], Claudio Ronco[3,4]

## Membrane Sieving Coefficients Curves




## Membrane Pore Size Distribution




**Účinnější clearance prozánětlivých cytokinů: IL-1, IL-6 a TNF konvekcí, vedla také k významné ztrátě albuminu ve srovnání s modalitami založenými na difúzi.**

Honore, P.M.; Jacobs, R.; Boer, W.; Joannes-Boyau, O.; De Regt, J.; De Waele, E.; Van Gorp, V.; Collin, V.; Spapen, H.D. New insights regarding rationale, therapeutic target and dose of hemofiltration and hybrid therapies in septic acute kidney injury. Blood Purif. 2012, 33, 44–51

Studie HICOSS

# Rozdíl: **HIGH CUTT OFF x HIGH FLUX**

**ANO: IL-6, myoglobin, b2- microglobulin**
**NE: AT III, Protein C a S, trombin, koag.f F V, F VIII, albumin**



Middle molecule clearance with high cut-off dialyzer versus high-flux dialyzer using continuous veno-venous hemodialysis with regional citrate anticoagulation: A prospective randomized controlled trial

Lorenz Weidhase[1]*, Elena Haussig[1], Stephan Haussig[2], Thorsten Kaiser[3], Jonathan de Fallois[1], Sirak Petros[1]

**Citation:** Weidhase L, Haussig E, Haussig S, Kaiser T, de Fallois J, Petros S (2019) Middle molecule clearance with high cut-off dialyzer versus high-flux dialyzer using continuous veno-venous hemodialysis with regional citrate anticoagulation: A prospective randomized controlled trial. PLoS ONE 14(4): e0215823. https://doi.org/10.1371/journal.pone.0215823

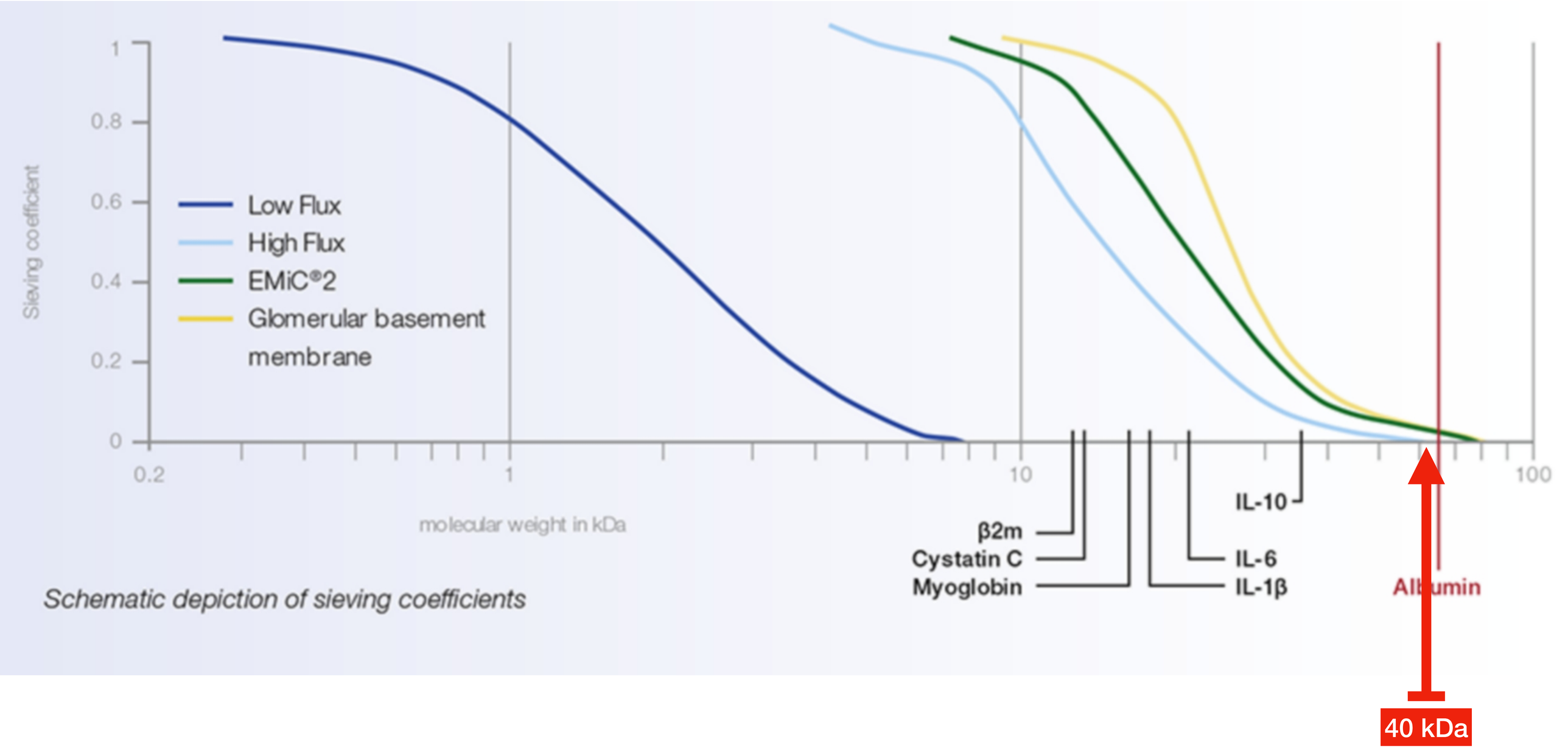
**Table 3. Mean plasma clearance (ml/min), n = 42.**

| Variable | control group (n = 20) | intervention group (n = 22) | *p* value |
|---|---|---|---|
| Urea | 20.7±8.7; (CI: 16.6–24.8) | 22.4±7.1; (CI: 19.2–25.5) | 0.488 |
| Creatinine | 22.9±9.0; (CI: 18.7–27.1) | 25.7±8.5; (CI: 21.9–29.5) | 0.279 |
| $\beta_2$-microglobulin | 12.2±3.6; (CI: 10.5–13.9) | 19.6±5.8; (CI: 17.0–22.1) | <0.001 |
| Myoglobin | 0.2±3.6; (CI: -1.5–1.9) | 8.0±4.5; (CI: 6.0–10.0) | <0.001 |
| IL-6 | -2.5±3.5; (CI: -4.1-(-0.9)) | 1.5±4.3; (CI: -0.4–3.4) | 0.002 |
| Albumin | -2.6±4.0; (CI: -4.5-(-0.8)) | -2.3±3.9; (CI: -4.1-(-0.6)) | 0.802 |

Data presented as mean ± standard deviation and confidence interval. *Abbreviations*: *CI* confidence interval, *ml/min* milliliters per minute, *IL-6* interleukin 6

* max. limit high cut off - 50 kDa, EMIC 2 40 kDA, Septex 45 kDa

# EMIC kapsle




*Schematic depiction of sieving coefficients*

# RRT - strategie

Fisher C, Baldwin I, Fealy N, Naorungroj T, Bellomo R: **Ammonia Clearance with Different Continuous Renal Replacement Therapy Techniques in Patients with Liver Failure**. Blood Purif 2022;51:840-846. doi: 10.1159/000521312

We found no significant difference in ammonia clearance according to CRRT technique and demonstrated that ammonia clearance is significantly less than urea or creatinine clearance.


**iHD - SLED - CRRT (CVVH, CVVHD, CVVHDF)**
**ale: CRRT rychlejší eliminace**
CVVHDF - pouze teoretická výhoda

**Amoniak** - toxicita, malá molekula, encefalopatie
——> riziko edému mozku, otok astrocytů, vazogenní edém a narušení hematoencefalické bariéry, což přispívá k edému mozku —-> determinanta mortality

norma: **< 50-70** umol/l …. hyperamonemie **> 100** umol/l (ped)…. (neonatologie: **> 50** umol/l)…
extrémní hyperamonemie: **> 150** umol/l

# Correction and Control of Hyperammonemia in Acute Liver Failure: The Impact of Continuous Renal Replacement Timing, Intensity, and Duration

Stephen Warrillow, MBBS, FRACP, FCICM[1,2,3]; Caleb Fisher, MBBS, FRACP, FCICM[1]; Rinaldo Bellomo, PhD, FRACP, FCICM[1,3,4,5]

Osoby, které přežily acetaminofen ALF bez OLTx, prokázaly **větší proporcionální snížení koncentrace amoniaku mezi 3. a 5. dnem** než osoby bez ELT (0,39 [IQR, 0,10–0,52] vs 0,03 [IQR, 0,14–0,26]; p = 0,05) a také **nižší absolutní koncentrace amoniaku 5. den** (48 µmol/L [IQR, 40–68] vs 65 µmol/L [IQR, 69–92]; p = 0,02).

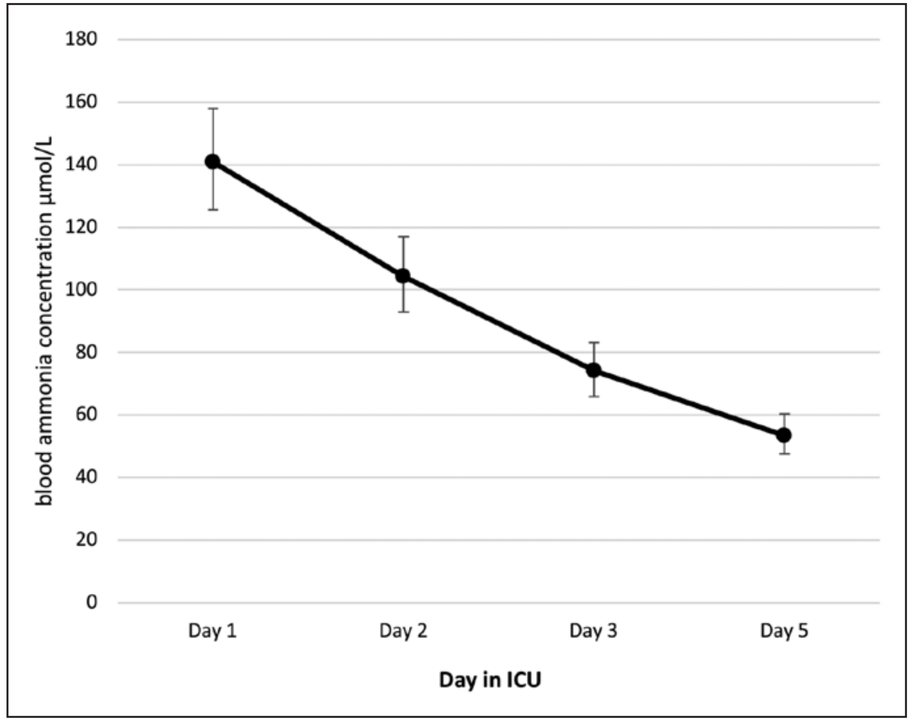



**Figure 1.** Ammonia dynamics over 5 d of treatment with continuous renal replacement therapy in acute liver failure. $p < 0.0001$. Geometric means of log transformed data. *Error bars* indicate 95% CI.

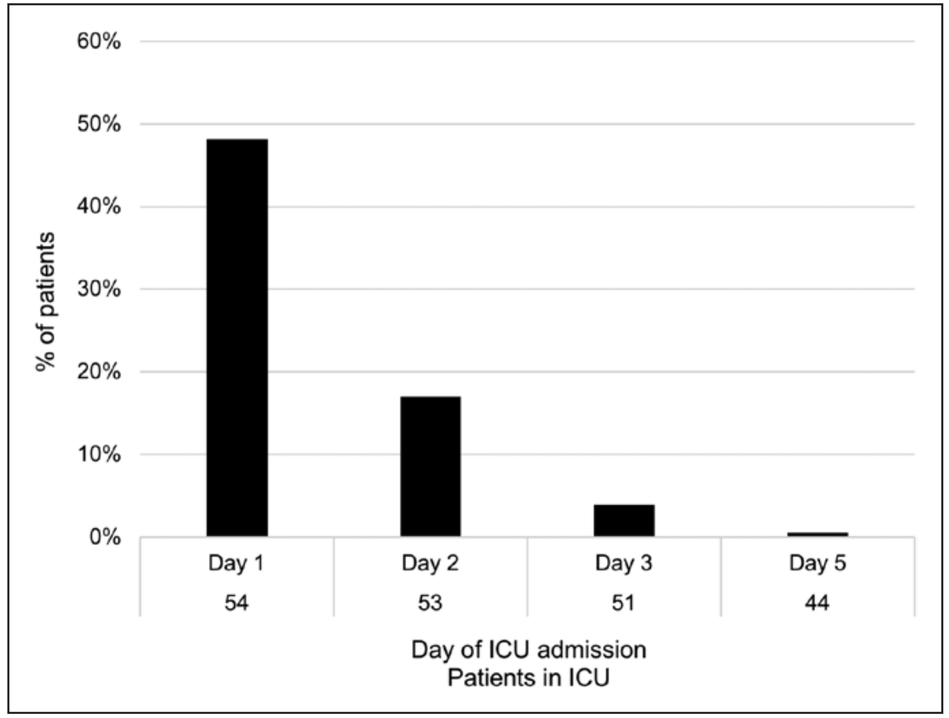



**Figure 2.** Proportion of patients with measured extreme hyperammonemia (> 150 µmol/L) over 5 d in ICU.

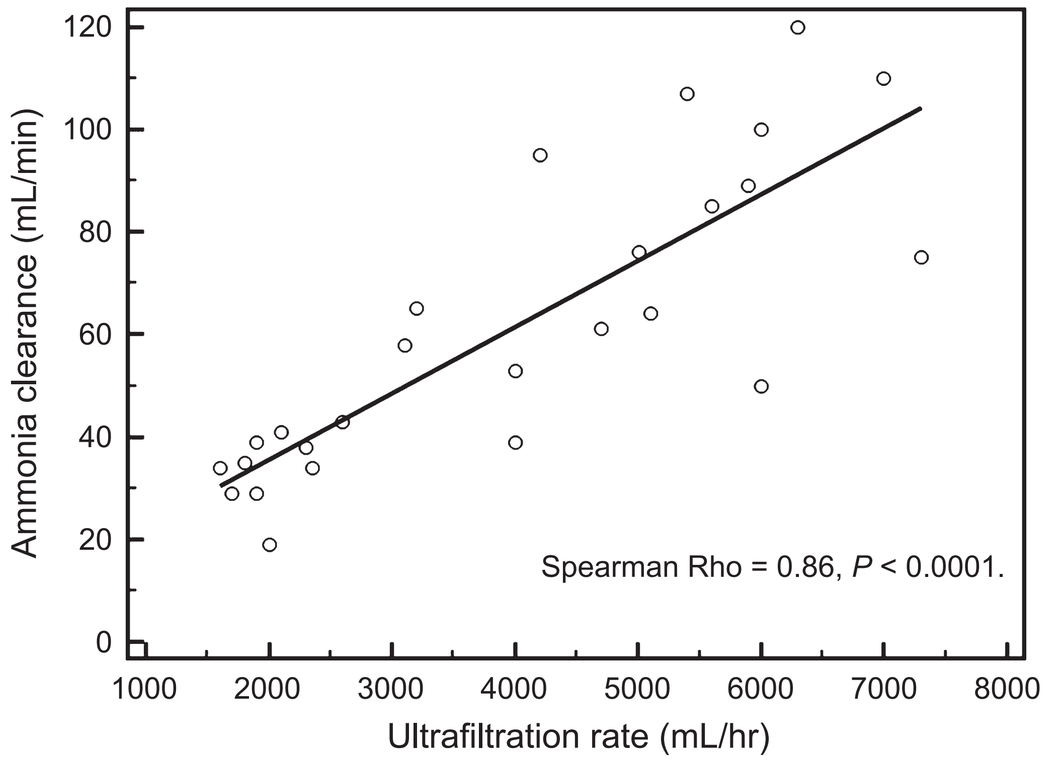



**Fig. 2.** Correlation between ultrafiltration rate and ammonia clearance after 1 h of continuous renal replacement therapy.



# Ammonia clearance with haemofiltration in adults with liver disease

Andrew J. Slack, Georg Auzinger, Chris Willars, Tracy Dew, Rebecca Musto, Daniel Corsilli, Roy Sherwood, Julia A. Wendon and William Bernal

Institute of Liver Studies, King's College Hospital Foundation Trust, London, UK

## Abstract

*Background & Aims:* Ammonia is recognized as a toxin central to complications of liver failure. Hyperammonaemia has important clinical consequences, but optimal means to reduce circulating levels are uncertain. In patients with liver disease, continuous renal replacement therapy (CRRT) with haemofiltration (HF) is often required to treat concurrent kidney injury, but its effects upon ammonia levels are poorly characterized. To evaluate the effect of HF at different treatment intensities on ammonia clearance (AC) and arterial ammonia concentration. *Methods:* Prospective study of adult patients with liver failure and arterial ammonia >100 μmol/L requiring CRRT using veno-venous HF. Arterial ammonia concentration and AC measured at 1 and 24 h after initiation of low (35 ml/kg/h) or high (90 ml/kg/h) filtration volume. *Results:* Twenty-four patients (10 acute liver failure, 10 chronic liver disease and 4 following liver resection) were studied. Clearance of urea and ammonia solutes correlated closely ($r = 0.819$, $P = 0.007$). Ammonia clearance correlated closely with ultrafiltration rate ($r = 0.86$, $P < 0.001$). At 1 h, AC was 39 (34–54) ml/min (low volume) vs 85 (62–105) ml/min (high volume) CRRT, ($P < 0.001$) and at 24 h 44 (34–63) vs 105 (82–109) ml/min, ($P = 0.01$). Overall, a 22% reduction in median arterial ammonia concentration was observed over 24 h of HF from 156 (137–176) to 122 (85–133) μmol/L, ($P \leq 0.0001$). *Conclusion:* Clinically significant ammonia clearance can be achieved in adult patients with hyperammonaemia utilizing continuous VVHF. Ammonia clearance is closely correlated with ultrafiltration rate. HF was associated with a fall in arterial ammonia concentration.

