4η Ετήσια Επιστημονική Εκδήλωση
Νεφρολογικού Τμήματος Γ.Ν "Παπαγεωργίου»

Περί θεραπευτικής αφαίρεσης

Αιμοπροσρόφηση :
Στις παθήσεις του ήπατος και τις δηλητηριάσεις

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In accordance with the “Consensous Conference on Biocompatibility”, absorptsion (and thus HP) is a method for removal of molecules from blood

Poison: A xenobiotic (exogenous chemical, including medication) or an endogenously found chemical (e.g., iron, copper, vitamins) resulting from exogenous exposure with the potential to cause toxicity

e

xtracorporeal

stances that absorb on

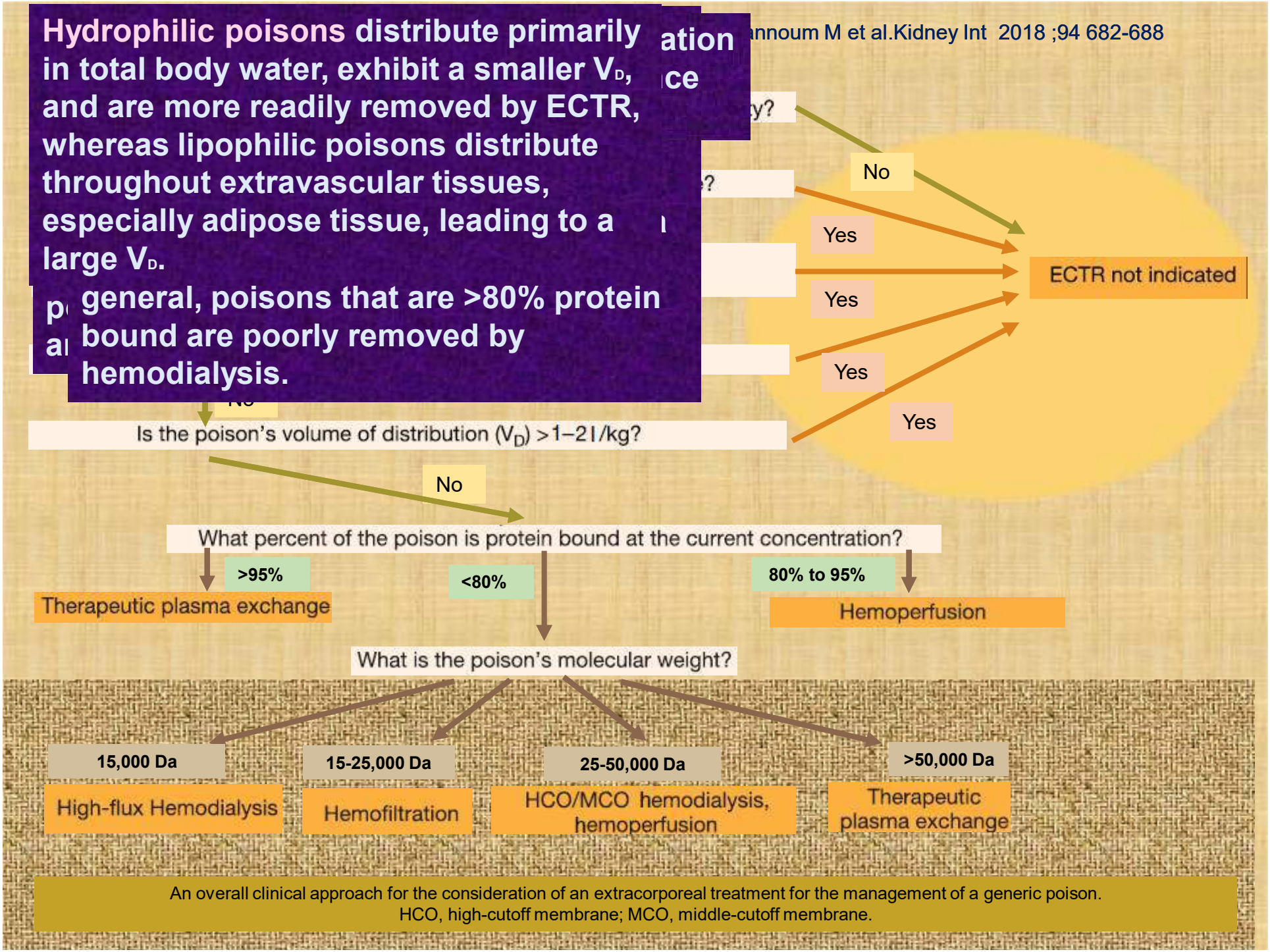
ts present in a fluid

sical and chemical

Poisoning: Exposure to a poison causing or capable of caus ing toxicity, regardless of intent. It includes intoxication, toxicity, and overdose.
Adverse outcome: Significant clinical effect following poisoning. An adverse outcome can be critical (death or major end-organ damage, such as blindness in methanol poisoning) or non-critical (minor end-organ damage, such as tremors in lithium poisoning).
Severe poisoning: Exposure to a poison causing or having the potential to cause an adverse outcome.

Hydrophilic poisons distribute primarily in total body water, exhibit a smaller V_D, and are more readily removed by ECTR, whereas lipophilic poisons distribute throughout extravascular tissues, especially adipose tissue, leading to a large V_D.

general, poisons that are >80% protein bound are poorly removed by hemodialysis.



An overall clinical approach for the consideration of an extracorporeal treatment for the management of a generic poison.
HCO, high-cutoff membrane; MCO, middle-cutoff membrane.

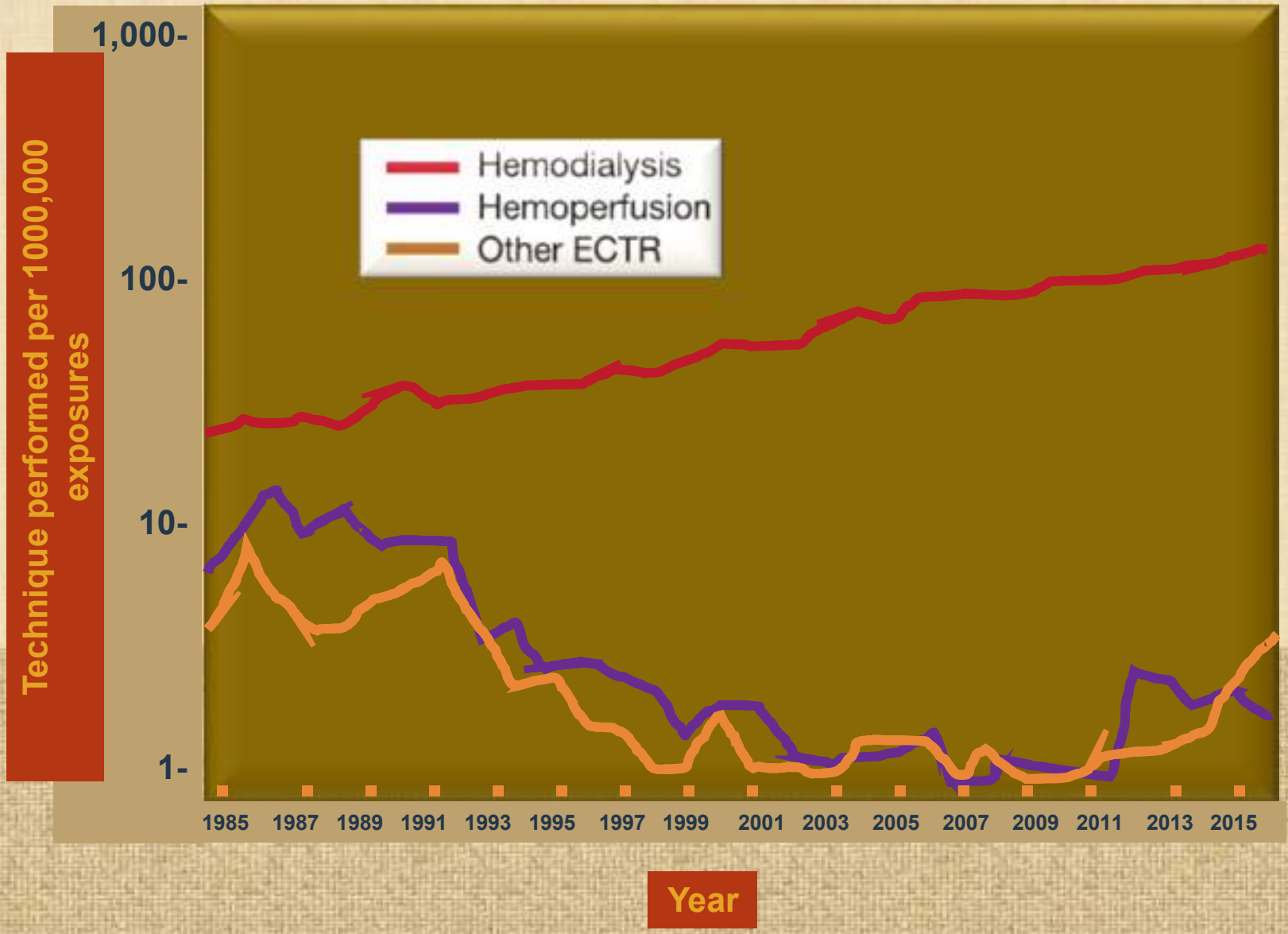
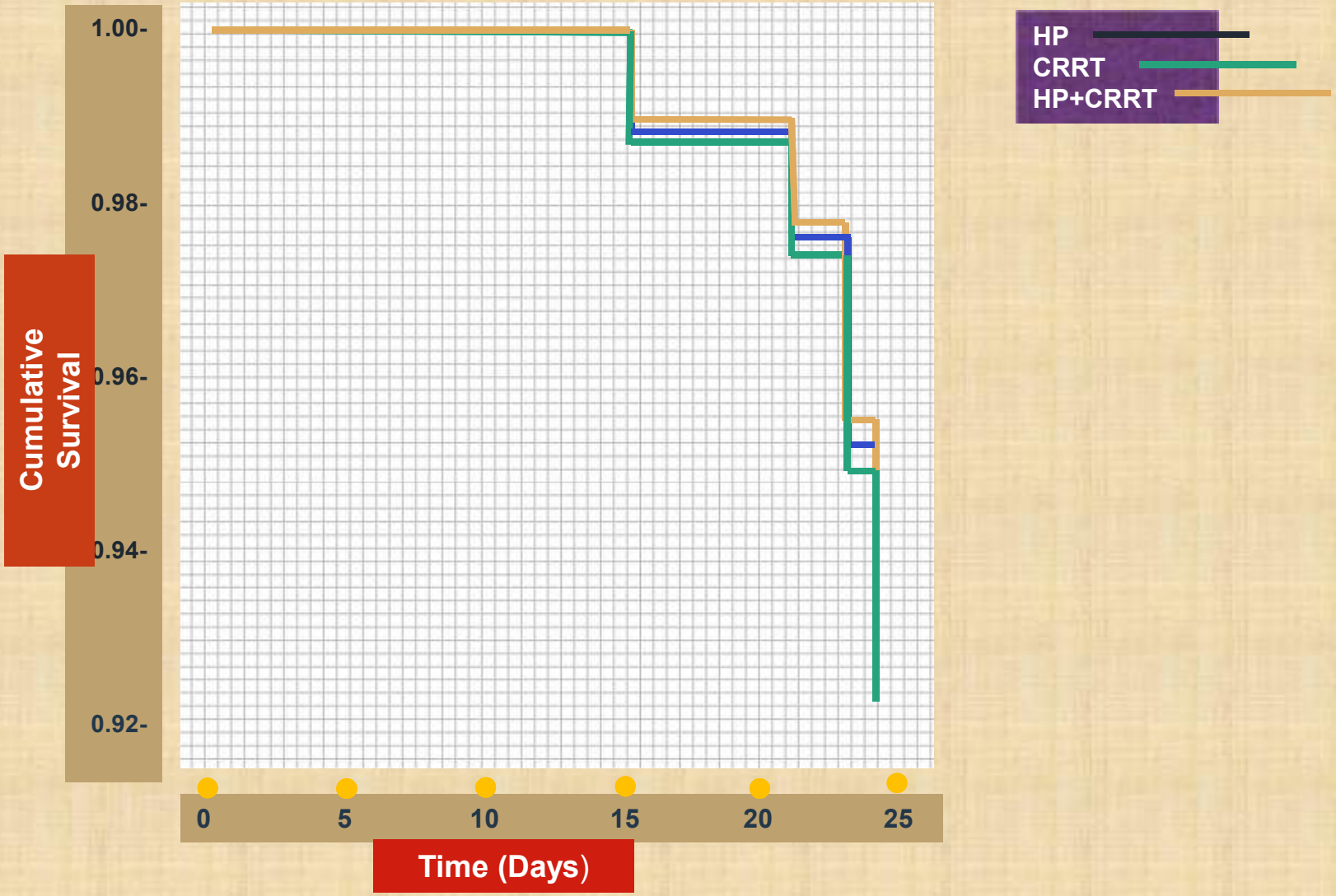