**PROTOKOL :**

**<u>časná indikace</u> - často před KDIGO AKI stage 2, dokonce jen v “mírné” acidémii**

<u>CRRT</u> - rychlá eliminace, redukce hladiny amoniaku (trend)

<u>“pokročilost” pacienta</u> - encefalopatie, INR, hypofibrinogenémia, trombocytopenie

**dávka: CRRT - CVVHD(F)**

<u>nastavení:</u>

**Qeff - 45-50 ml/kg/h*** (dávka dialýzy)**, Qb 80-120-250 ml/min, UF dp.**

**(cave: poměr pro RCA - 1:20!)**

vaky: Na - 133! (cíl: 145-150 mmol/)

<u>antikoagulace</u>: RCA (metabolizmus, nastavení)

Bikarbonátové vaky (bez) - druhá volba, závažný met. rozvrat

<u>stav koagulace</u>: suplementace AT III, TEG!

* min. prvních 12 hodin ——> TPE/DPMAS

# Kombinace:

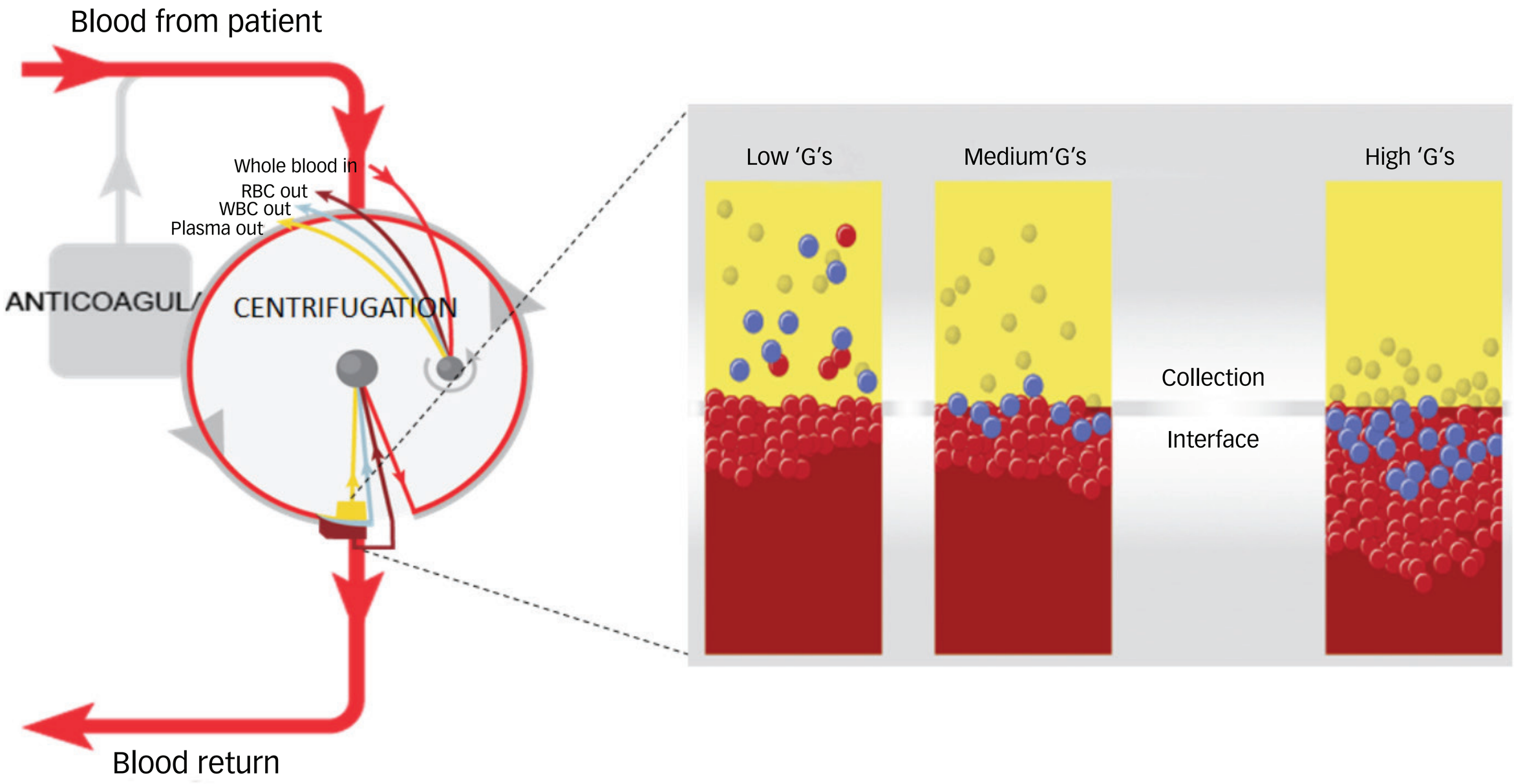
DPMAS (HA) + TPE

TPE + HD(F)

HD(F) + DPMAS (HA)

DPMAS + PE + HD(F)

# (Terapeutická) výměna plazmy
# (T)PE, PLEX, PEX


Blood from patient
Whole blood in
RBC out
WBC out
Plasma out
ANTICOAGUL/
CENTRIFUGATION
Blood return
Low ‘G’s
Medium‘G’s
High ‘G’s
Collection
Interface

FRESENIUS KABI

caring for life



# COM.TEC®

## Therapeutic apheresis and cell collection

### Intuitive graphical user interface (GUI)

- Connects you to the relevant information using a high-resolution, color touch screen
- Guides you through each step of the procedure
- Helps you enter the necessary patient and procedure information
- Gives you the right information at the right time to enhance procedure efficiencies
- Provides clear alarm messages that you can see at a glance

### Incorporated Seal Safe System for sealing tubes

### Ready-to-use tubing sets designed to handle multiple procedure types

- You can load the snap-in-place cassette in a few steps
- The system verifies when you have the correct tubing set in place for the selected procedure
- Low-volume tubing set accommodates your smaller patients
- With minimal set types to keep in inventory, you can achieve storage efficiencies

### Highly maneuverable system

- Telescoping IV pole that you can easily raise or lower
- Folding screen to help you simplify moving and storage
- Large, durable wheels on pivoting casters brings you a high level of system maneuverability
- Advanced wheel pedal enables you to move or secure the system depending on your needs

### Dimensions

- Weight: 91.6 kg (220 lbs)
- Height (lowered IV pole): 115.6 cm (45.5 in)
- Height (extended IV pole): 174 cm (68.5 in)
- Width: 52.7 cm (20.75 in)
- Depth: 81.3 cm (32.0 in)
- Floor space required: 0.43 $m^2$ (4.6 $ft^2$)

Shown with a tubing set for therapeutic plasma exchange procedures.

# Plasma exchange in the intensive care unit: a narrative review

Philippe R. Bauer[2*], Marlies Ostermann[12], Lene Russell[15], Chiara Robba[14], Sascha David[6], Bruno L. Ferreyro[7], Joan Cid[5], Pedro Castro[4], Nicole P. Juffermans[8], Luca Montini[10], Tasneem Pirani[13], Andry Van De Louw[17], Nathan Nielsen[11], Julia Wendon[18], Anne C. Brignier[3], Miet Schetz[16], Jan T. Kielstein[9], Jeffrey L. Winters[19], Elie Azoulay[1] on behalf of the Nine-I Investigators

**Eliminace: - nahrazení vylučovacích a metabolických funkcí selhávajících jater - extrakce proteinů váz. i neváz. na alb. navázané HMW molekuly (vč. amoniak, endotoxin, indol, merkaptan) ——-> zlepšení jat. komatu a hyperkinetického syndromu !**

**- úprava koagulace ———> zabránění krvácení**

**- odstranění škodlivých DAMP a cytokinů (patologická ohromující imunitní odpověď —->MOF)**

**úprava: CBF, CPP, ICP a MAP ——> lepší průtok krve orgány (vč. jater)**

**TPE - koriguje zvýšený multimer von Willebrandova faktoru a sníženou aktivitu ADAMTS13**

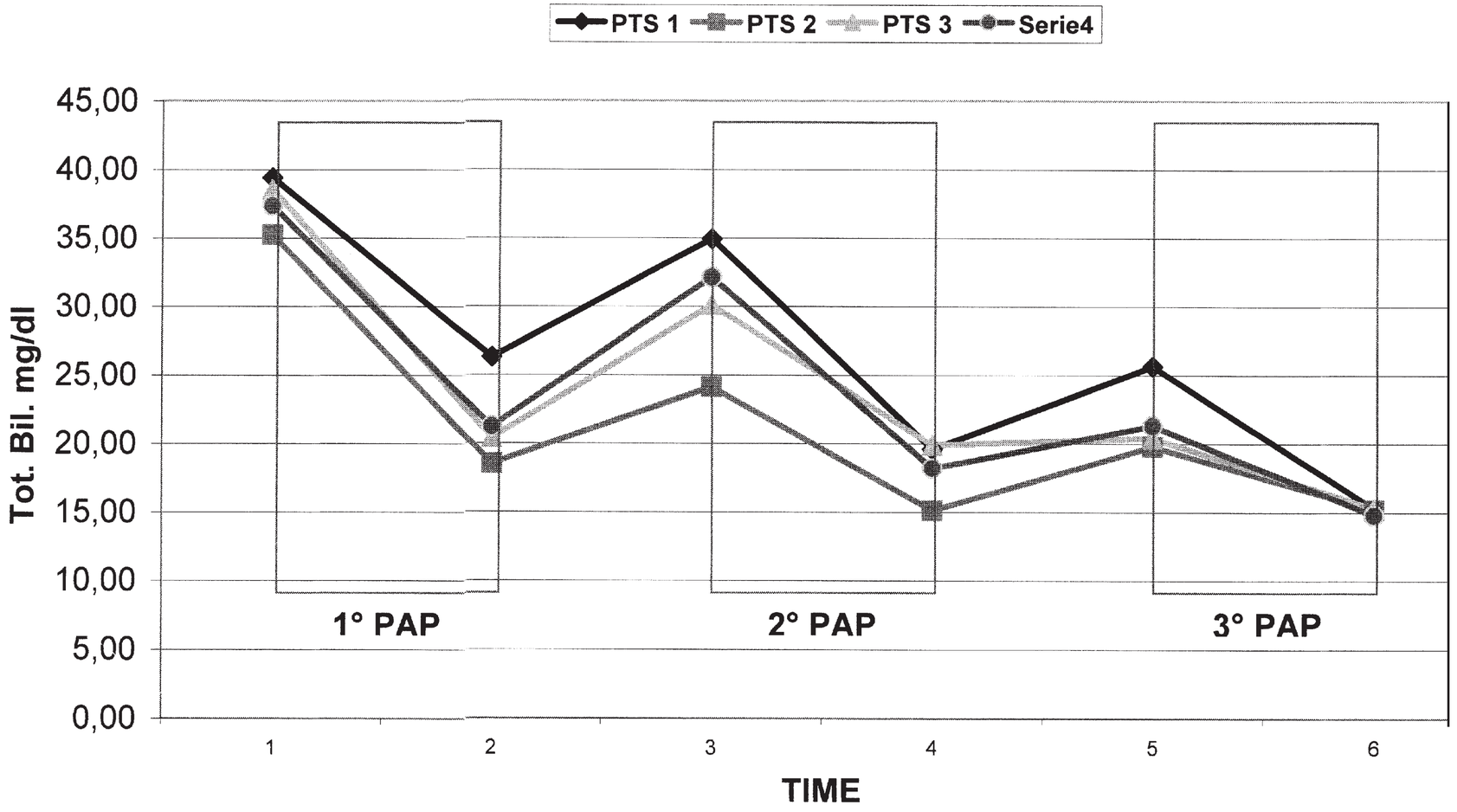
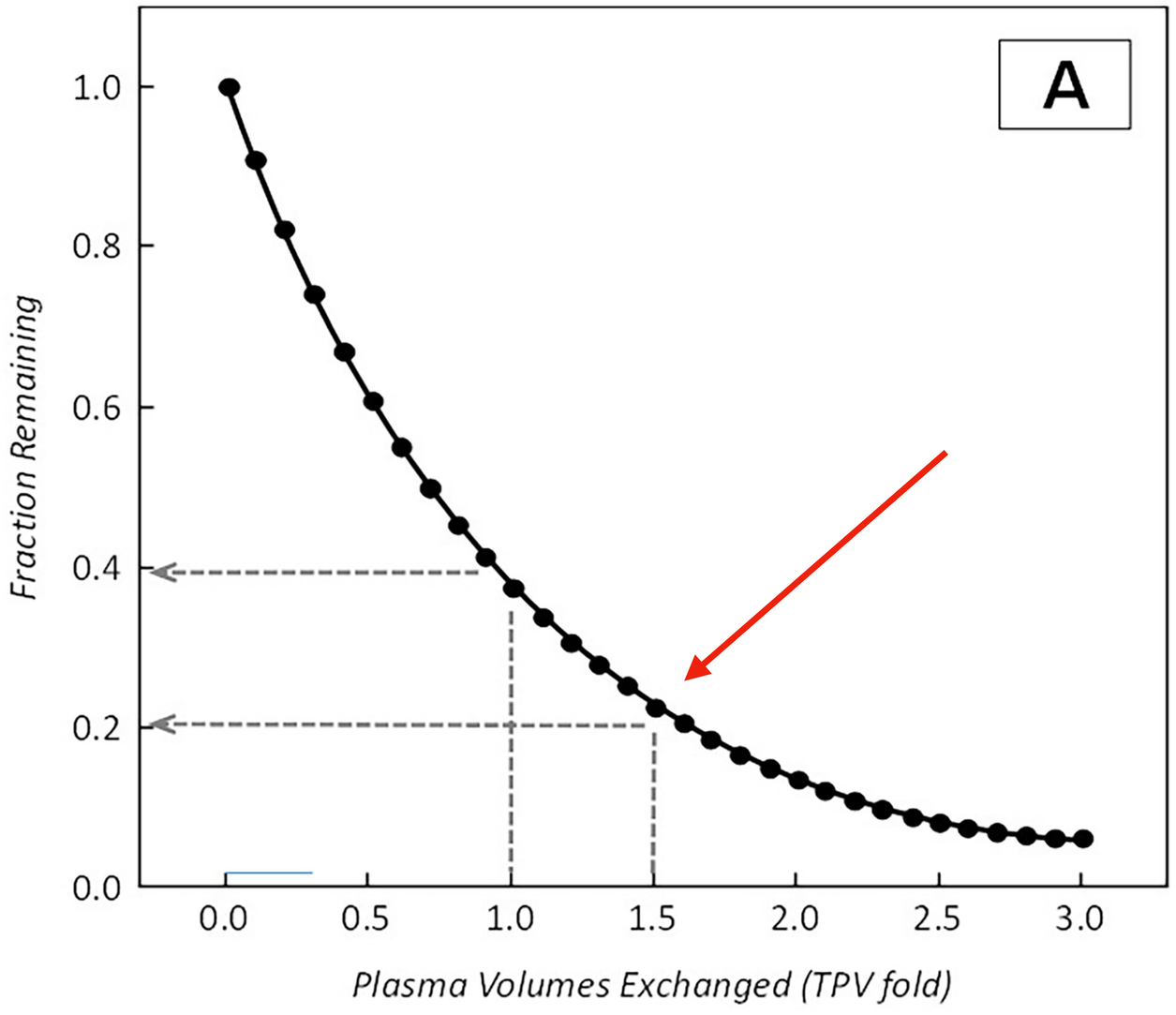
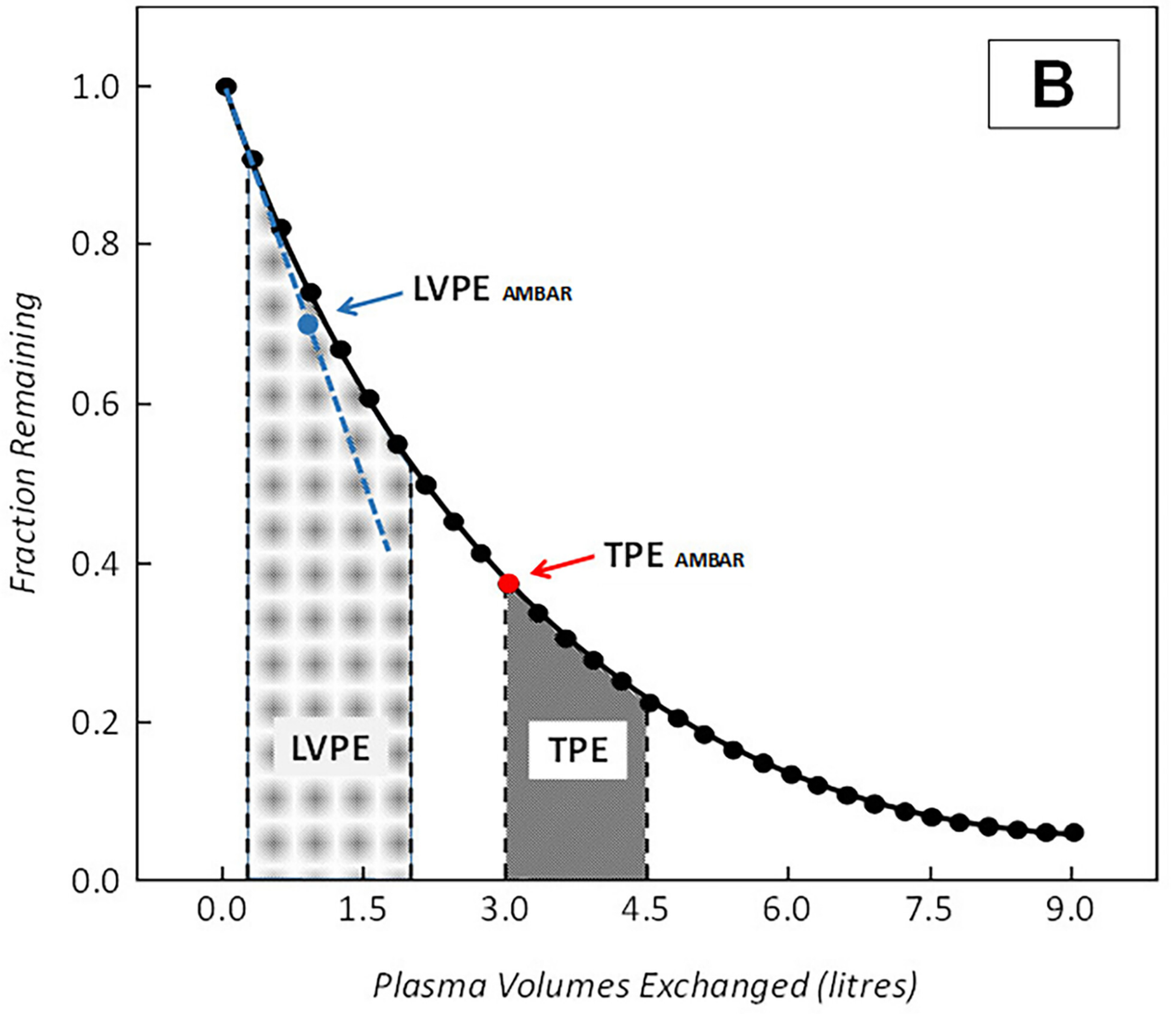



**Fig 1.** Total bilirubin level during PAP with Plasorba BR-350.


A
1.0
0.8
0.6
0.4
0.2
0.0
Fraction Remaining
0.0
0.5
1.0
1.5
2.0
2.5
3.0
Plasma Volumes Exchanged (TPV fold)


B
1.0
0.8
0.6
0.4
0.2
0.0
Fraction Remaining
LVPE AMBAR
TPE AMBAR
LVPE
TPE
0.0
1.5
3.0
4.5
6.0
7.5
9.0
Plasma Volumes Exchanged (litres)

**Therapeutic plasma exchange in acute liver failure**

Klaus Stahl[1] | Johannes Hadem[2] | Andrea Schneider[1] | Michael P. Manns[1] | Olaf Wiesner[3] | Bernhard M. W. Schmidt[4] | Marius M. Hoeper[3] | Markus Busch[1] | Sascha David[4]

Received: 7 February 2019

# HV-TPE ——-> 15% IBW ( 8-12 litrů FFP na 7 hodin)
# LV-TPE ——> 6% IBW (12 FFP - 3 litry na 2 hodiny)
# nejnovější ———> 3% IBW (1 hodina + steroidy)

**Dávka TPE byla zvolena libovolně a nižší i vyšší dávky mohly mít stejné příznivé účinky.**

Americká společnosti pro aferézu (**ASFA**) - silné doporučení stupně 1A/III pro HV-TPE, ale pouze **slabé doporučení stupně 2B/III pro použití jakéhokoli jiného než HV-TPE u ALF** vzhledem k nedostatku spolehlivých údajů pro přiblížení LV-TPE.

.

**3000ml (á 200ml = 2850 Kč) —-> 42.750 Kč**

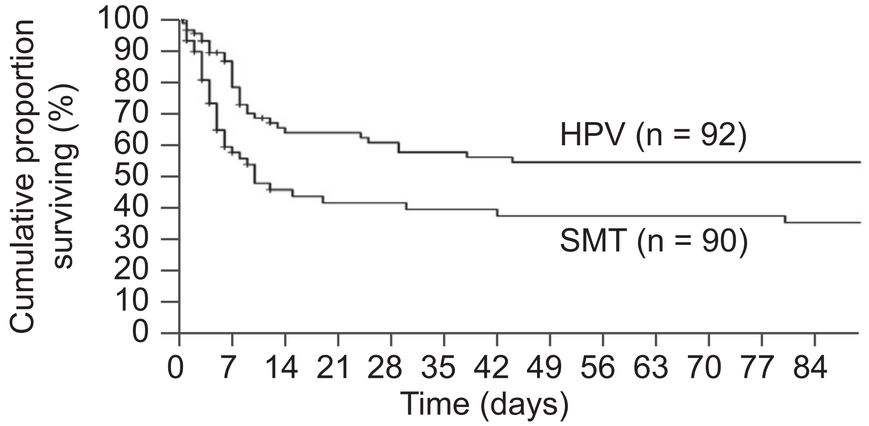



**Fig. 1. Main results of the intention-to-treat analysis survival data in the standard medical treated group (SMT) compared to the high-volume plasma exchange (HVP) treated group** (LogRank: $p = 0.0058$).

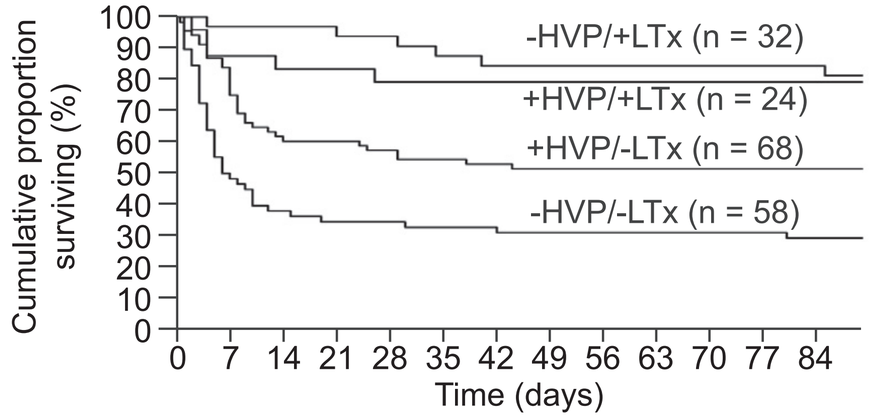



**Fig. 2. Survival in the groups, in the two groups receiving SMT (standard medical treated group) with and without emergency transplantation (−HVP +LTx *vs.* +HVP−LTx) and the two group receiving SMT with and without emergency transplantation (−HVP−LTx *vs.* +HVP−LTx)** (LogRank: $p = 0.0058$) and Cox proportional hazard: LTx: $p < 0.0001$; HVP: $p = 0.0076$).

## High-volume plasma exchange in patients with acute liver failure: An open randomised controlled trial

Fin Stolze Larsen[1,*], Lars Ebbe Schmidt[1], Christine Bernsmeier[2], Allan Rasmussen[3], Helena Isoniemi[4], Vishal C. Patel[2], Evangelos Triantafyllou[2], William Bernal[2], Georg Auzinger[2], Debbie Shawcross[2], Martin Eefsen[1], Peter Nissen Bjerring[1], Jens Otto Clemmesen[1], Krister Hockerstedt[4], Hans-Jørgen Frederiksen[5], Bent Adel Hansen[1], Charalambos G. Antoniades[2,6,†], Julia Wendon[2,†]

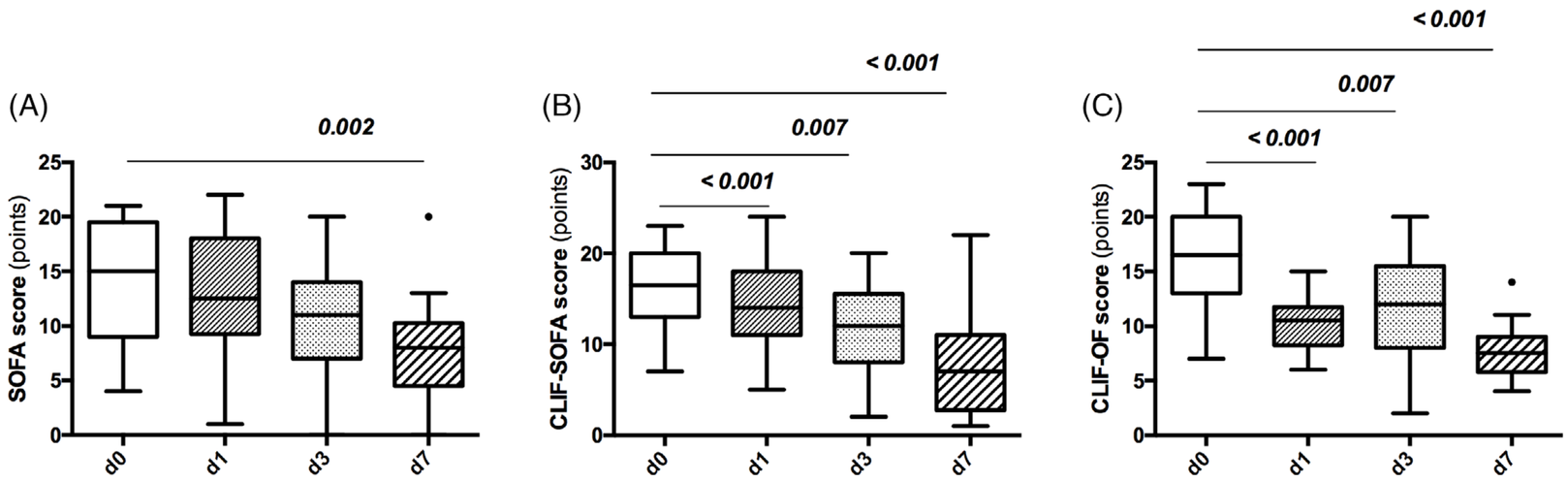



**FIGURE 3** Effect of LV-TPE on organ dysfunction. Box and whisker blots showing SOFA (A), CLIF-SOFA (B), and CLIF-OF scores (C) immediately before (d0) and at 24 hours (d1), 72 hours (d3) as well as a week (d7) after first LV-TPE treatment. CLIF, chronic liver failure; LV-TPE, low-volume therapeutic plasma exchange; OF, organ failure; SOFA, sequential organ failure assessment

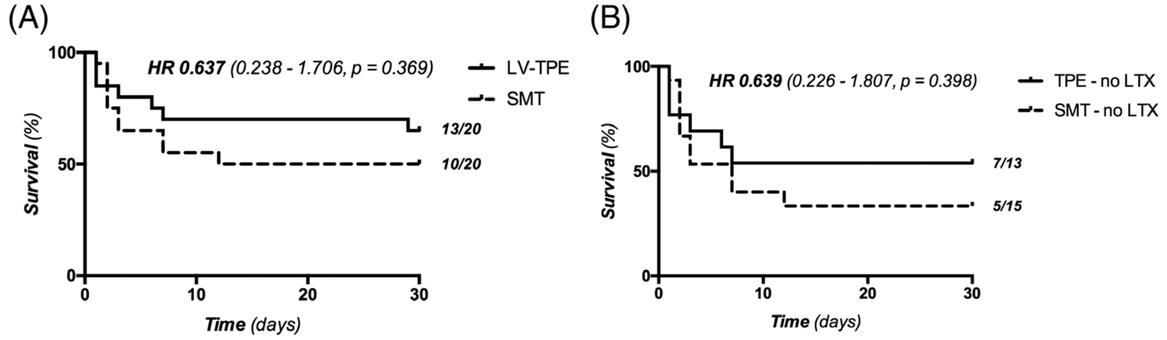



**FIGURE 4** Thirty-day survival in patients receiving LV-TPE compared to SMT. Kaplan-Meier graphs showing the 30-day survival course in patients with standard supportive medical therapy (SMT) only and additional LV-TPE demonstrating an observed survival of 50% and 65%, respectively (A). As survival was comparable in LV-TPE and SMT patients receiving a liver transplant, survival differences (33% vs 54%) were mainly attributable to patients in both cohorts receiving no liver transplant (B)

# Low-Volume Plasma Exchange and Low-Dose Steroid to Treat Severe Liver Injury

2020

**Uday Zachariah, Santhosh E. Kumar, Vijay Alexander, Lalji Patel[1], Ashish Goel, C. E. Eapen**
Departments of Hepatology and [1]Gastroenterology, Christian Medical College, Vellore, Tamil Nadu, India

**1-1,5-2 litru + "malá dávka” steroidu (50 mg prednison) - 3 dny po sobě**

## Jak zlepšuje léčba výměnou plazmy s nízkou dávkou a steroidem s nízkým objemem přežití u syndromů akutního selhání jater?

Pokud je indikována včas ——>

**vWF <— —> ADAMTS13**

redukce MOF, MODS, zlepšení regenerace

měření: prognostické márkery

# Growing Evidence for Survival Benefit with Plasma Exchange to Treat Liver Failure

Ashish Goel , Uday Zachariah, Dolly Daniel, Chundamannil E. Eapen

*Departments of Hepatology and Transfusion Medicine and Immunohaematology, Christian Medical College, Vellore, Tamil Nadu, India*

2024

## Různé dávky plazmatického objemu k léčbě selhání jater

Průměrný dospělý má asi 5 1 krve (asi 2,5 l je plazma).

**Vysoký, standardní a nízký objem** - 10 l (4násobek plazmatického objemu), 2,5–5 l (1–2násobek objemu plazmy) nebo **1,2 l plazmy (0,5násobek plazmatického objemu)**.

*TPE s nízkým objemem může být také prospěšný pro léčbu pacientů s ALF.*

Tlak na TS/Octaplas (potřebné velké objemy FFP), riziko akutních plicních komplikací - TRALI, riziko infekce.