Figure 2 | US poison center trends in the use of hemodialysis, hemoperfusion, and other extracorporeal treatments.

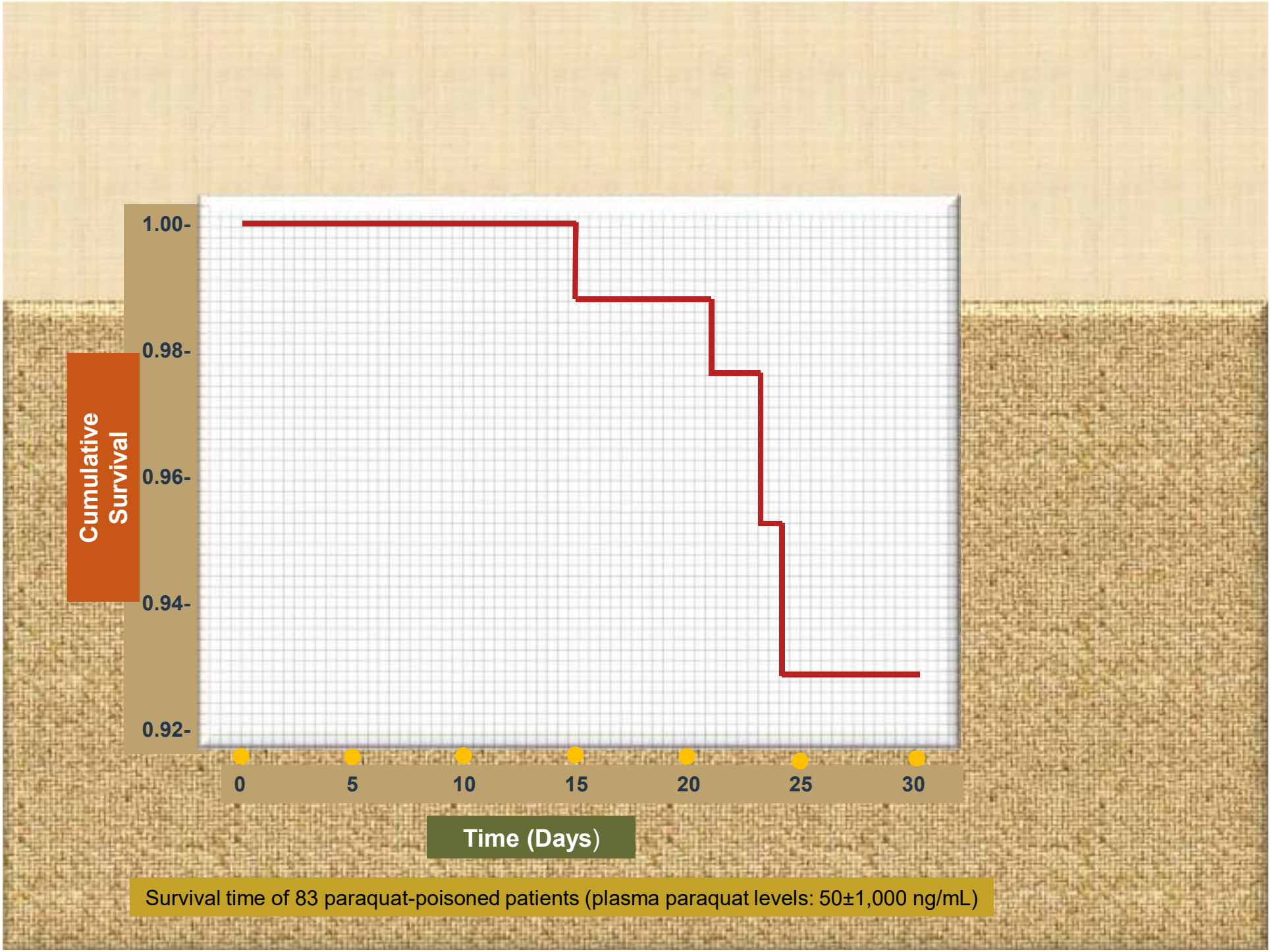
Effects of hemoperfusion and continuous renal replacement therapy on patient survival following paraquat poisoning. Wang Y et al. PLOS July 13,2017

Fatality times and rates of paraquat-poisoned patients with low plasma paraquat levels (50±1,000 ng/mL, n = 83)

Treatment group	Death (<10 d)		Death (10±30 d)		Total Death	
	N	Fatality (%)	N	Fatality (%)	N	Fatality (%)
HP	0	0	2	7.1	2	7.1
CRRT	0	0	2	7.7	2	7.7
HP+CRRT	0	0	2	6.9	2	6.9