# Hemoadsorpce

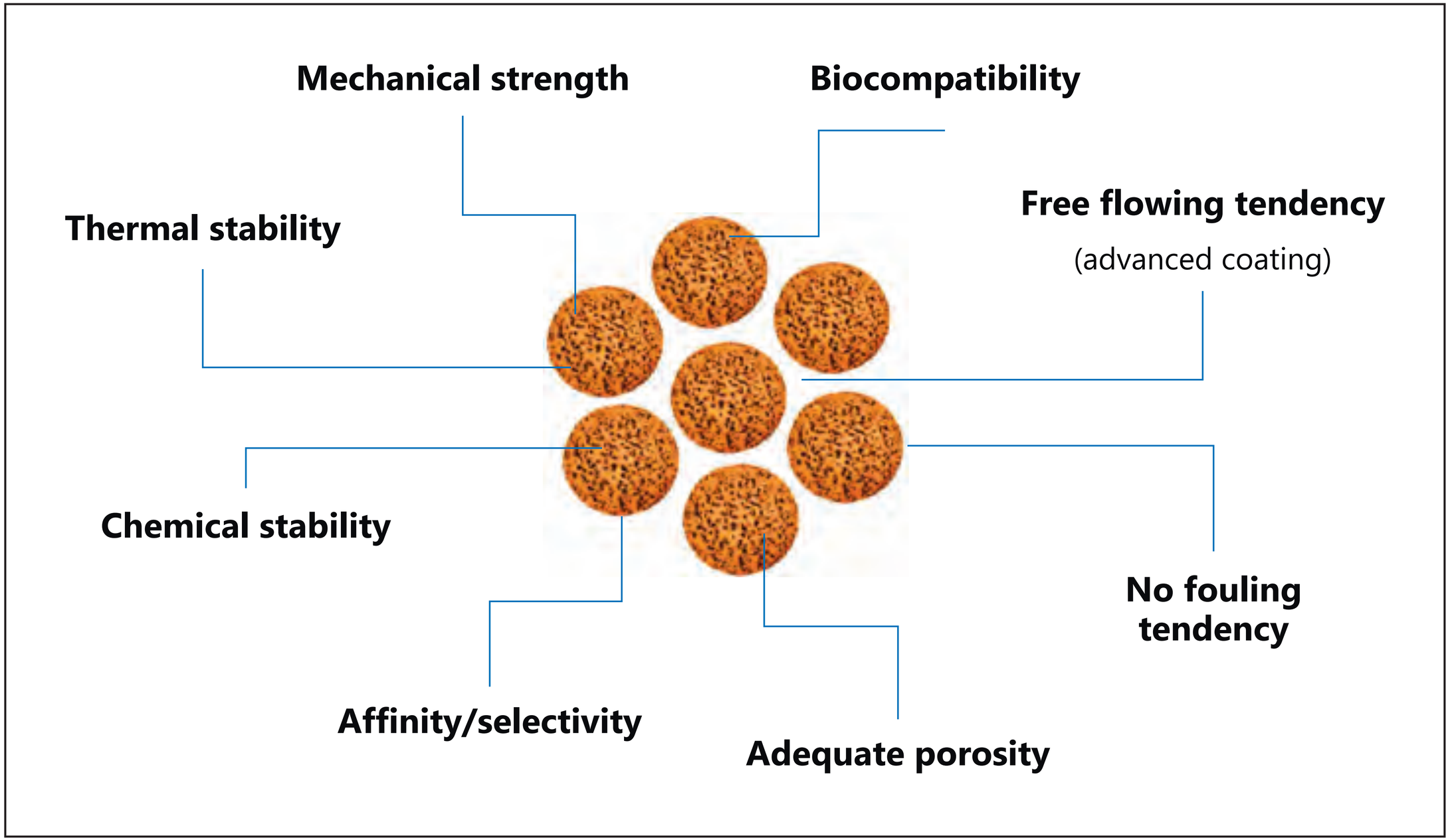
# Historie

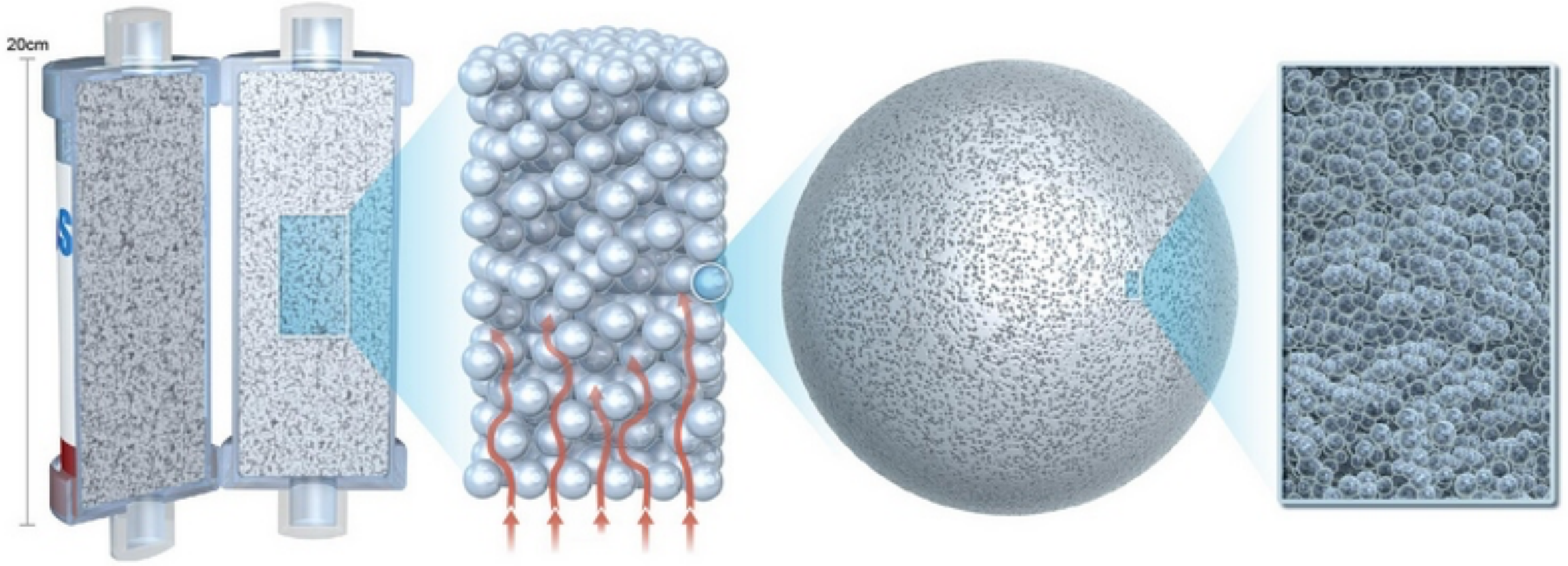
**Table 1.** Development of sorbents in extracorporeal blood therapies

| | |
|---|---|
| 1850 | First inorganic aluminosilicates (zeolites) used to exchange $NH_4$ and Ca |
| 1910 | Water softeners using zeolites display instability in the presence of mineral acids |
| 1935 | Adams and Holmes synthetized the first organic polymer ion exchange resin |
| 1950s | Application of synthetic porous polymers (styrene or acrylic acid based) (spherical beads; trade names were Amberlite, Duolite, Dowex, Ionac, and Purolite) |
| 1960s | Manipulation of physical-chemical characteristics (commercial use) |
| 1970s | Application in blood purification techniques such as hemoperfusion |
| 1980–2000 | Improved design and coating for better hemocompatibility of adsorbent materials |
| 2000–2010 | Focus on critical illness and sepsis with removal of cytokines |
| 2010–2023 | New clinical applications and development of a neutral microporous resin optimized by advanced surface coating and nanoscale molecular sieve control technology |

2000

RenalTech - biokompatibilní pryskyřici potažená tenkým polysulfonovým filmem ——> **BetaSorb** (New Jersey, USA, Robert Albright) ——-> “doplňkový nástroj” pro kombinaci s hemodialýzou ke snížení hladin beta-2 mikroglobulinu u CKD-HD.

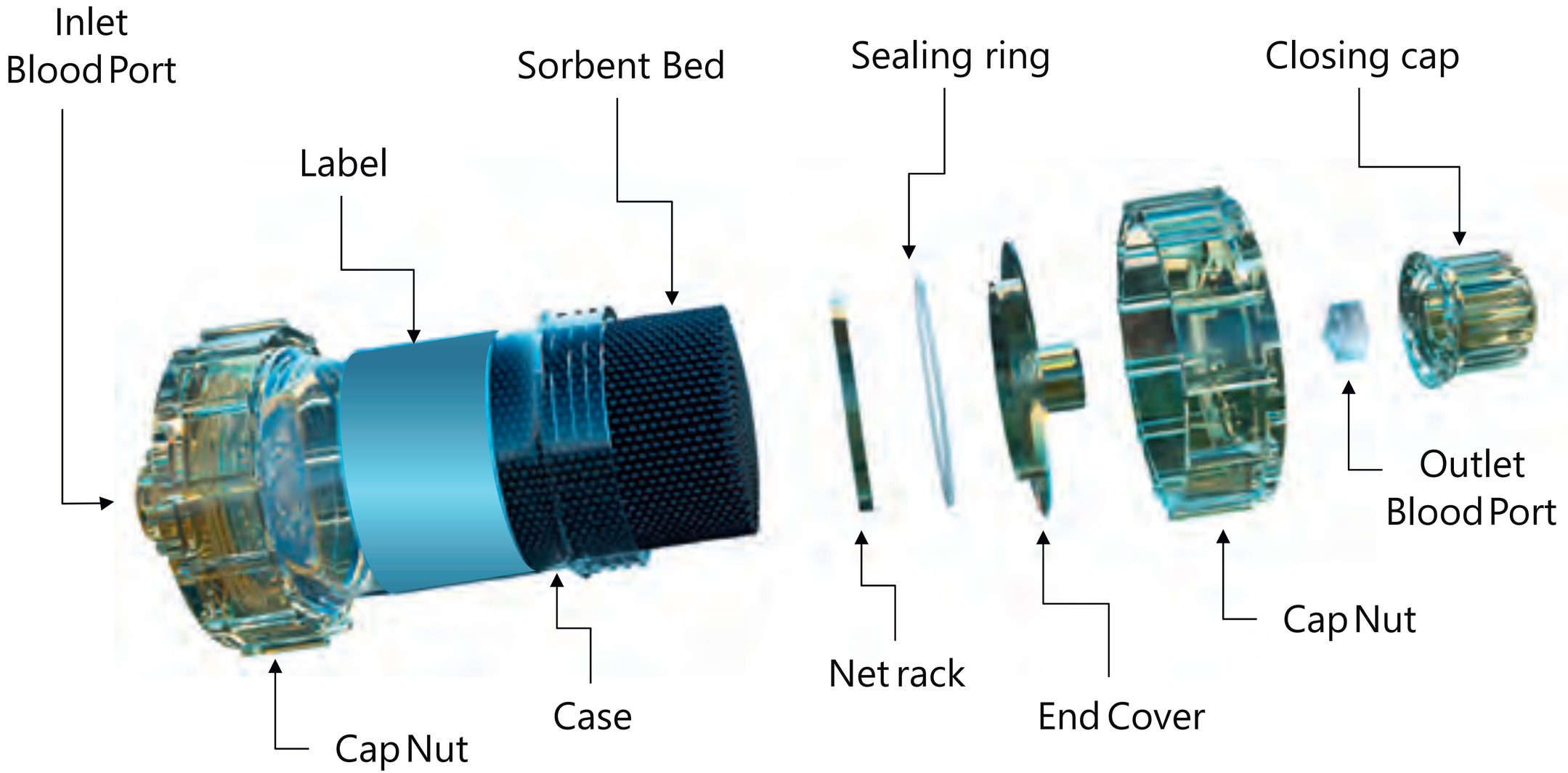

Mechanical strength
Biocompatibility
Thermal stability
Free flowing tendency
(advanced coating)
Chemical stability
No fouling tendency
Affinity/selectivity
Adequate porosity