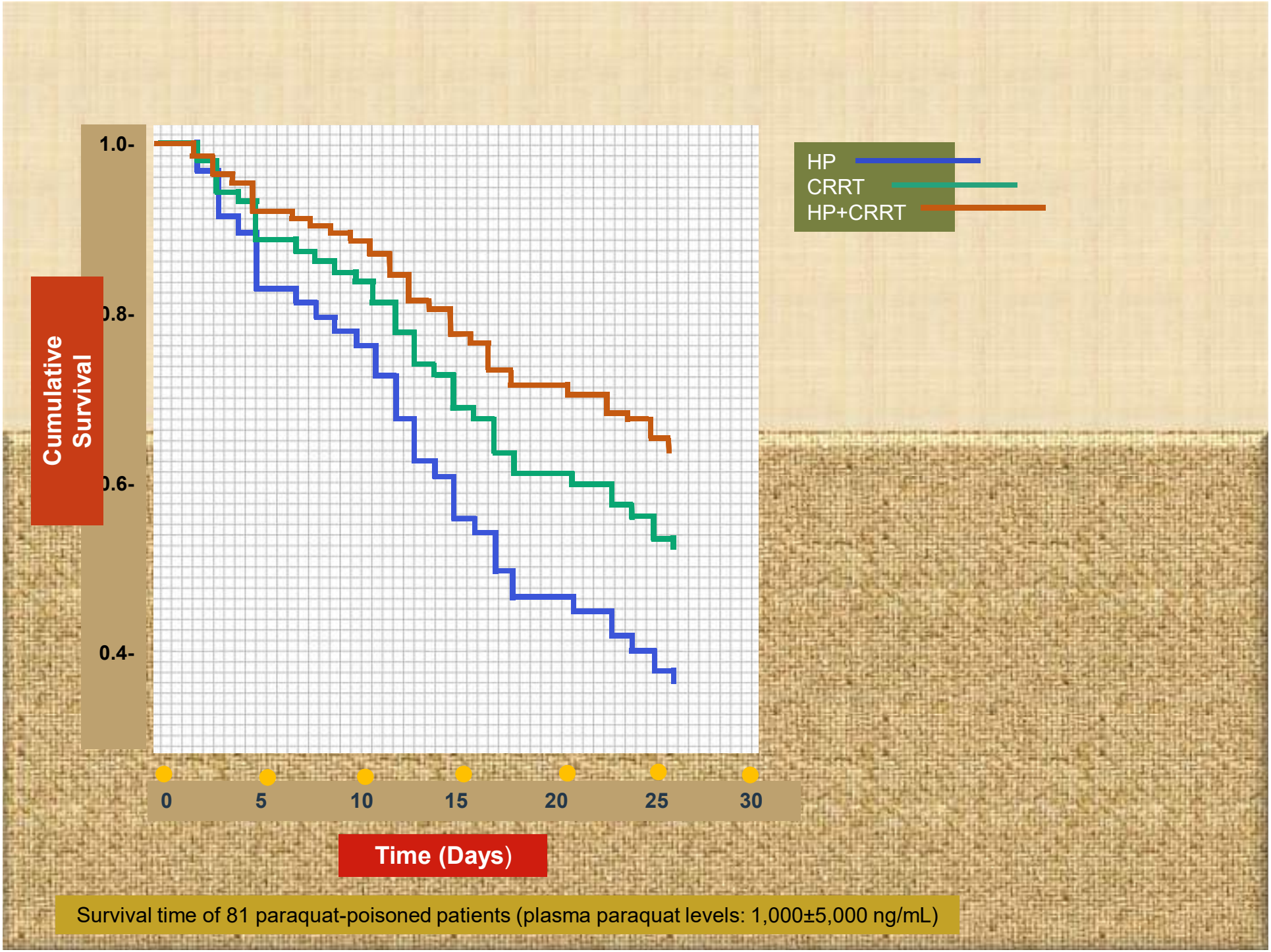
Comparison of survival curves for three treatments. Hemoperfusion (HP), continuous renal replacement therapy (CRRT), and combined treatment (HP+CRRT) in patients with plasma paraquat levels between 50 and 1,000 ng/mL. The chi-squared value between HP and CRRT was 1.056; $p>0.05$. The chisquared value between HP and HP+CRRT was 1.136; $p>0.05$.



Survival time of 83 paraquat-poisoned patients (plasma paraquat levels: 50±1,000 ng/mL)

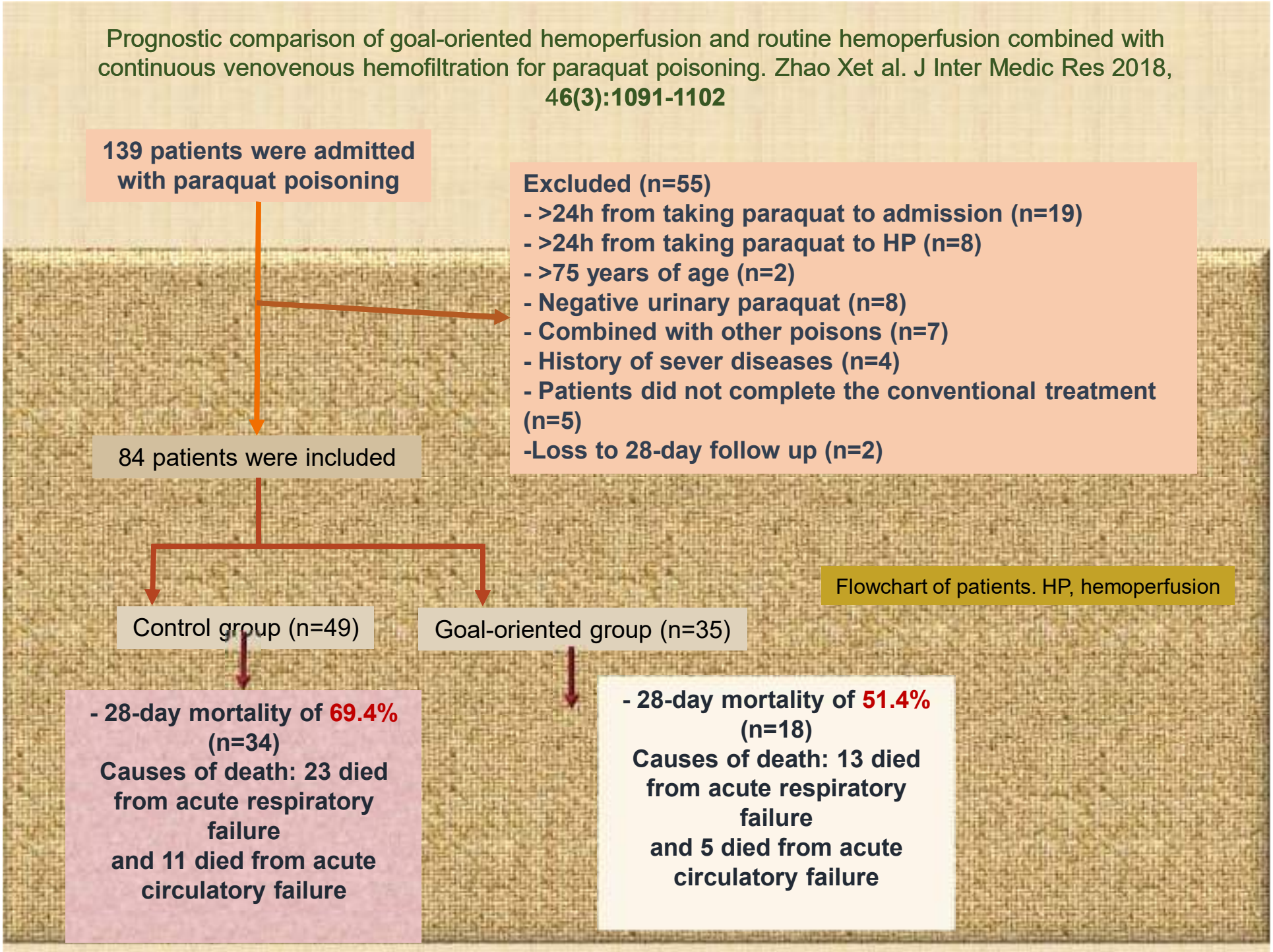
Fatality times and rates of paraquat-poisoned patients with high plasma paraquat levels (1,000±5,000 ng/mL, n = 81)

Treatment group	Death (<10 d)		Death (10±30 d)		Total Death	
	N	Fatality (%)	N	Fatality (%)	N	Fatality (%)
HP	7	25.9	9	33.3	19	**59.2**
CRRT	4	16	8	32	12	**48**
HP+CRRT	2	6.9	9	31	11	**37.9**


1.0-
0.8-
0.6-
0.4-
Cumulative Survival
HP
CRRT
HP+CRRT
0
5
10
15
20
25
30
Time (Days)
Survival time of 81 paraquat-poisoned patients (plasma paraquat levels: 1,000±5,000 ng/mL)

Survival time of 81 paraquat-poisoned patients (plasma paraquat levels: 1,000±5,000 ng/mL)

Prognostic comparison of goal-oriented hemoperfusion and routine hemoperfusion combined with continuous venovenous hemofiltration for paraquat poisoning. Zhao Xet al. J Inter Medic Res 2018, 46(3):1091-1102

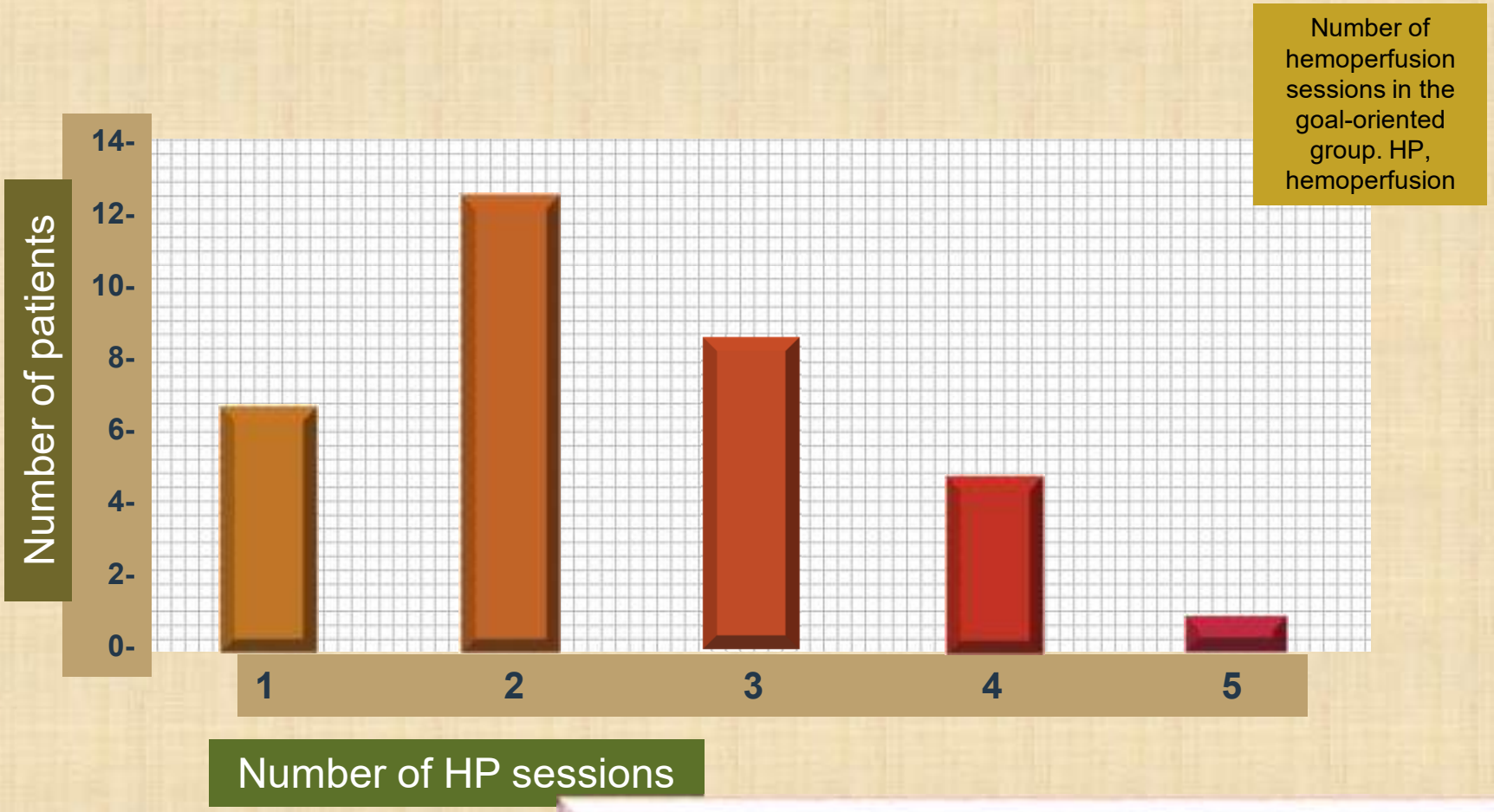


Flowchart of patients. HP, hemoperfusion

Color scale for semi-quantitative analysis of urine paraquat concentration.

To investigate the impact of goal-oriented hemoperfusion (HP) with monitoring of the paraquat concentration on the prognosis of patients with acute paraquat poisoning.

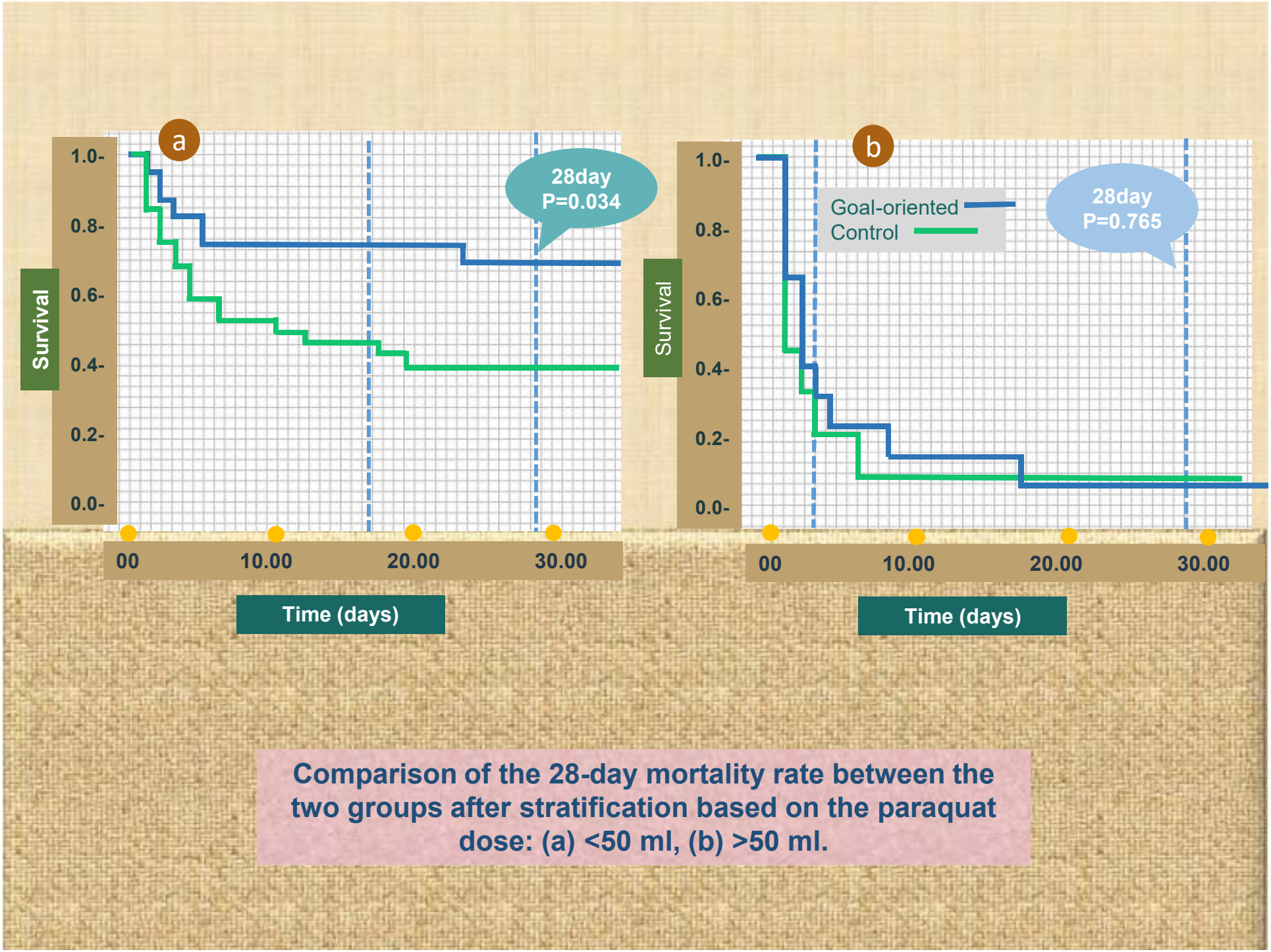
The primary endpoint was 28-day mortality after poisoning. The secondary endpoints were the incidence of organ dysfunction within 7 days and 7-day mortality.



If the results suggested that the content was >or=3 μg/ml, HP was continued until the urine detection turned negative.

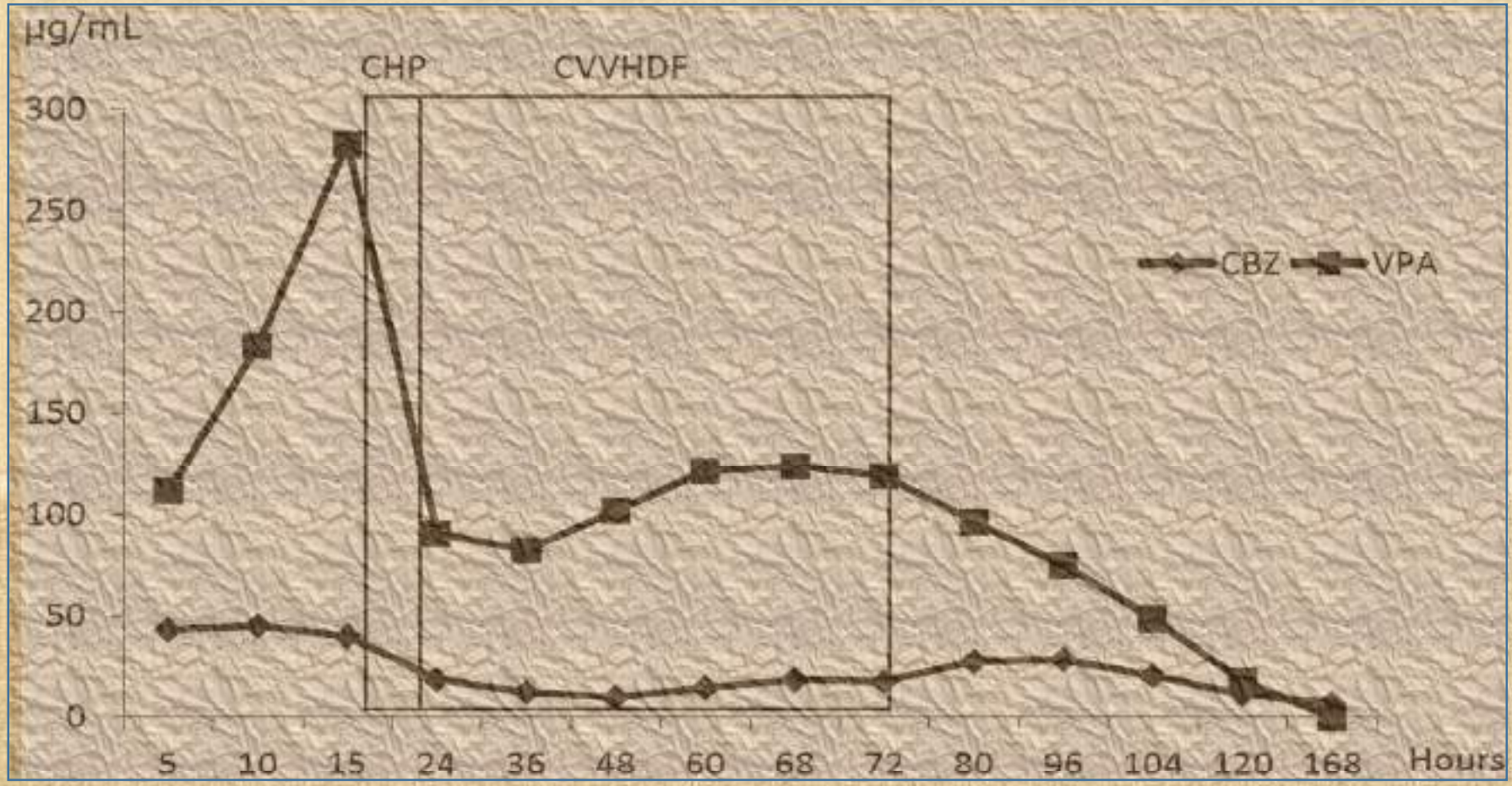
During subsequent 48 h, the urine paraquat concentration was detected every 6h, and if the concentration was again >or=3 μg/ml, another HP session was performed. This protocol was repeated until negative urine detection was achieved as the standard of stopping HP. If the patients did not develop acute renal injury, sequential CVVH was not per- formed after HP.