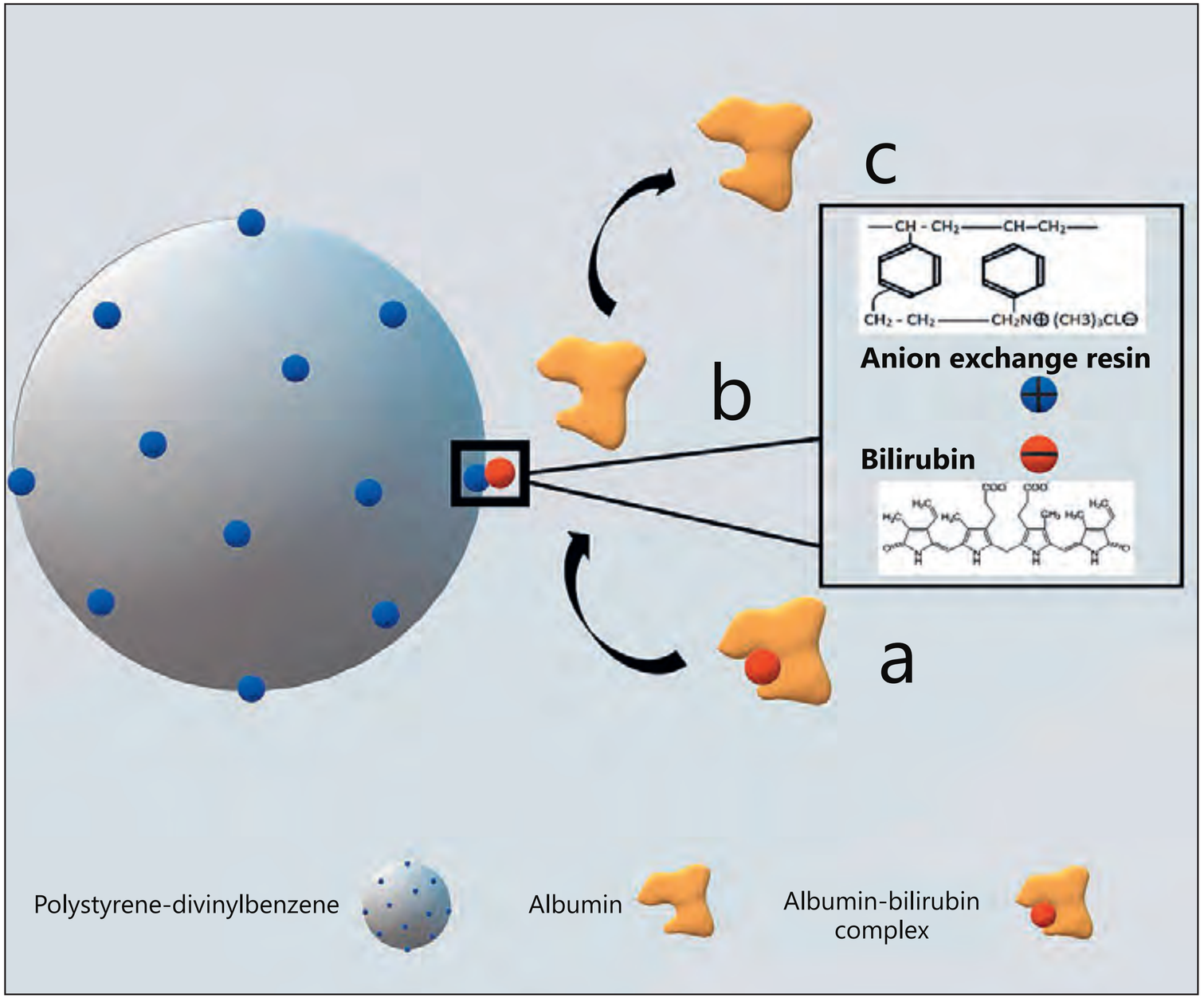


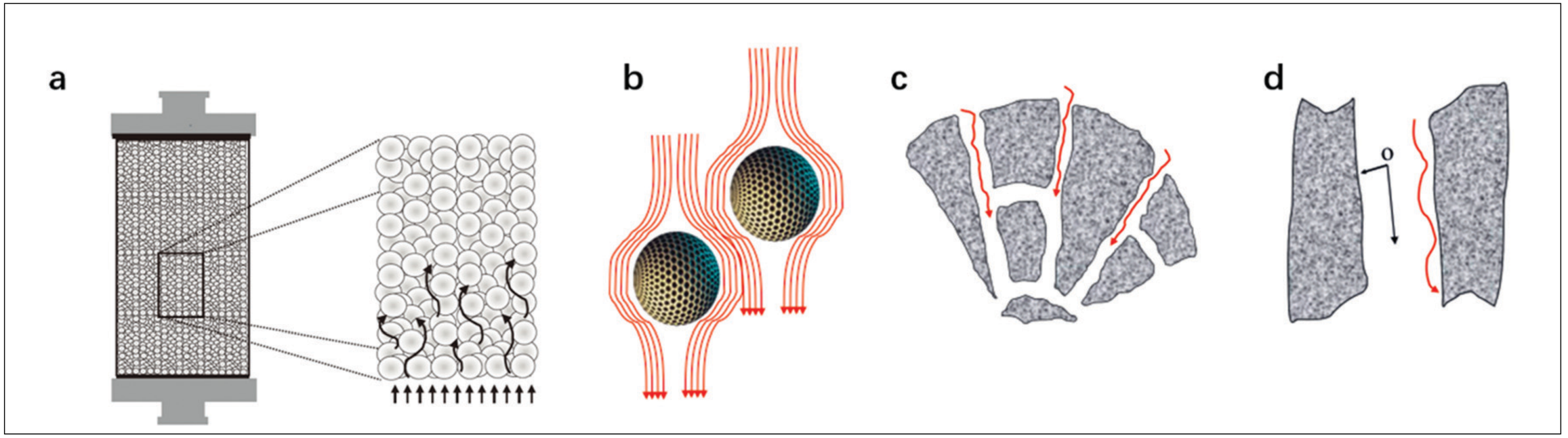

Section through an adsorber

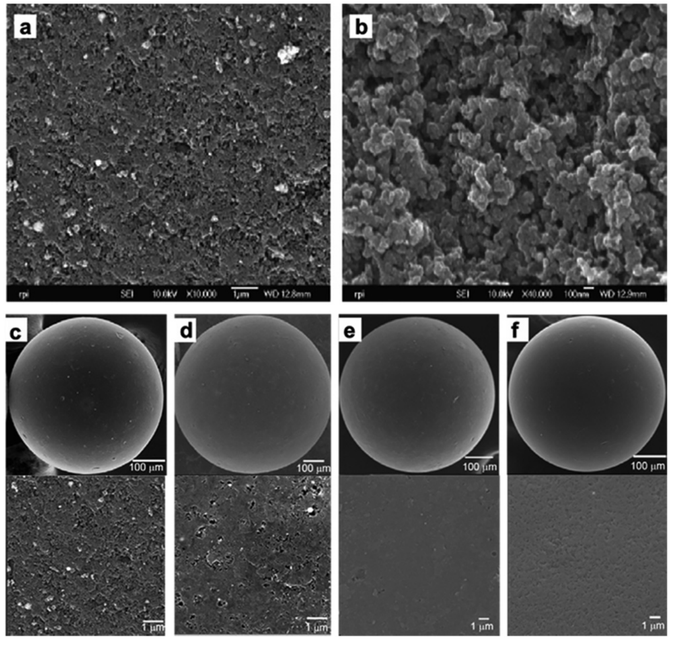
Adsorber bead

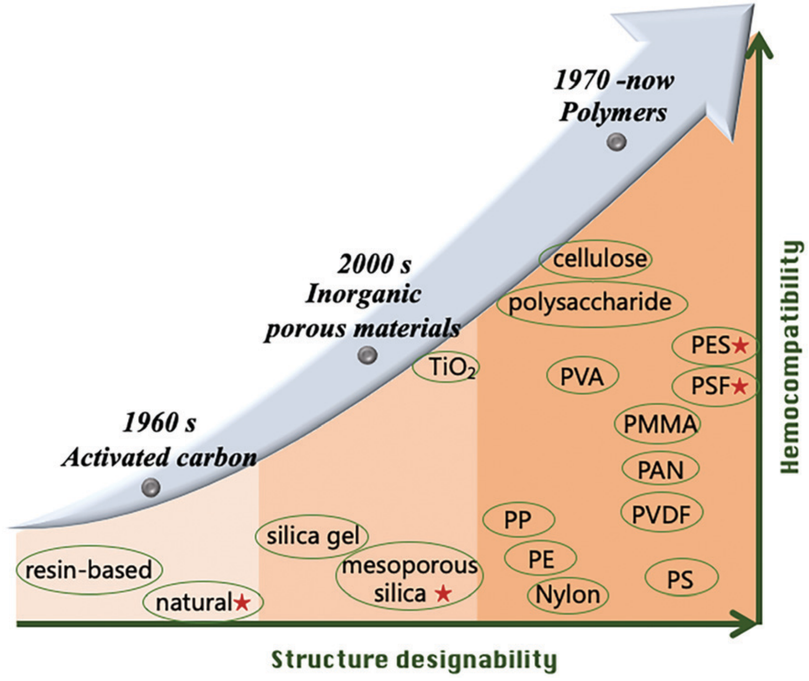
Internal structure

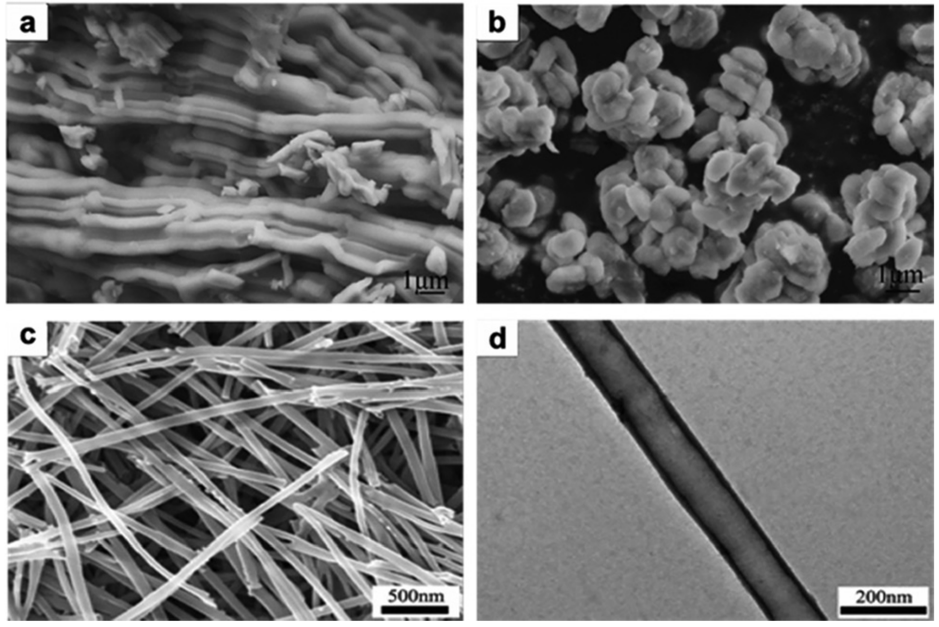

Inlet
Blood Port
Label
Sorbent Bed
Sealing ring
Closing cap
Outlet
Blood Port
Cap Nut
Net rack
End Cover
Case
Cap Nut


c
b
a
Anion exchange resin
Bilirubin
Polystyrene-divinylbenzene
Albumin
Albumin-bilirubin complex


a
b
c
d


a
b
c
d
e
f
100 μm
1 μm


1970 -now
Polymers
2000 s
Inorganic
porous materials
1960 s
Activated carbon
cellulose
polysaccharide
PES★
PSF★
TiO2
PVA
PMMA
PAN
PVDF
PP
PE
PS
Nylon
silica gel
mesoporous
silica ★
resin-based
natural★
Hemocompatibility
Structure designability


a
b
c
d
1μm
1μm
500nm
200nm

NARRATIVE REVIEW

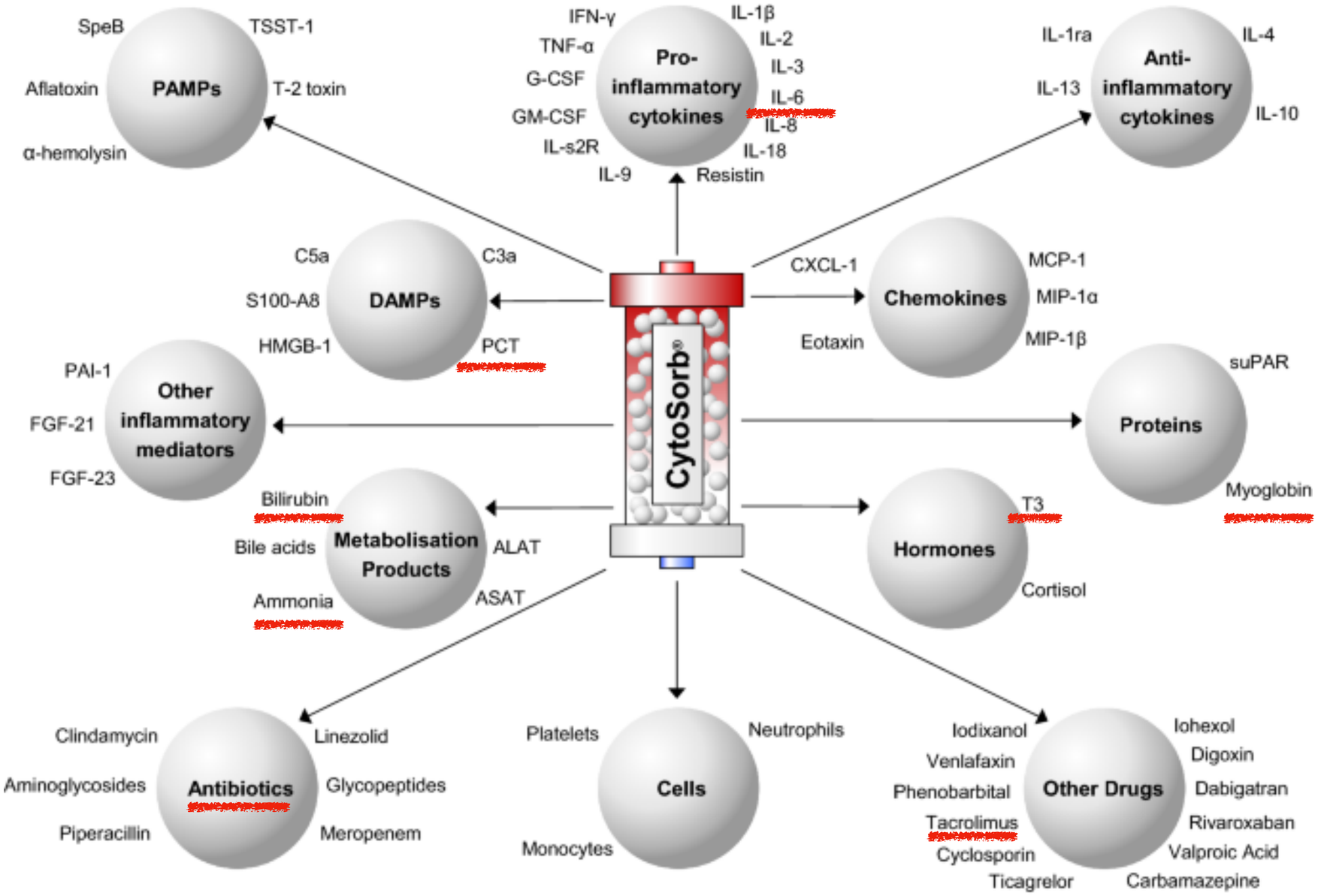
# Hemoperfusion in the intensive care unit

Zaccaria Ricci[1,2*], Stefano Romagnoli[2,3], Thiago Reis[4,5,6], Rinaldo Bellomo[7,8] and Claudio Ronco[9]

## Table 1 Currently available technologies

| Sorbent polymer | Commercial name (manufacturer) | Amount of sorbent | Coating |
|---|---|---|---|
| Norit charcoal | Adsorba (Gambro) | 100–300 g | Cellulose acetate |
| Polymyxin B | Toraymyxin (Estor) | – | – |
| Spherical charcoal | Hemosorba (Asahi) | 170 g | Polyhema |
| Polystyrene divinyl benzene | HA 130/230/330 (Jafron) | – | None |
| Polystyrene divinyl benzene | Cytosorb (Aferetica) | 300 g | None |
| Ultra-high molecular weight polyethylene beads with end-point-attached heparin | Seraph-100 (ExThera Medical) | – | – |

**— —> 100 a 300 g aktivního uhlí nebo mezi 300 a 650 g pryskyřice. Průtok krve pro účinné odstranění léčiva je přibližně 300 ml/min, až 450 ml/min a intermitentní hemoperfuze se obvykle provádí po dobu 4 hodin.**


SpeB
TSST-1
Aflatoxin
PAMPs
T-2 toxin
α-hemolysin
IFN-γ
IL-1β
TNF-α
IL-2
G-CSF
Pro-inflammatory cytokines
IL-3
GM-CSF
IL-6
IL-8
IL-s2R
IL-18
IL-9
Resistin
IL-1ra
IL-4
IL-13
Anti-inflammatory cytokines
IL-10
C5a
C3a
S100-A8
DAMPs
HMGB-1
PCT
CXCL-1
MCP-1
Chemokines
MIP-1α
Eotaxin
MIP-1β
PAI-1
Other inflammatory mediators
FGF-21
FGF-23
CytoSorb®
suPAR
Proteins
Myoglobin
Bilirubin
Bile acids
Metabolisation Products
ALAT
Ammonia
ASAT
T3
Hormones
Cortisol
Clindamycin
Linezolid
Aminoglycosides
Antibiotics
Glycopeptides
Piperacillin
Meropenem
Platelets
Neutrophils
Cells
Monocytes
Iodixanol
Iohexol
Venlafaxin
Digoxin
Phenobarbital
Other Drugs
Dabigatran
Tacrolimus
Rivaroxaban
Cyclosporin
Valproic Acid
Ticagrelor
Carbamazepine


# DPMAS

## double plasma molecular adsorption system

B|BRAUN
SHARING EXPERTISE

JaFron健帆

**Table 1.** The main characteristics of the HA adsorption cartridges

| | HA-130 | HA-230 | HA-330 |
|---|---|---|---|
| Indications | Chronic dialysis complications | Intoxication | Acute conditions with cytokines storm such as sepsis |
| Molecular weight removed | 5–30 kDa | 500 Da–10 kDa | 10–60 kDa |
| Resin pore size distribution | 500 Da–40 kDa | 200 Da–10 kDa | 500 Da–60 kDa |
| Toxins removed | Middle uremic toxins<br>Protein-bound uremic toxins | Hydrophobic or protein-bound exogenous substances | Cytokines, complements, free hemoglobin, etc |

kDa, kilodalton; Da, daltons.

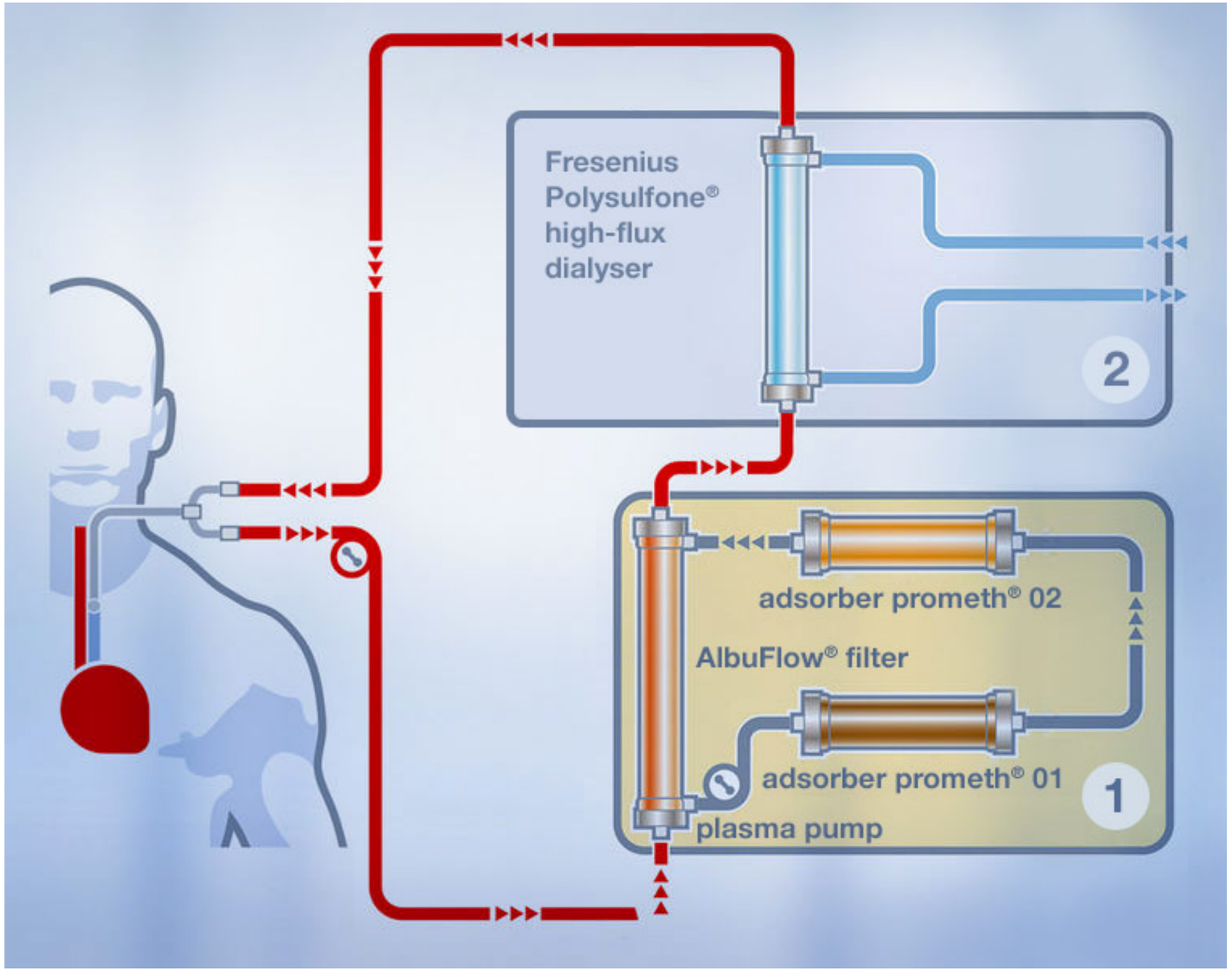

**A New Series of Sorbent Devices for Multiple Clinical Purposes: Current Evidence and Future Directions**

Ghada Ankawi[a, b] Weixuan Fan[a, c] Diego Pomarè Montin[a] Anna Lorenzin[a, d]
Mauro Neri[a, d] Carlotta Caprara[a, e] Massimo de Cal[d] Claudio Ronco[a, d]

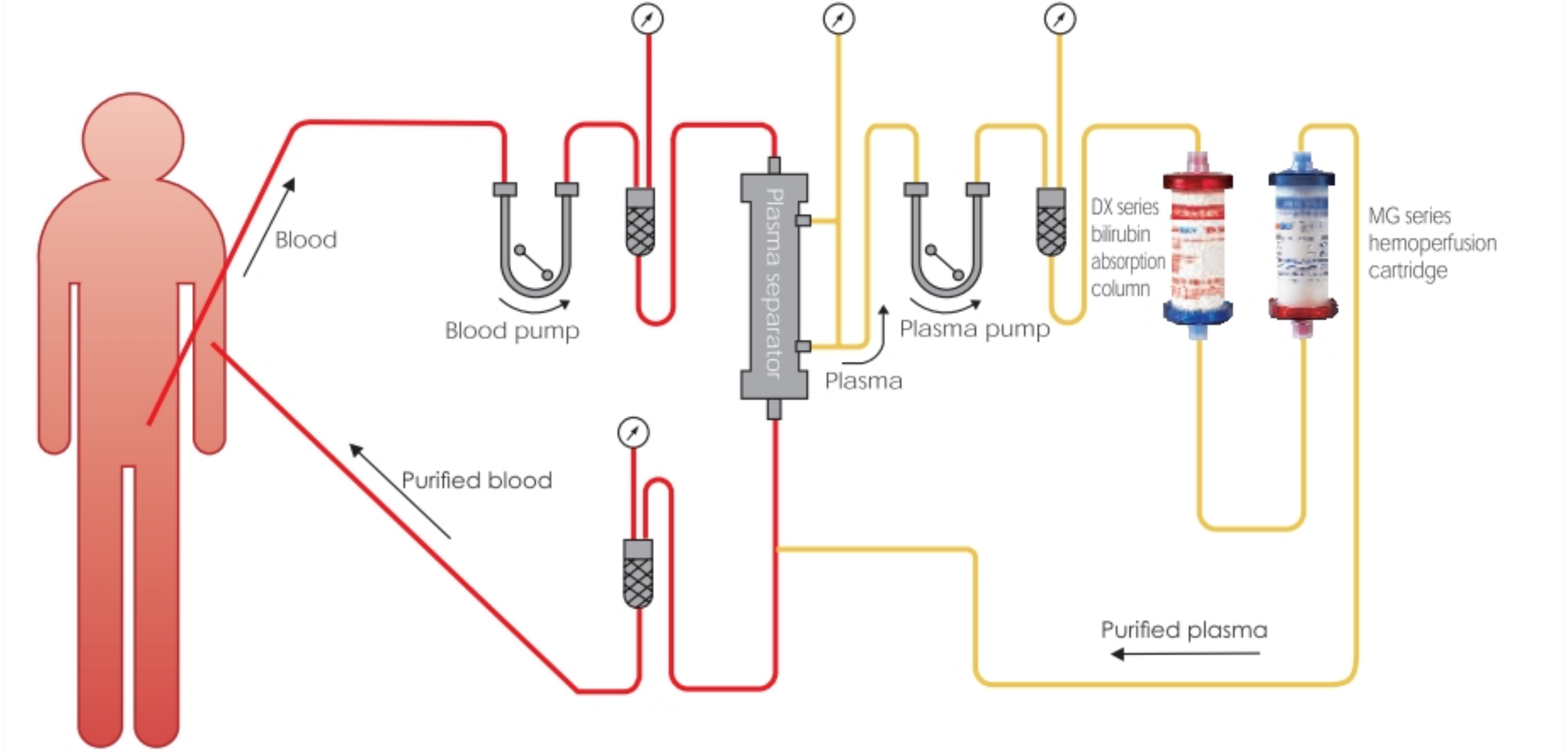
**Table 1.** Characteristics of the HA330 and HA380 Jafron cartridges

| Product parameter | HA330 |
|---|---|
| Sorbent volume (mL) | 330 ± 3 |
| Volume (mL) | 185 ± 5 |
| Absorbent material | Styrene-divinylbenzene copolymers |
| Housing material | Polycarbonate |
| Sterilization method | Irradiation sterilization |
| Packaging size | 290 mm (*L*) × 105 mm (*W*) × 105 mm (*H*) 0.90 kg |
| Product parameter | HA380 |
| Sorbent volume (mL) | 380 ± 3 |
| Volume (mL) | 145 ± 5 |
| Absorbent material | Styrene-divinylbenzene copolymers |
| Housing material | Polycarbonate |
| Sterilization method | Irradiation sterilization |
| Packaging size | 290 mm (*L*) × 105 mm (*W*) × 105 mm (*H*) 0.90 kg |

| Product Parameters | BS330 Disposable Plasma Bilirubin Adsorption Column | HA330-II Disposable Hemoperfusion Cartridge |
|---|---|---|
| Adsorbent Volume(mL) | 330 | 330 |
| Adsorbent Material | Polystyrene Divinylbenzene Anion Exchange Resin | Double Cross-linked Styrene-divinylbenzene Copolymers |
| Housing Material | Polypropylene | Polycarbonate |
| Sterilization Method | Moist Heat Sterilization | Irradiation Sterilization |
| Unit Package | 280mm(L)×105mm(W)×108mm(H) | 285±2mm(L)*117±2mm(W)*108±2mm(H) |