Survival
1.0-
0.8-
0.6-
0.4-
0.2-
0.0-
7d
28d
.00
5.00
10.00
15.00
20.00
25.00
30.00
Time (Days)
Goal-oriented
Control
51.4
69.4%
Kaplan–Meier survival analysis of the patients in the two groups.



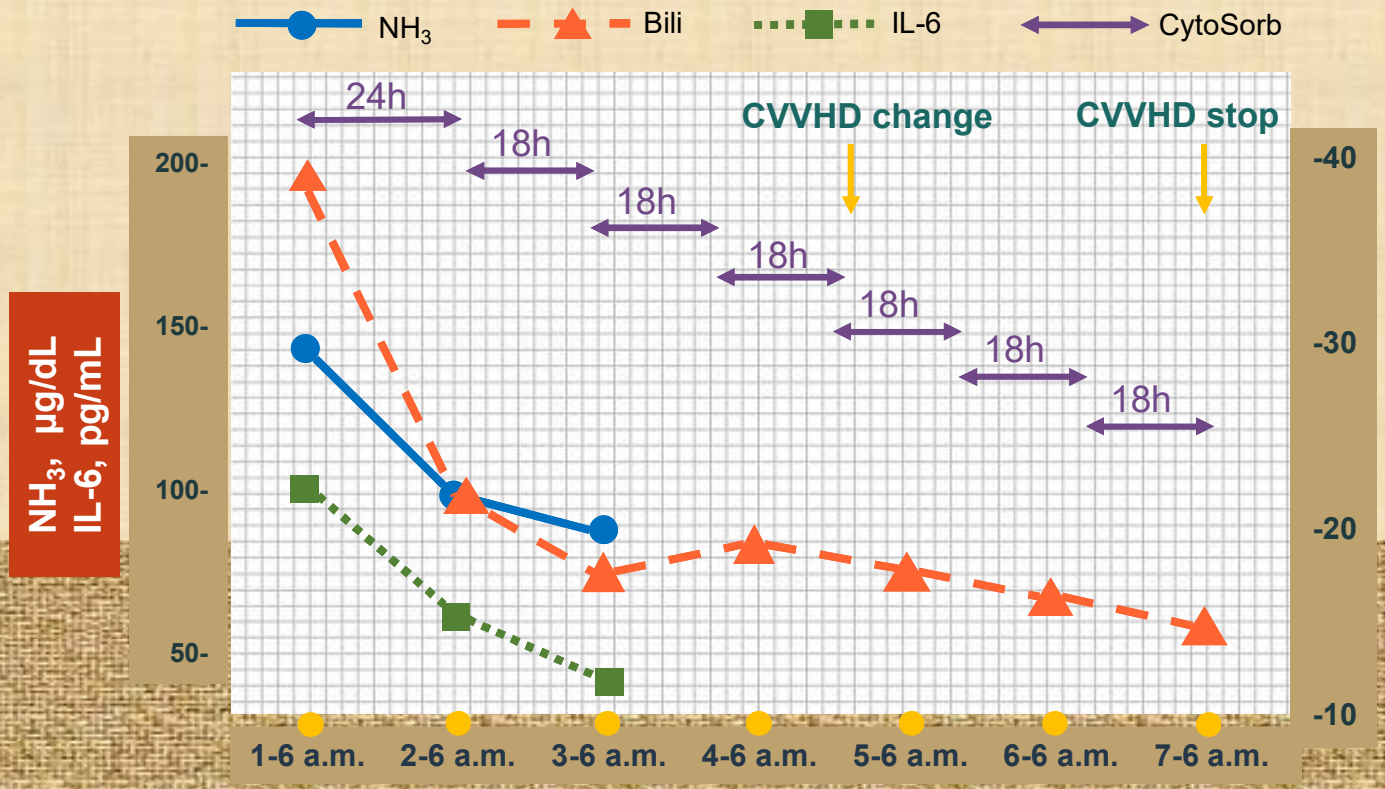
Comparison of the 28-day mortality rate between the two groups after stratification based on the paraquat dose: (a) <50 ml, (b) >50 ml.

Overdose with antiepileptic drugs: the efficacy of extracorporeal removal techniques. Moinho R, et al. BMJ Case Rep 2014. doi:10.1136/bcr-2014-207761



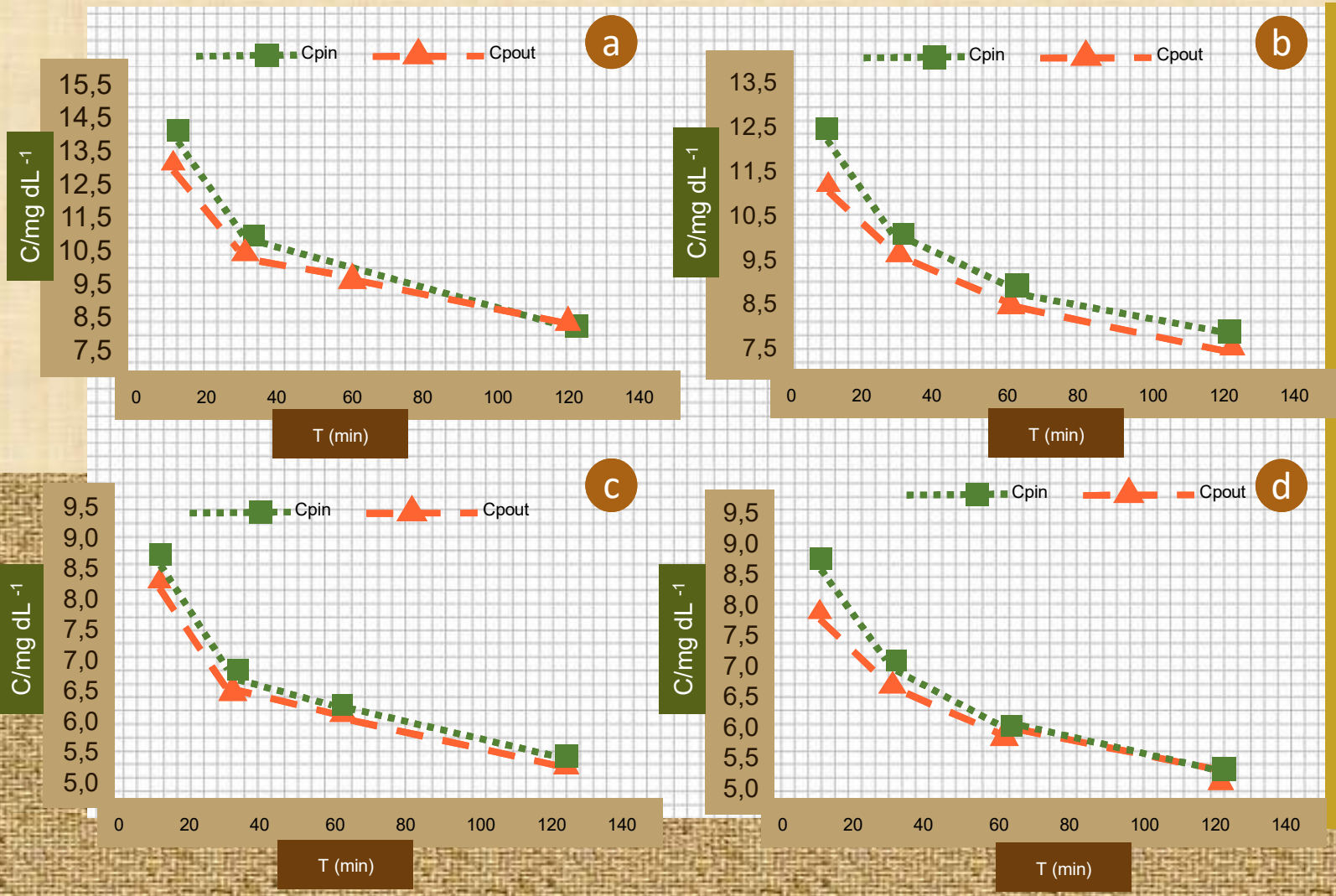
Carbamazepine (CBZ) and valproic acid (VPA) serum concentration evolution before, during and after the treatment with charcoal haemoperfusion (CHP) and continuous venovenous hemodiafiltration (CVVHDF). Therapeutic levels of CBZ=4–12 µg/mL and of VPA=50–100 µg/mL.