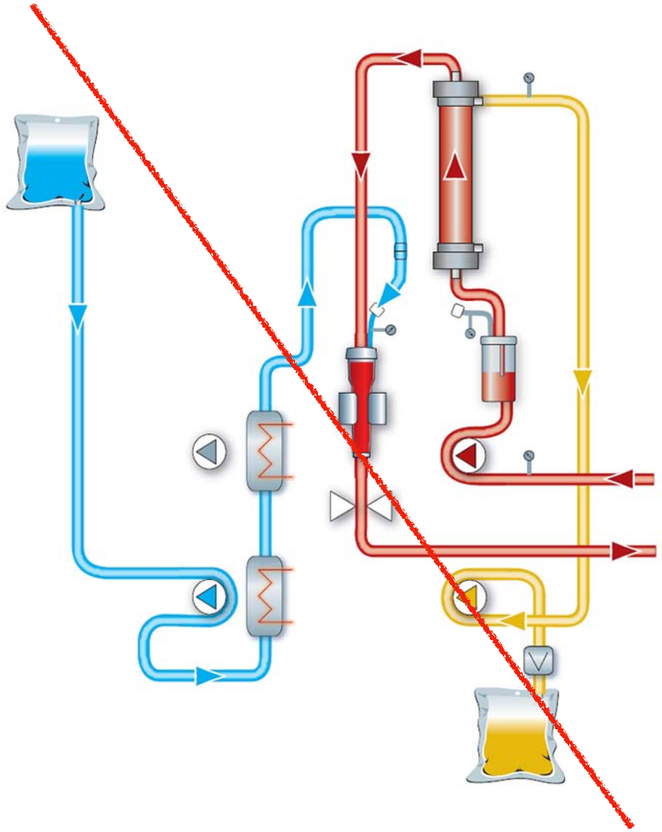




**Tohle už známe z FPSA**

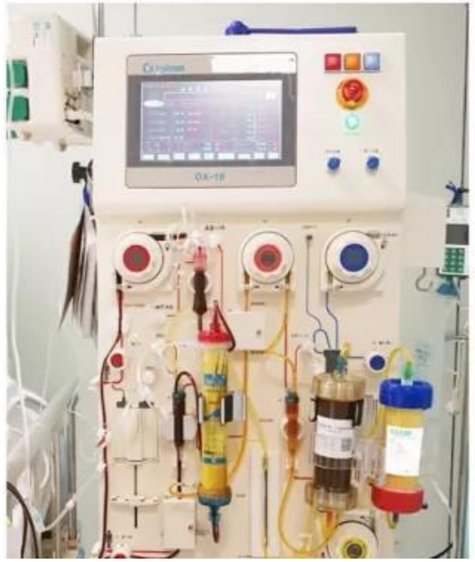



**Dálka terapie: 4-6 h**

# MPS - kit pro plazmaferézu? —-> ano, ale s CVVH nastavením

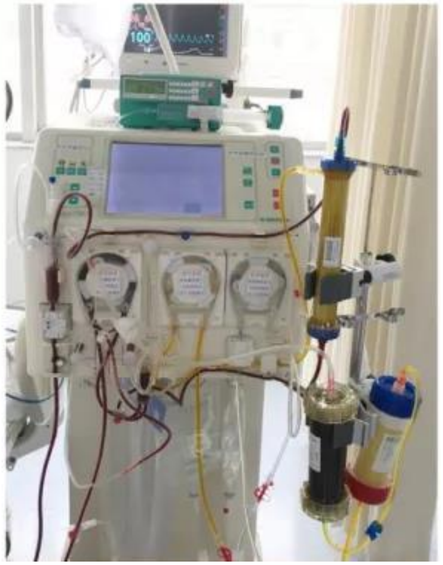


**DPMAS compatible with different machines**



DPMAS on Jafron (DX-10) machine

DPMAS on Fresenius Machine

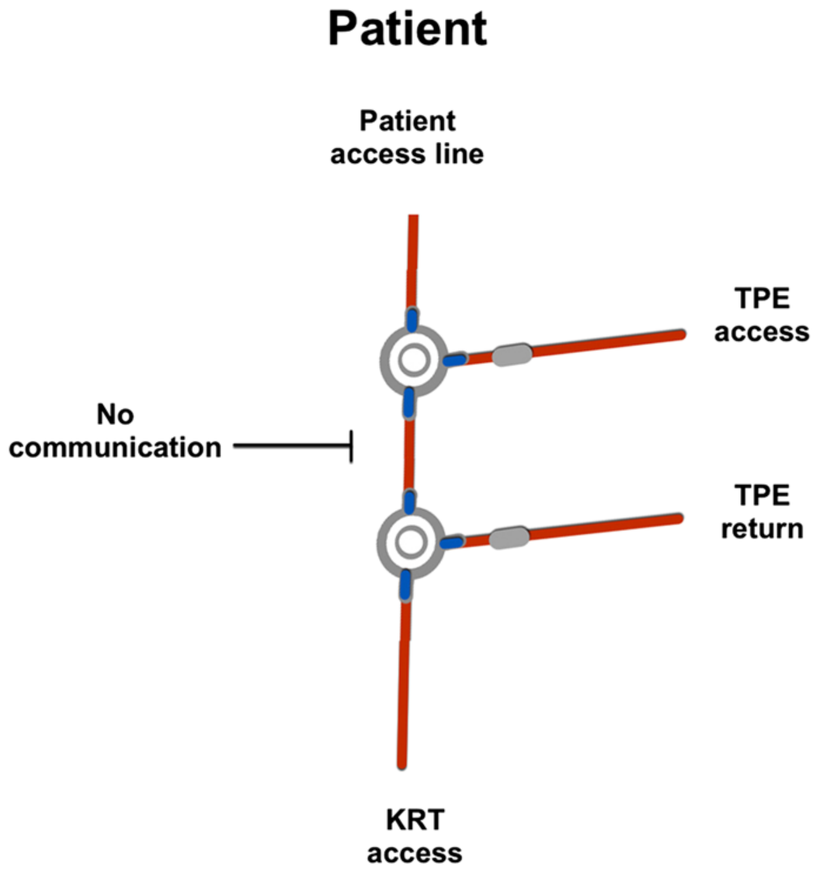


DPMAS on B. Braun Machine

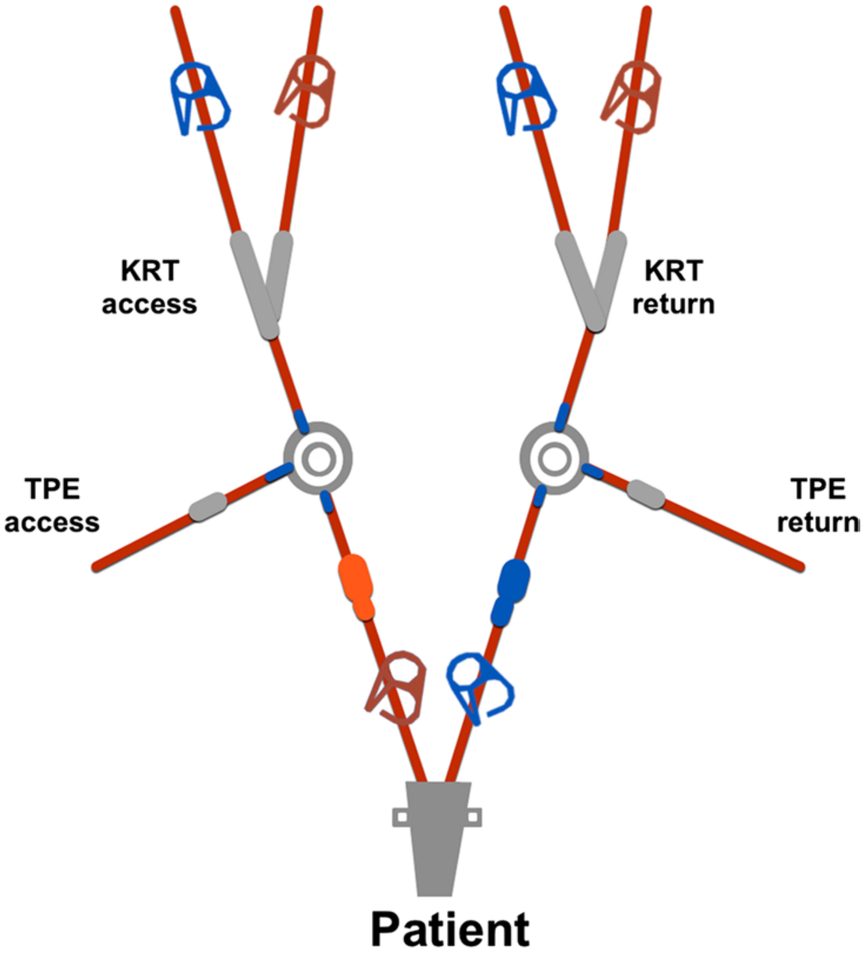

START RESET
STOP
ESC
10 L
Filtrate bag


BS330
A330-II

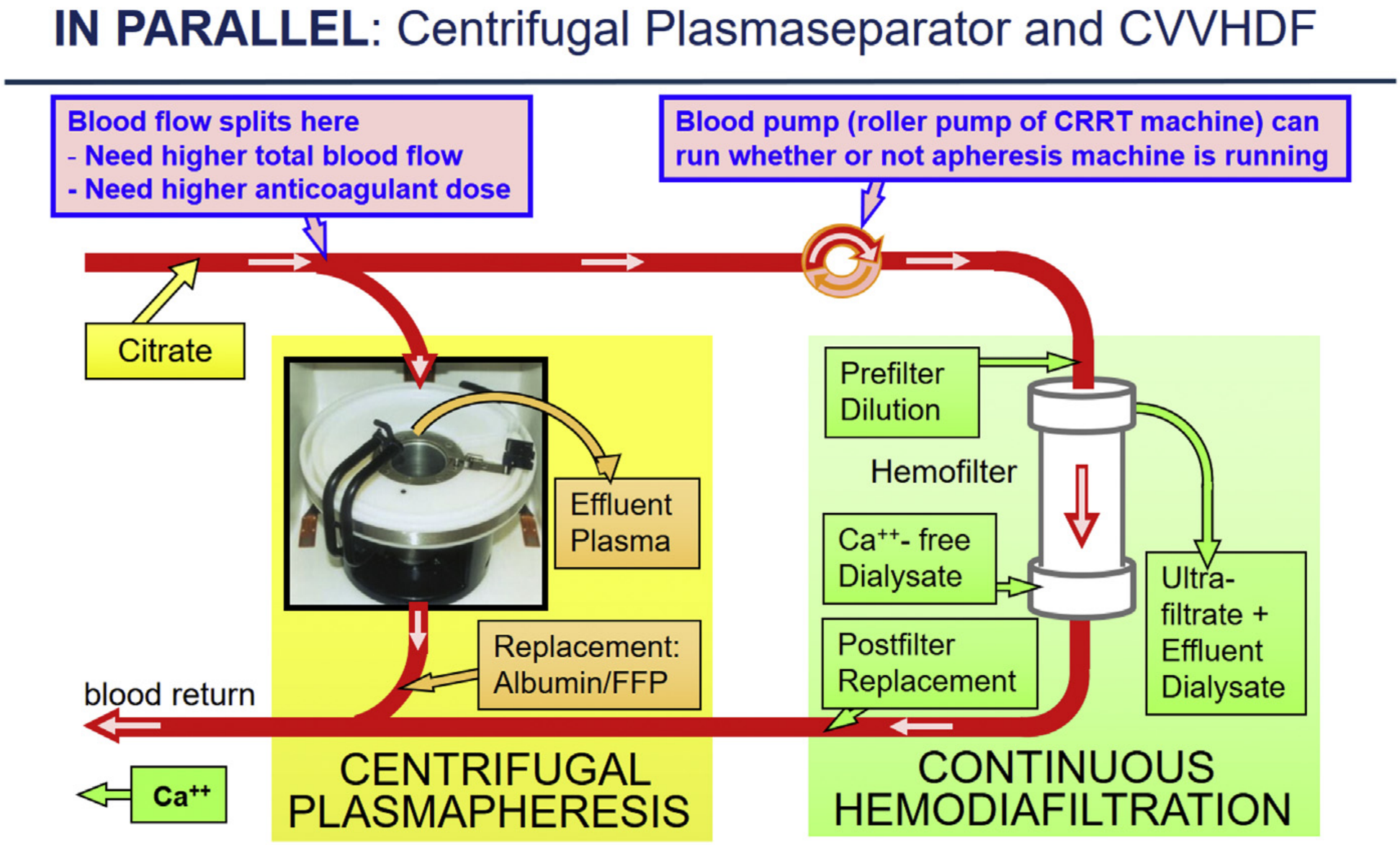
# Připojení

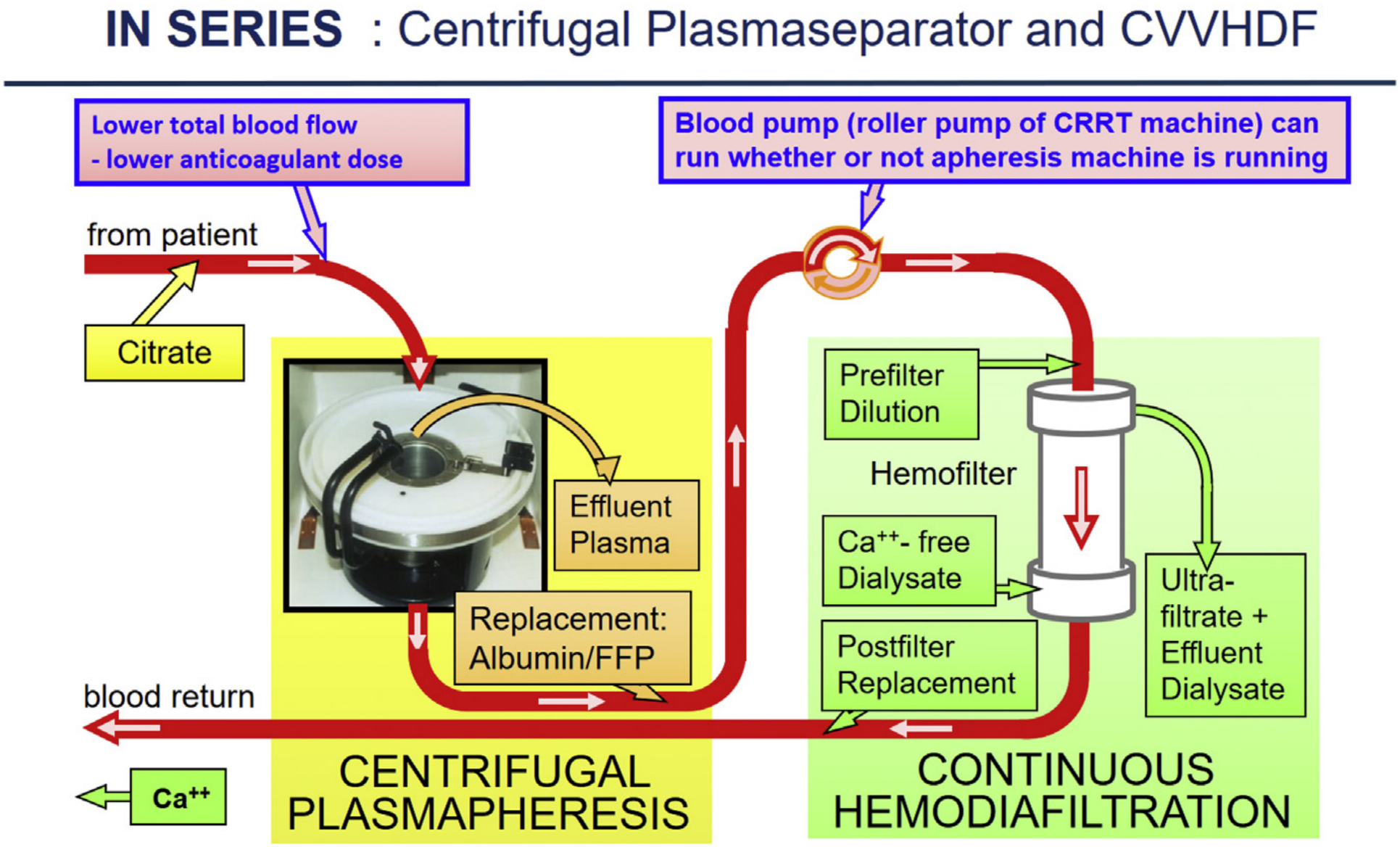



*In Series*




*Parallel*


IN PARALLEL: Centrifugal Plasmaseparator and CVVHDF
Blood flow splits here
- Need higher total blood flow
- Need higher anticoagulant dose
Blood pump (roller pump of CRRT machine) can run whether or not apheresis machine is running
Citrate
Effluent Plasma
Replacement: Albumin/FFP
blood return
Ca++
CENTRIFUGAL PLASMAPHERESIS
Prefilter Dilution
Hemofilter
Ca++- free Dialysate
Postfilter Replacement
Ultra-filtrate + Effluent Dialysate
CONTINUOUS HEMODIAFILTRATION


IN SERIES : Centrifugal Plasmaseparator and CVVHDF
Lower total blood flow
- lower anticoagulant dose
Blood pump (roller pump of CRRT machine) can run whether or not apheresis machine is running
from patient
Citrate
Effluent Plasma
Replacement: Albumin/FFP
blood return
Ca++
CENTRIFUGAL PLASMAPHERESIS
Prefilter Dilution
Hemofilter
Ca++- free Dialysate
Postfilter Replacement
Ultra-filtrate + Effluent Dialysate
CONTINUOUS HEMODIAFILTRATION


Arteriální tlak
-80 mmHg
Venózní tlak
98 mmHg
Předfiltrační tlak
142 mmHg
Průtok krve
150 ml/min
TMP
12 mmHg
Konec léčby za
0h 23min
B|BRAUN
PLAZMAFERÉZA
- svij ohnis


CVVHD
PLAZMAFERÉZA
CVVHD
PLAZMAFERÉZA

# TPE + DPMAS (HA)

Received: 19 November 2018 | Revised: 7 January 2019 | Accepted: 17 January 2019
DOI: 10.1002/jca.21690

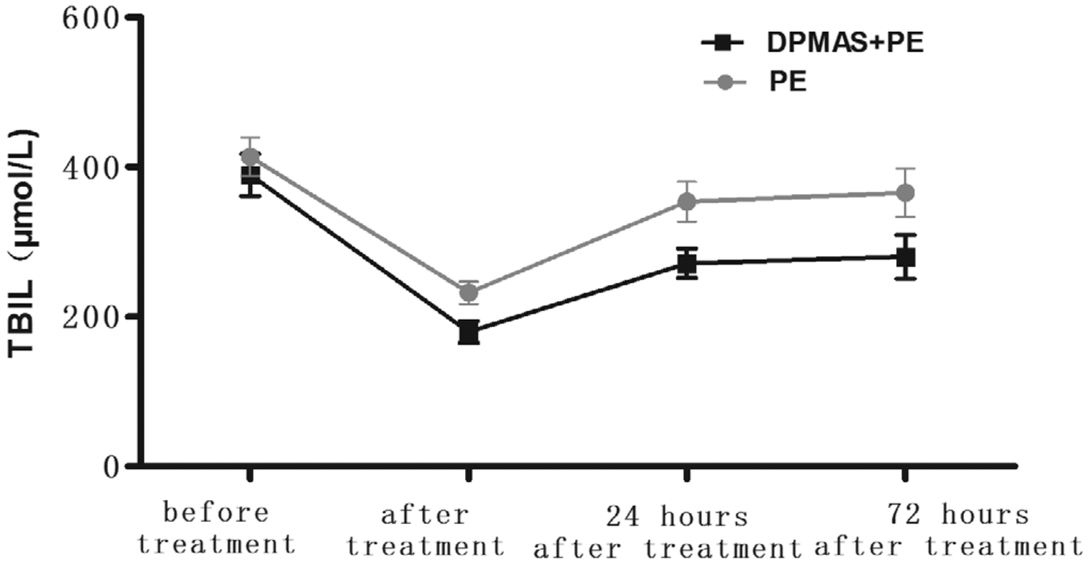
Journal of Clinical Apheresis ASFA WILEY

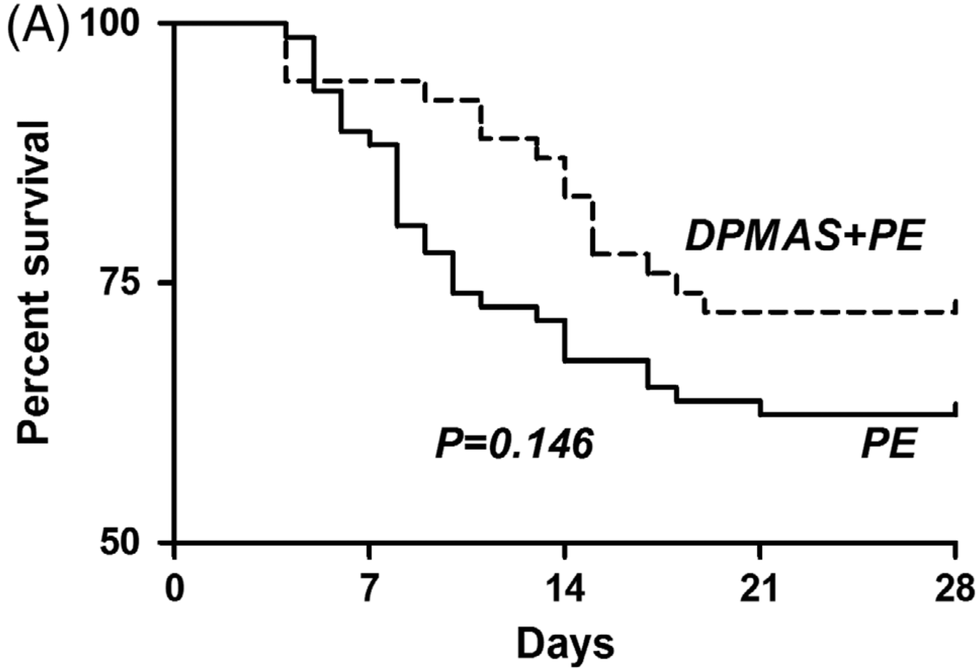
RESEARCH ARTICLE

# Therapeutic effect of double plasma molecular adsorption system and sequential half-dose plasma exchange in patients with HBV-related acute-on-chronic liver failure

Jia Yao[1] | Shuang Li[2,3] | Li Zhou[2,3] | Lei Luo[4] | Lili Yuan[1] | Zhongping Duan[2,3] | Jun Xu[1] | Yu Chen[2,3]

single treatment by DPMAS was approximately 5.5 to 6 L. The PE group was treated with PE alone, and the amount of fresh frozen plasma was 2200 to 2400 mL per treatment, and the time for a single treatment was about 2 hours. The DPMAS +PE group was treated with DPMAS first, followed by sequential PE treatment, with the fresh frozen plasma volume of 1100 to 1200 mL for each treatment, and the time for a single treatment was about 3 to 4 hours. According to the severity of the disease, each patient received 1 to 4 times of artificial liver support therapy.



Received: 1 November 2016 | Revised: 4 February 2017 | Accepted: 5 March 2017

DOI: 10.1002/jca.21535

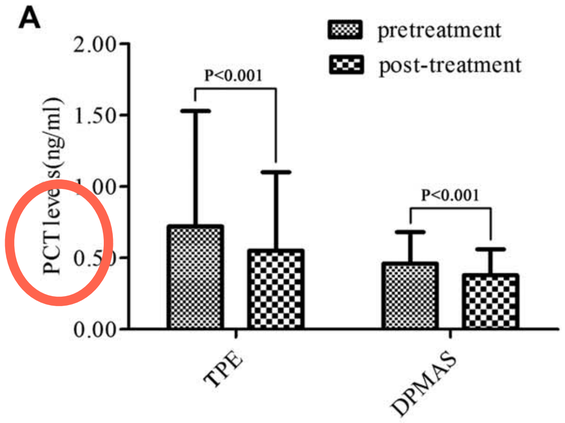
RESEARCH ARTICLE

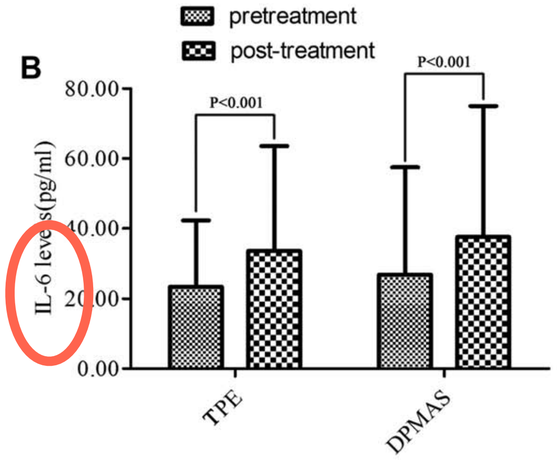
WILEY Journal of Clinical Apheresis ASFA

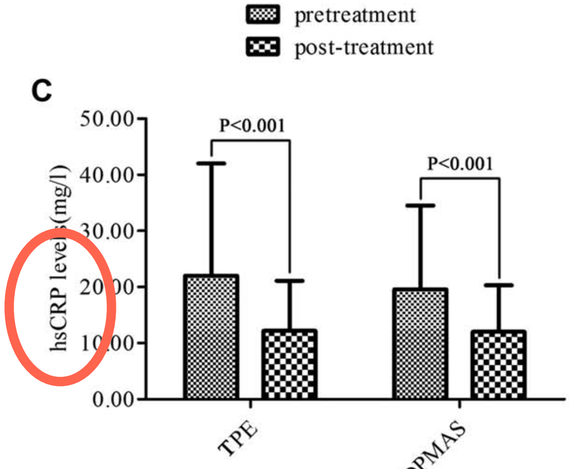
# Therapeutic plasma exchange versus double plasma molecular absorption system in hepatitis B virus-infected acute-on-chronic liver failure treated by entercavir: A prospective study

Yue-Meng Wan[1,2] | Yu-Hua Li[1] | Zhi-Yuan Xu[1] | Jing Yang[1] | Li-Hong Yang[1] | Ying Xu[1] | Jin-Hui Yang[1]

**Conclusion:** Compared to DPMAS, TPE was more efficient in eliminating TBIL, DBIL, and hsCRP, but it was associated with higher loss rate of albumin. TPE and DPMAS were similar in improving 12-week survivals in HBV-ACLF.



| | TPE ($n = 104$) | DPMAS ($n = 69$) | [a]$P$ value |
|---|---|---|---|
| Albumin(35-50 g/l) | | | |
| pretreatment | 28.2 ± 3.5 | 28.9 ± 3.8 | .161 |
| post-treatment | 19.8 ± 3.4 | 24.3 ± 2.9 | .000 |
| ALT(5-40 U/l) | | | |
| pretreatment | 94.9 ± 109.3 | 138.3 ± 134.0 | .027 |
| post-treatment | 67.2 ± 75.7 | 104.2 ± 98.1 | .009 |
| AST(8-40 U/l) | | | |
| pretreatment | 119.6 ± 154.4 | 152.3 ± 128.4 | .147 |
| post-treatment | 79.0 ± 84.5 | 118.5 ± 95.0 | .006 |
| TBA(0-10.0 μmol/l) | | | |
| pretreatment | 209.5 ± 76.9 | 268.5 ± 113.9 | .000 |
| post-treatment | 160.0 ± 64.1 | 214.9 ± 96.5 | .000 |
| TBIL(3.4-17.1 μmol/l) | | | |
| pretreatment | 271.9 ± 93.2 | 291.9 ± 81.8 | .150 |
| post-treatment | 160.5 ± 64.8 | 184.5 ± 56.0 | .015 |
| DBIL(0-5.1 μmol/l) | | | |
| pretreatment | 222.6 ± 74.2 | 255.5 ± 72.9 | .004 |
| post-treatment | 130.2 ± 55.7 | 160.5 ± 52.4 | .000 |

# Therapeutic plasma exchange versus double plasma molecular absorption system in hepatitis B virus-infected acute-on-chronic liver failure treated by entercavir: A prospective study

Yue-Meng Wan[1,2] | Yu-Hua Li[1] | Zhi-Yuan Xu[1] | Jing Yang[1] | Li-Hong Yang[1] | Ying Xu[1] | Jin-Hui Yang[1]

**Background:** Therapeutic plasma exchange (TPE) and double plasma molecular absorption system (DPMAS) were two extracorporeal liver support systems. Few studies compared their efficacy profile.

**Objective:** This study was to compare the efficacy of TPE and DPMAS on acute-on-chronic liver failure (ACLF) caused by hepatitis B virus (HBV-ACLF).

**Methods:** 60 HBV-ACLF patients were enrolled and prospectively studied. All patients received entecavir therapy, and were assigned to TPE group ($n = 33$) and DPMAS group ($n = 27$). Primary end-points were the effects of TPE and DPMAS on liver function and serum inflammatory markers.

**Results:** Serum procalcitonin, interleukin (IL)−6, and high sensitive C-reactive protein (hsCRP) were significantly elevated in patients with HBV-ACLF. TPE achieved significantly higher removal rates of total bilirubin (TBIL, $P = .002$), direct bilirubin (DBIL, $P = .006$), and hsCRP ($P = .010$) than DPMAS, but DPMAS displayed lower loss rate of albumin ($P = .000$). TPE and DPMAS resulted in similarly increased serum IL-6 levels and comparable 12-week survivals ($P > .05$). Multivariate analysis showed that hospital stay (Relative Risk [RR]: 1.062, 95% Confidence Interval [CI]: 1.011-1.115, $P = .016$), prothrombin time (RR: 1.346, 95% CI: 1.077-1.726, $P = .010$), and international normalized ratio (RR: 0.013, 95% CI: 0.006-0.788, $P = .041$) were independent predictors for 12-week survival. Both TPE and DPMAS treatments were well-tolerated.

**Conclusion:** Compared to DPMAS, TPE was more efficient in eliminating TBIL, DBIL, and hsCRP, but it was associated with higher loss rate of albumin. TPE and DPMAS were similar in improving 12-week survivals in HBV-ACLF.