Use of Hemoabsorption in a Case of Severe Hepatic Failure and Hyperbilirubinemia. Andreas Falthauser and Frank Kullmann. Blood Pueif 2017;44:98-99



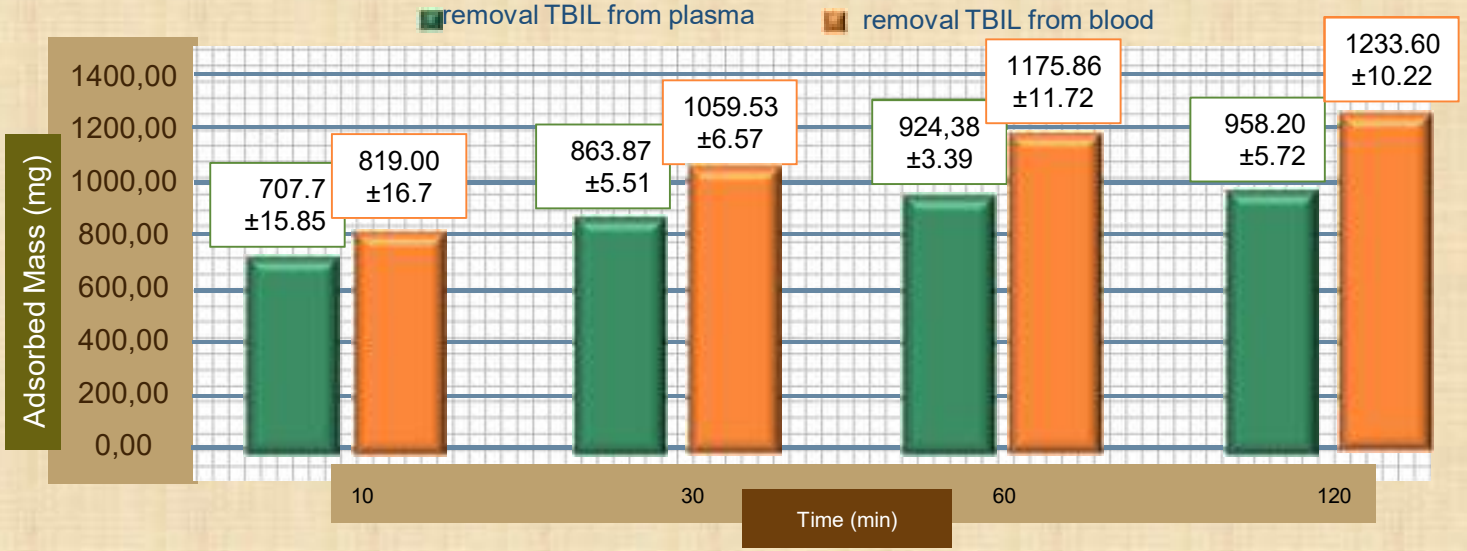
Course of bilirubin, ammonia, and IL-6 during the hemoadsorption treatment over 7 days.

New option for the treatment of hyperbilirubinemia: in vitro direct hemoperfusion with the Lixelle S-35.Santori et al. Int.J. Artif.Org 2014;37(11):815-823

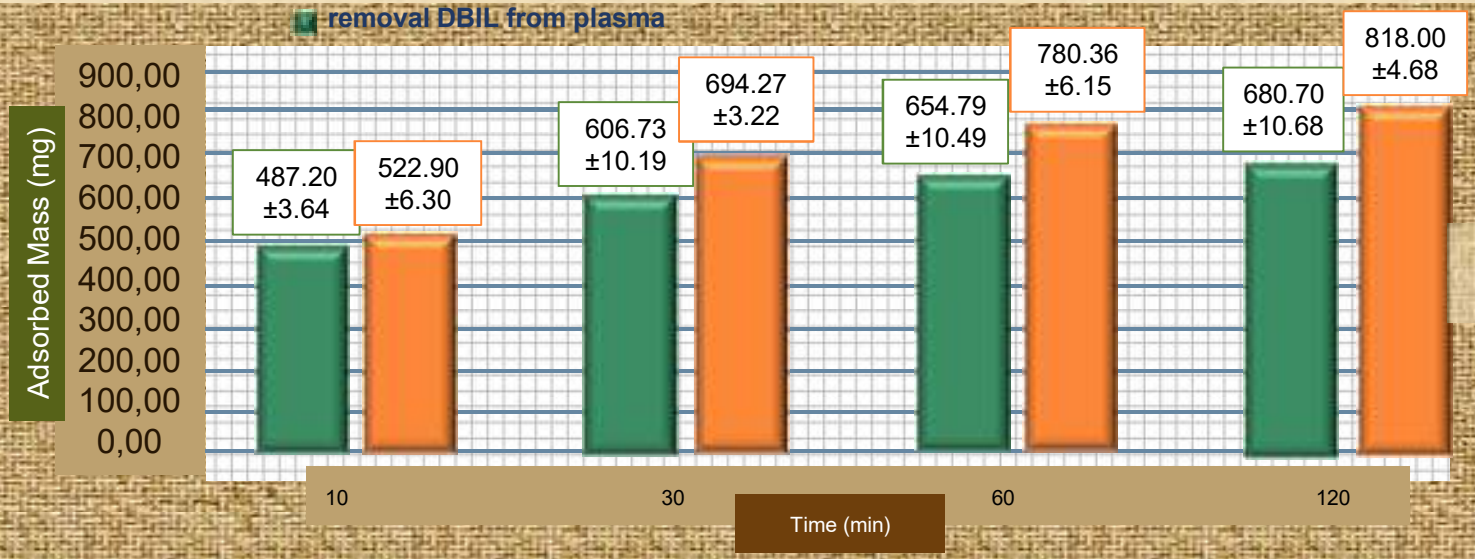


Change in arterial-venous concentrations during mock DHP: in a levels of total bilirubin in blood (baseline concentration 23.10 ± 0.47 mg/dl); in b levels of total bilirubin in plasma (baseline concentration 17.57 ± 0.53 mg/dl); in c levels of direct bilirubin in blood (baseline concentration 15.37 ± 0.24 mg/dl); in d levels of direct bilirubin in plasma (baseline concentration 12.57 ± 0.23 mg/dl).

New option for the treatment of hyperbilirubinemia: in vitro direct hemoperfusion with the Lixelle S-35

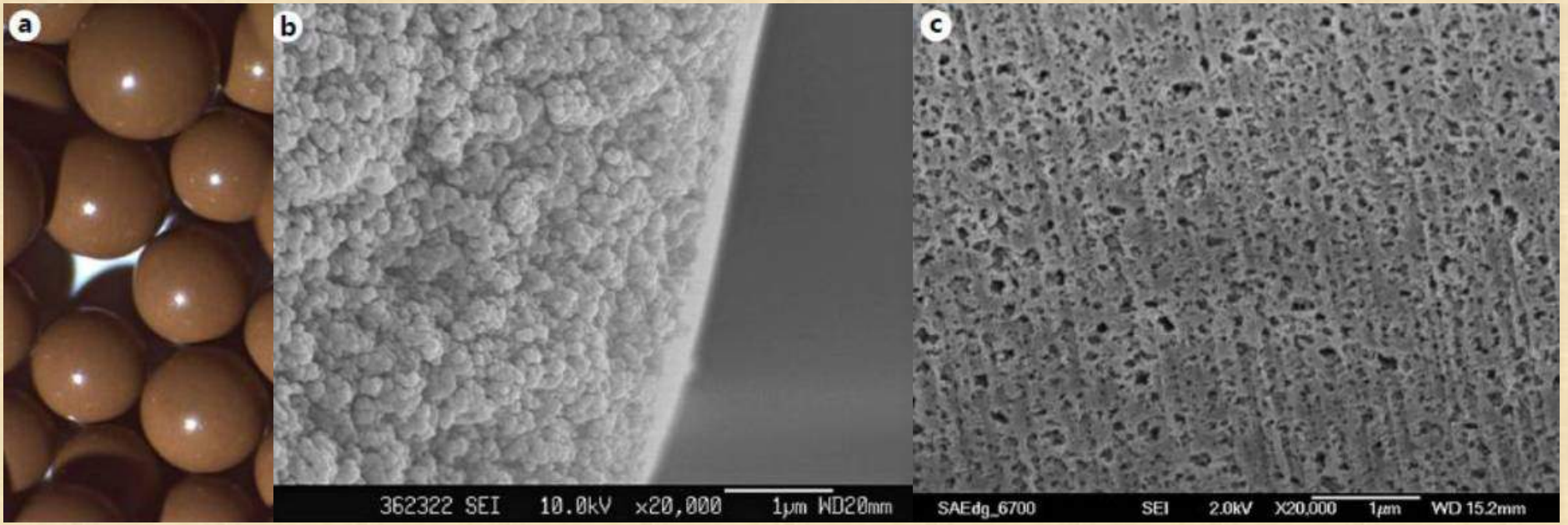


Mass Balance Analysis at 10, 30, 60 and 120 minutes. TBIL = total bilirubin; DBIL = direct bilirubin



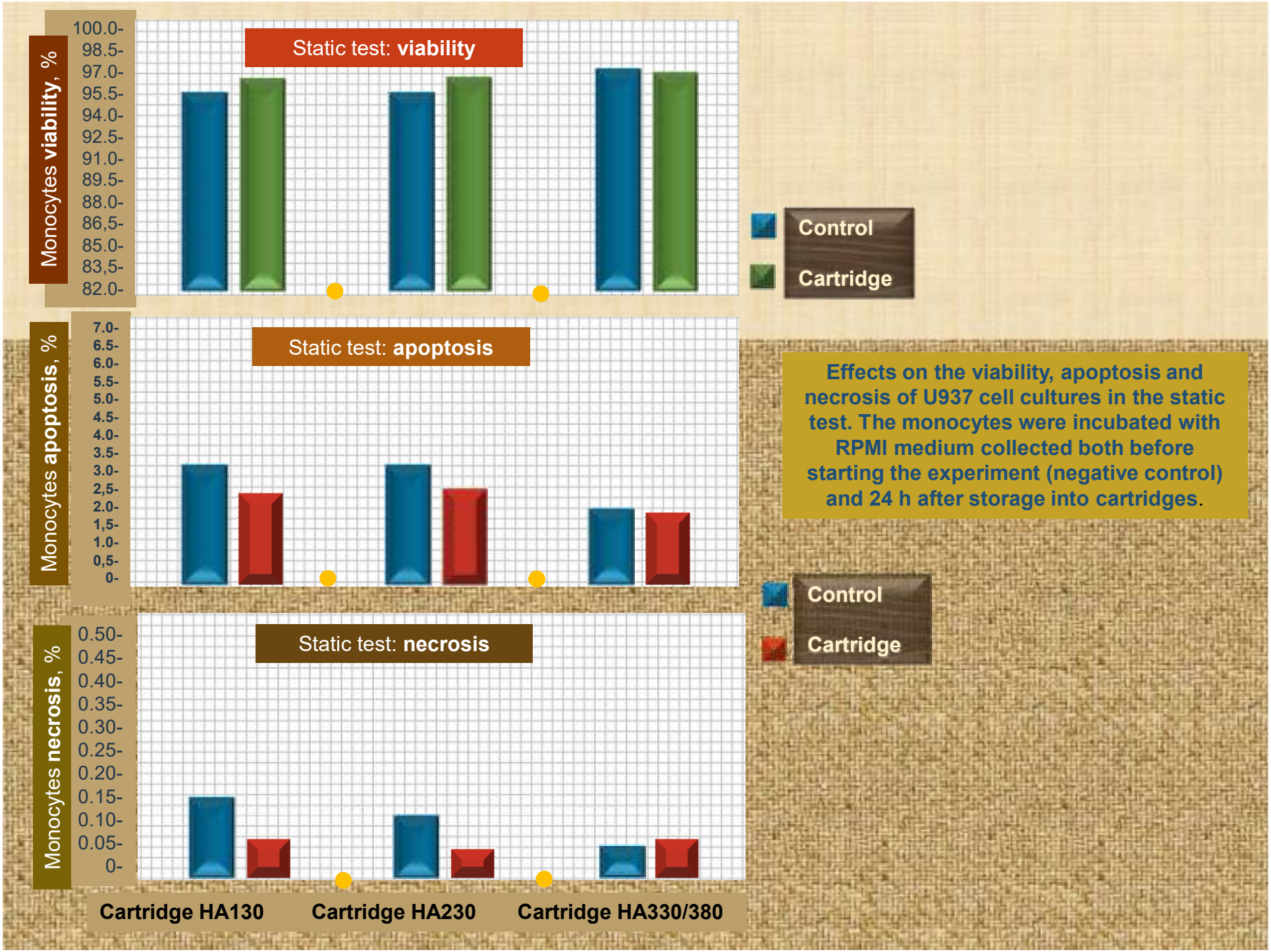
removal DBIL from blood

Biocompatibility and Cytotoxic Evaluation of New Sorbent Cartridges for Blood Hemoperfusion. Montin DP et al. Blood Purif 2018;46:187-195

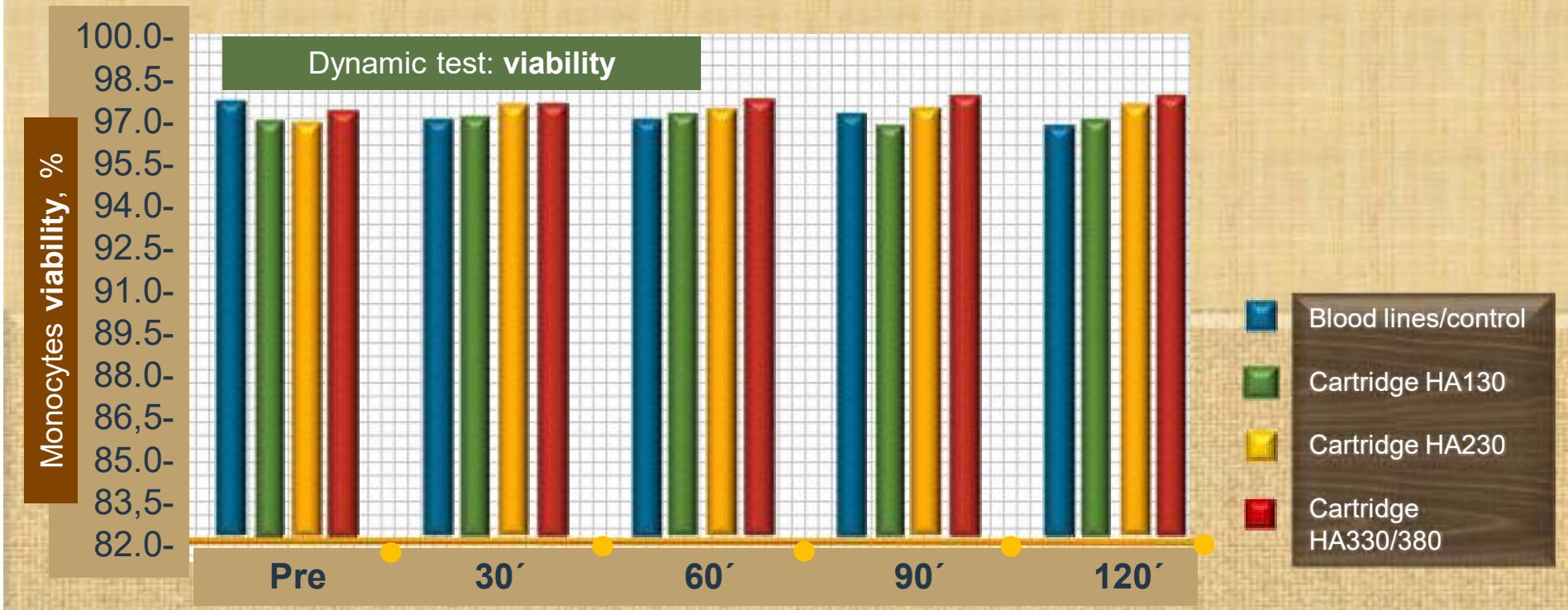


Neutro-macroporous resin adsorbing beads made of styrene-divinylbenzene copolymer (a). In (b.c), pics made by transmission electron microscopy (TEM) of beats surface and section with the poor.

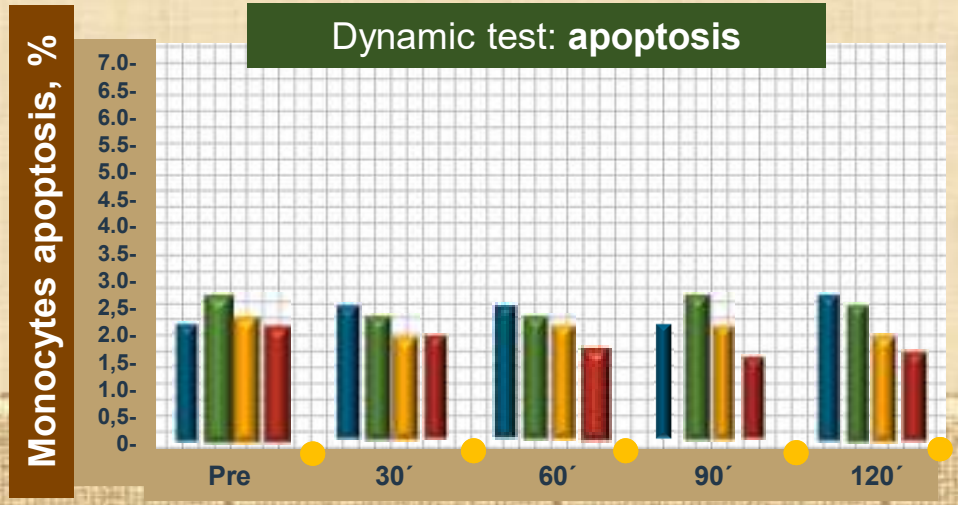
	HA130	HA230	HA330/380
Indications	Long term dialysis complications-itching renal osteodystrophy,hypertension, malnutrition	Intoxication poisong of herbicide, rodenticide, pesticide,biotoxin, drug overdose	Critical ill patients suffered from cytokine stom-sepsis pancreatitis, trauma, cardiac surgery, inflammation
Toxins removal	Middle uremic toxins, protein-bound uremic toxins	Ydrofobic or protein-bound exogenous substances	Cytokines, complement ,free hemoglobin and so on
Main removed molecular range	5-30kDa	500Da-10kDa	10-60kDa
Resin pore size distribution	500Da-40kDa	200Da-10kDa	500Da-60kDa
Specification			
Resin loading capacity	130	230	330/380
Blood volume	110	145	170/185
Material of absorbent		Styrene divinylbenzene Copolymers	
Material of housing		PC	
Parietal filter		Yes	
Sterilization method		Irradiation sterilization	