*Research Article*

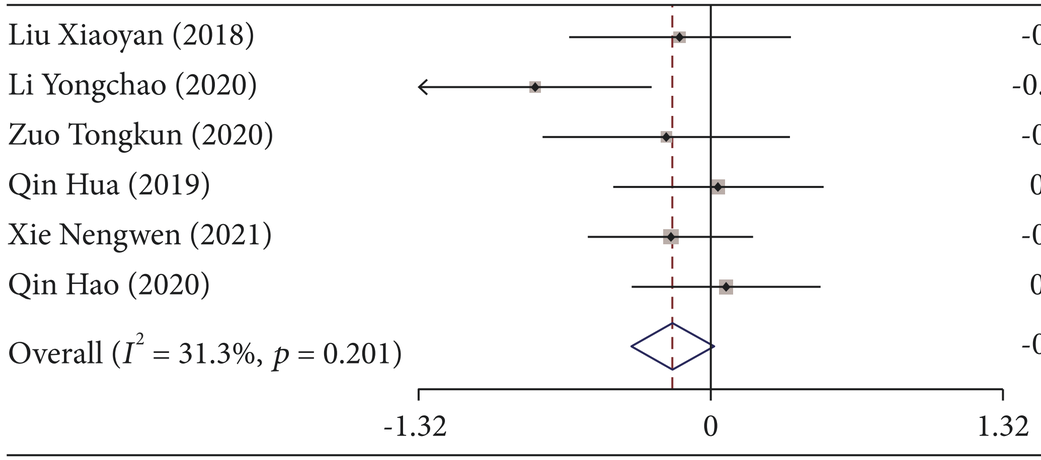
# The Clinical Efficacy of Double Plasma Molecular Absorption System Combined with Plasma Exchange in the Treatment of Acute-on-Chronic Liver Failure: A Systematic Review and Meta-Analysis

**Wenjie Bai,[1] Chun Yao,[1] Dewen Mao,[2] Jinyu Wu,[2] Kejing Wang,[3] Huazhu Wei,[1] Zuhong Huang,[1] Qinglan Shi,[2] and Na Wang[2]**

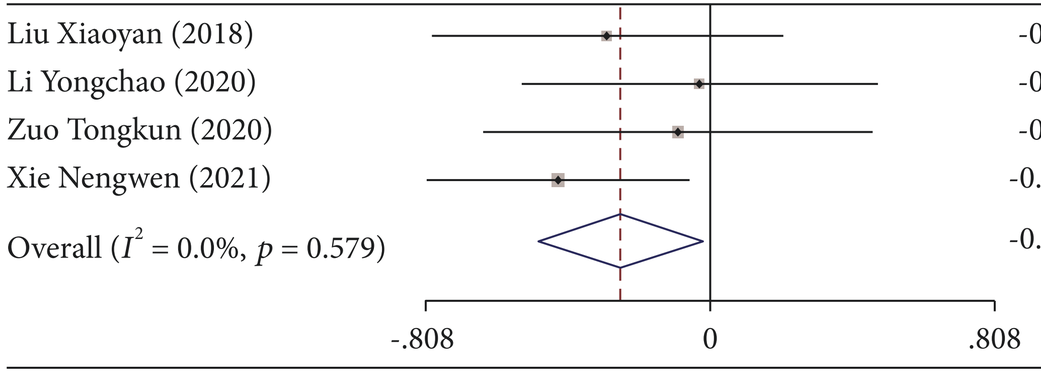
[1]*Guangxi University of Chinese Medicine, Nanning 530200, China*
[2]*The First Affiliated Hospital of Guangxi University of Chinese Medicine, Nanning 530023, China*
[3]*Ruikang Hospital Affiliated to Guangxi University of Chinese Medicine, Nanning 530200, China*

Correspondence should be addressed to Qinglan Shi; bshiqinglan@163.com and Na Wang; wangna0607mm@163.com

Received 16 December 2021; Accepted 17 February 2022; Published 25 March 2022




(b)




(c)

# DPMAS (jak dlouho?)


# Extracorporeal adsorption of protective and toxic bile acids and bilirubin in patients with cholestatic liver dysfunction: a prospective study

Antonia Greimel[1†], Katharina Habler[2†], Caroline Gräfe[1], Nils Maciuga[1], Clara Isabell Brozat[1], Michael Vogeser[2], Michael Zoller[1], Felix L. Happich[2], Uwe Liebchen[1], Sandra Frank[1], Michael Paal[2] and Christina Scharf[1*]

Greimel *et al. Annals of Intensive Care* (2023) 13:110
https://doi.org/10.1186/s13613-023-01198-7

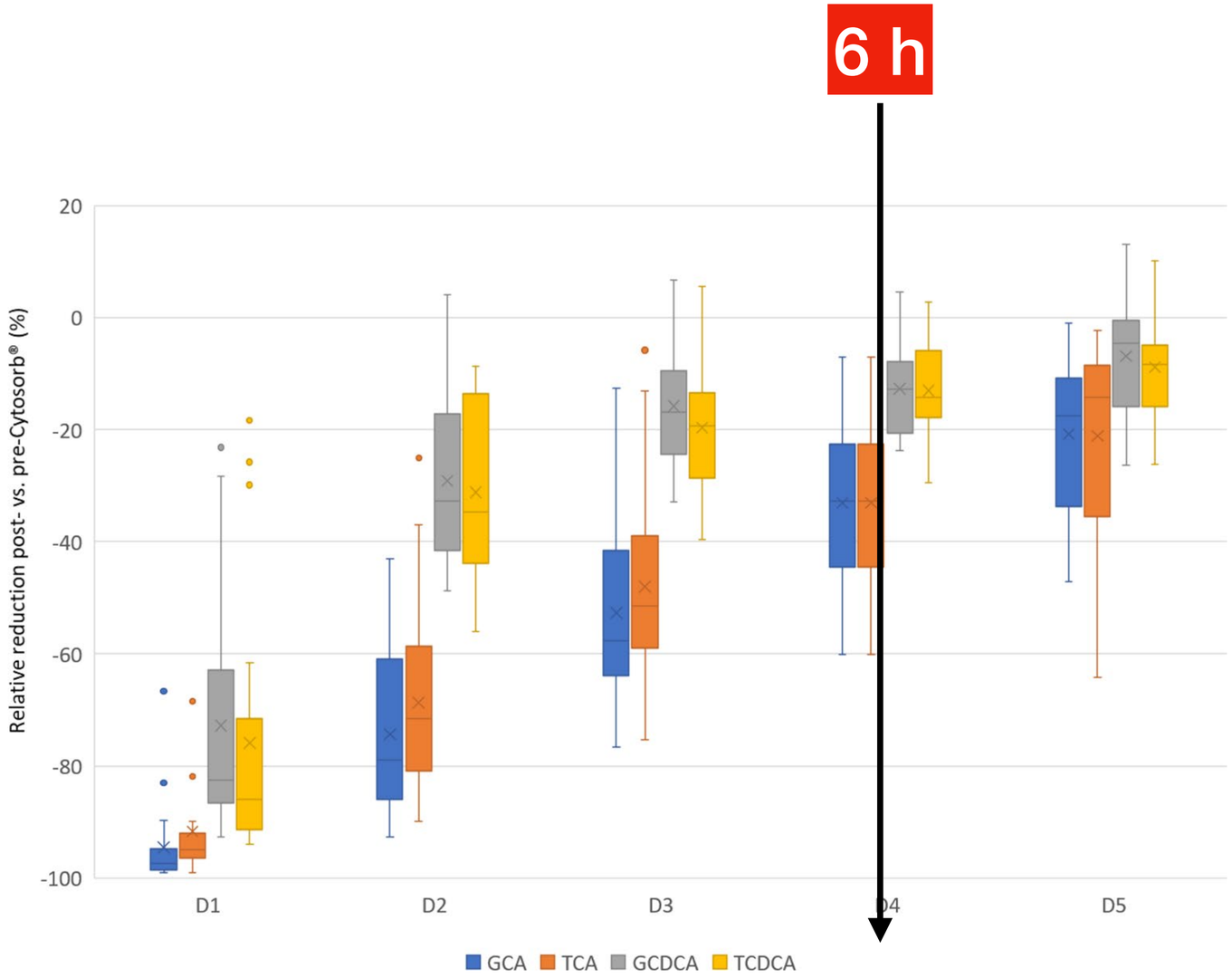



**Fig. 1** Relative reduction (%) of toxic bile acids with Cytosorb®. D1: 10 min after initiation of Cytosorb®, D2: 1 h after initiation of Cytosorb®, D3: 3 h after initiation of Cytosorb®, D4: 6 h after initiation of Cytosorb®, D5: 12 h after initiation of Cytosorb®, blue boxplots represent the relative reduction of GCA, orange ones of TCA, grey ones of GCDCA, and yellow ones of TCDCA. The boxes of the boxplots represent the interquartile range (IQR) and the line the median. Whiskers were limited to 1.5 times the IQR. The cross represents the mean

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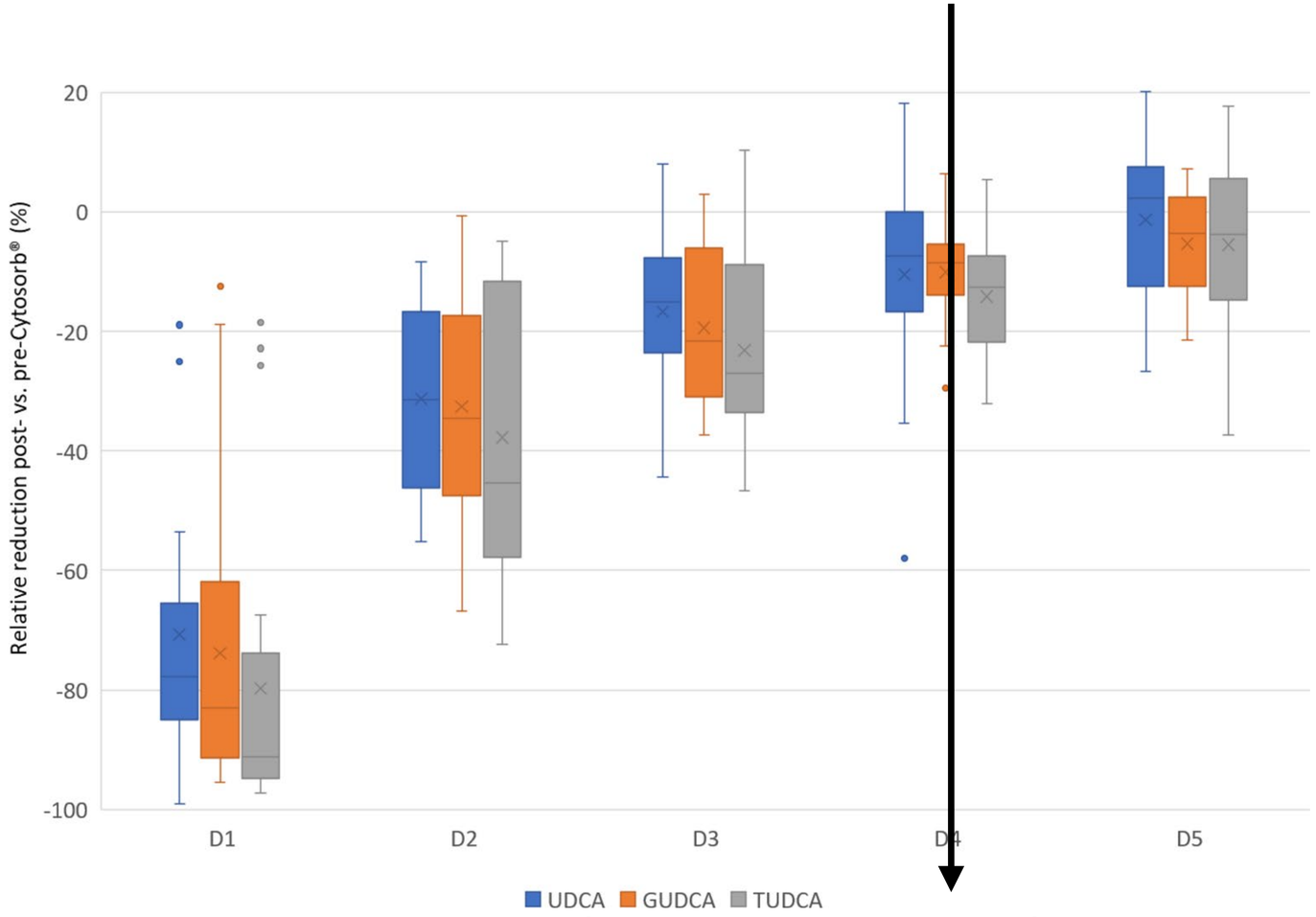



**Fig. 2** Relative reduction (%) of protective bile acids with Cytosorb®. D1: 10 min after initiation of Cytosorb®, D2: 1 h after initiation of Cytosorb®, D3: 3 h after initiation of Cytosorb®, D4: 6 h after initiation of Cytosorb®, D5: 12 h after initiation of Cytosorb®, blue boxplots represent the relative reduction of UDCA, orange ones of GUDCA, and grey ones of TUDCA. The boxes of the boxplots represent the interquartile range (IQR) and the line the median. Whiskers were limited to 1.5 times the IQR. The cross represents the mean

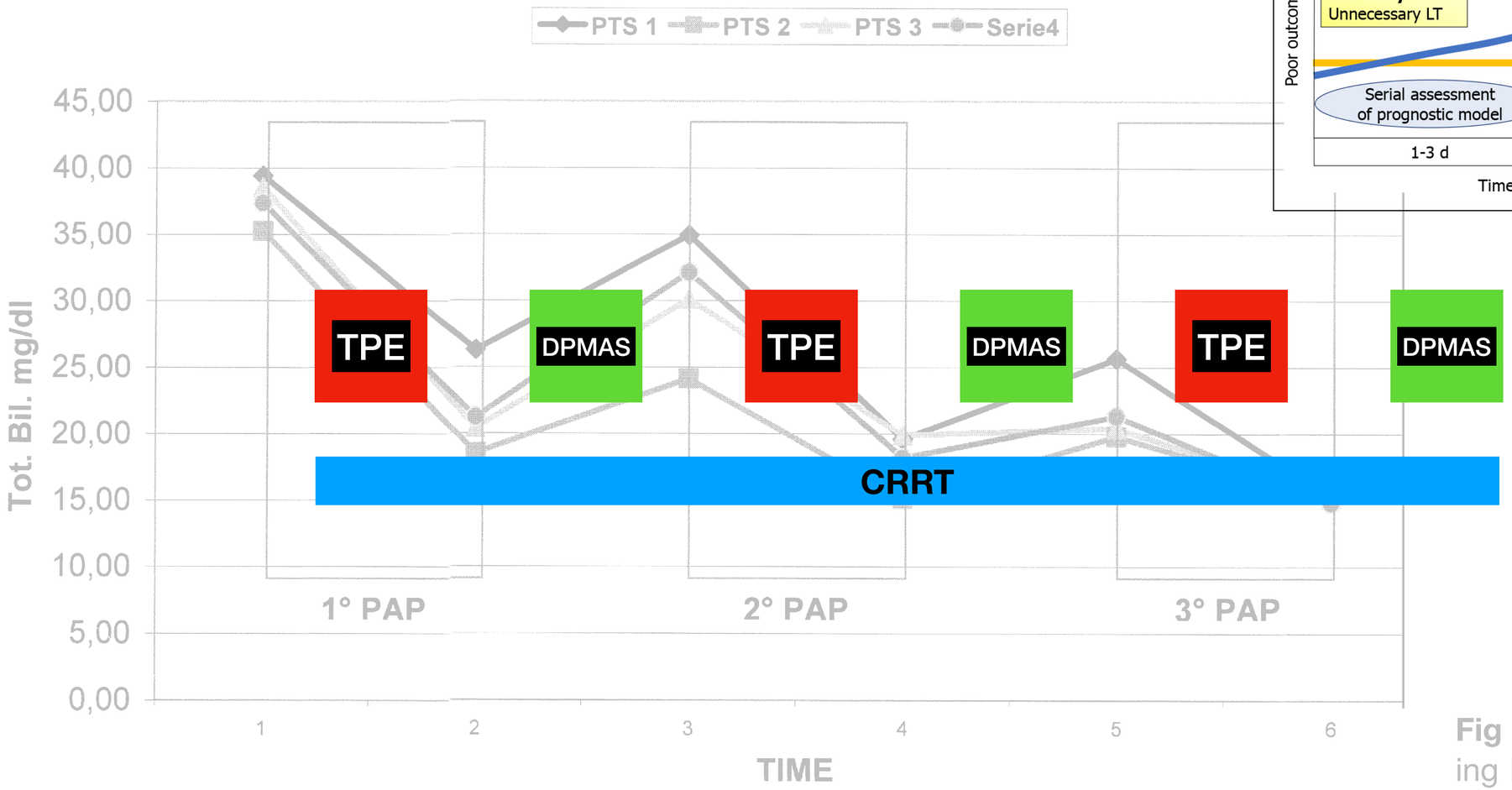
# Závěr:

indikace: ALF/ACLF

TPE + DPMAS + CRRT(HD)

- LV-TPE (výpočet, 1,5-3L)
- DPMAS (6h)
- ~~iHD~~xCRRT - CVVHD (EMIC)

SELECTIVE BILIRUBIN REMOVAL



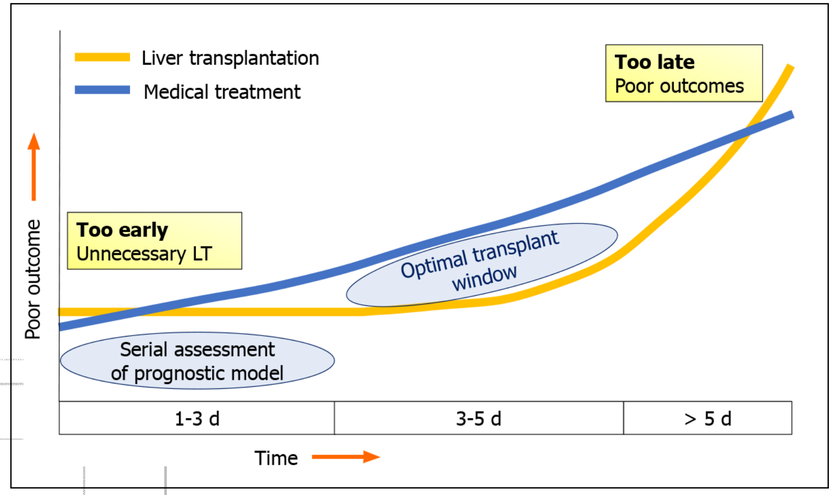




**Fig 1.** Total bilirubin level during PAP with Plasorba BR-350.



**Děkuji za pozornost**

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