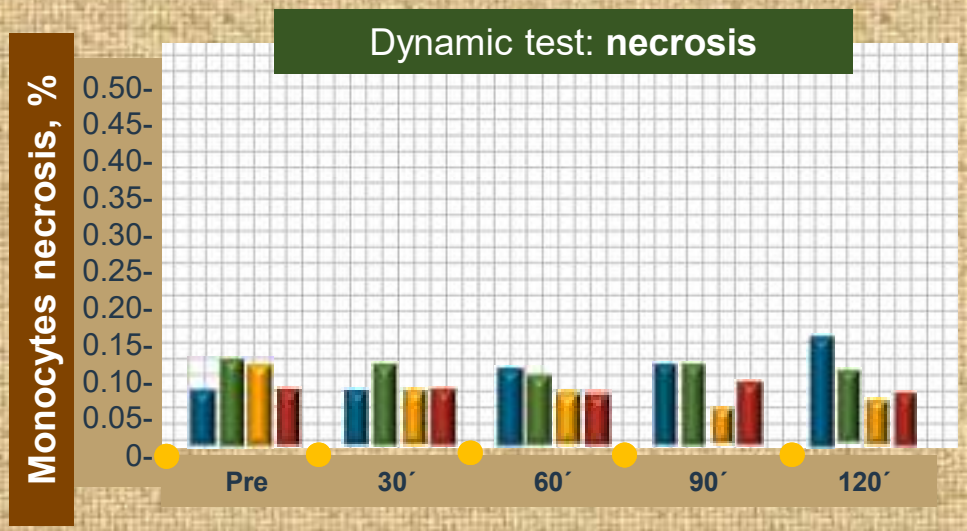

Monocytes viability, %
100.0-
98.5-
97.0-
95.5-
94.0-
92.5-
91.0-
89.5-
88.0-
86,5-
85.0-
83,5-
82.0-
Static test: viability
Control
Cartridge
Monocytes apoptosis, %
7.0-
6.5-
6.0-
5.5-
5.0-
4.5-
4.0-
3.5-
3.0-
2,5-
2.0-
1,5-
1.0-
0,5-
0-
Static test: apoptosis
Effects on the viability, apoptosis and necrosis of U937 cell cultures in the static test. The monocytes were incubated with RPMI medium collected both before starting the experiment (negative control) and 24 h after storage into cartridges.
Control
Cartridge
Monocytes necrosis, %
0.50-
0.45-
0.40-
0.35-
0.30-
0.25-
0.20-
0.15-
0.10-
0.05-
0-
Static test: necrosis
Cartridge HA130
Cartridge HA230
Cartridge HA330/380

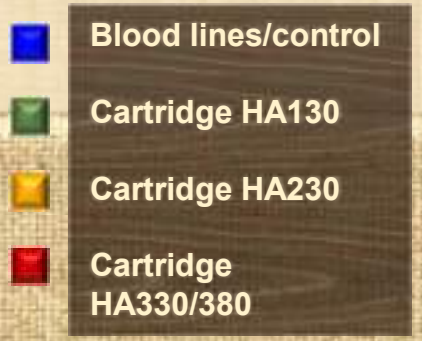
Percentage of viability, apoptosis, and necrosis of monocytes (U937 cell line) after 24 h of incubation for each cartridge type and controls, as negative control RPMI medium samples were collected before starting the experiment



Percentage of viability, apoptosis, and necrosis of monocytes (U937 cell line) after 24 h of incubation for each cartridge type and controls, as negative control RPMI medium samples were collected before starting the experiment

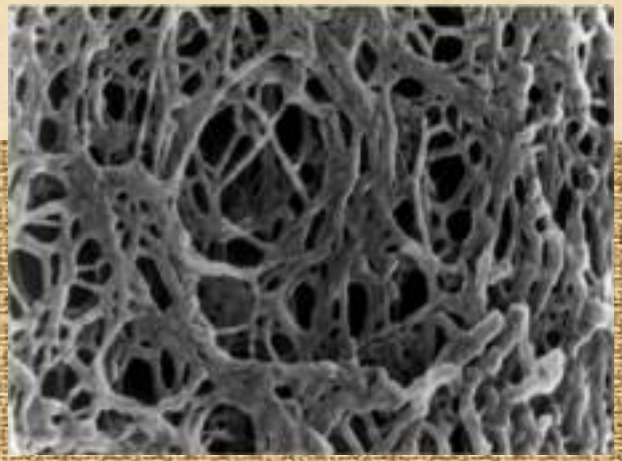


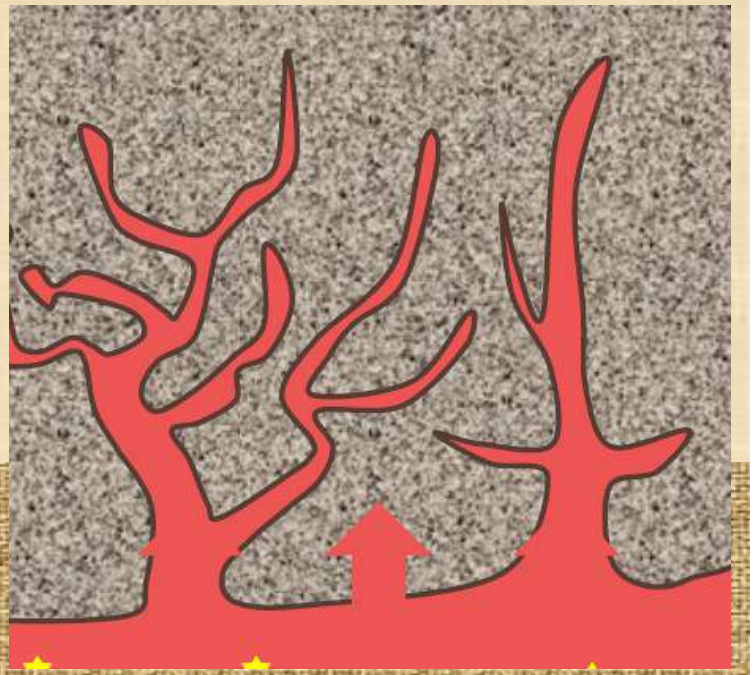




HA230 HEMOPERFUSION CARTRIDGE

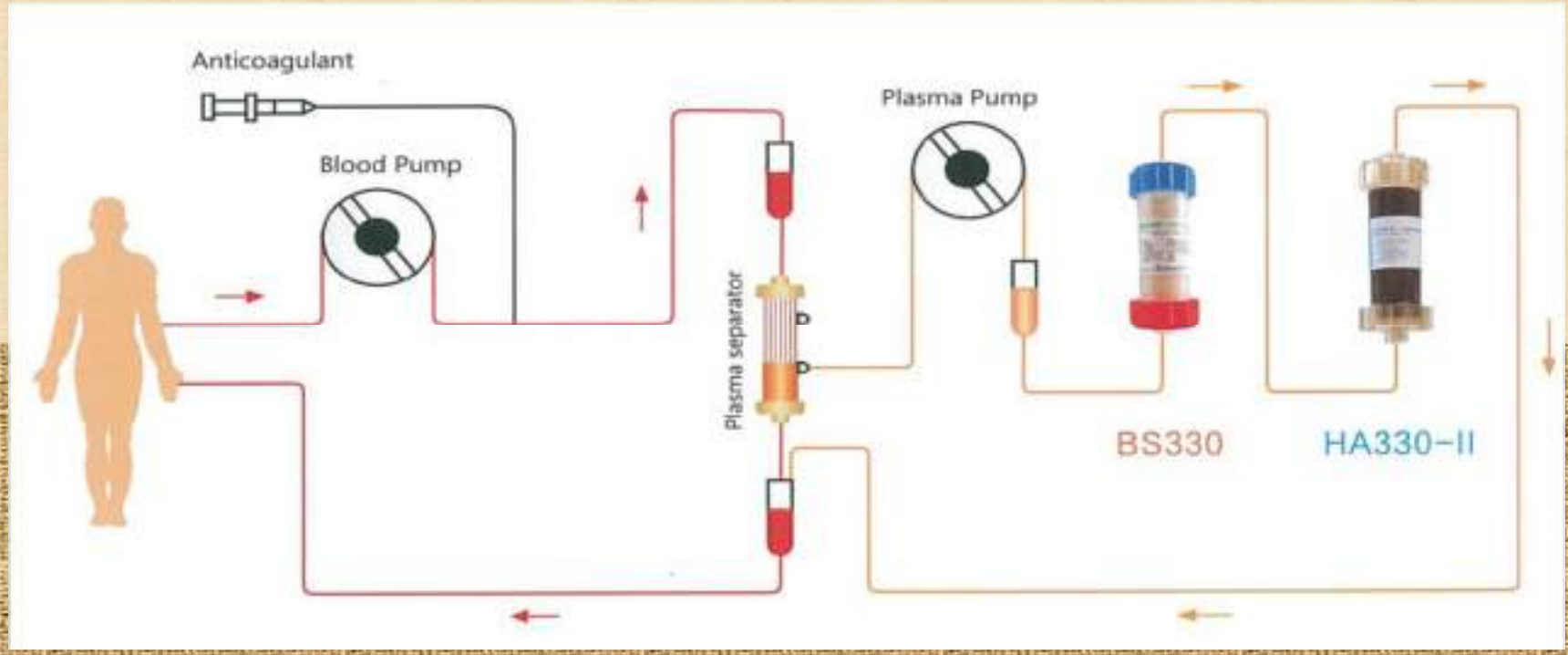
HA230 for Poisoning





- Hydrophobicity
- Molecular Sieve
- Physical adsorption/Van der Waals
- Electrostatic interaction

DPMAS – Efficient Liver Support System
Double Plasma Molecular Adsorption System



BS330+HA330-II Plasma adsorption

DPMAS

BS330 specifically adsorbs bilirubin, bile acid and endotoxin

BS330 Disposable Plasma Bilirubin Adsorption Colum

Anion-exchange resin

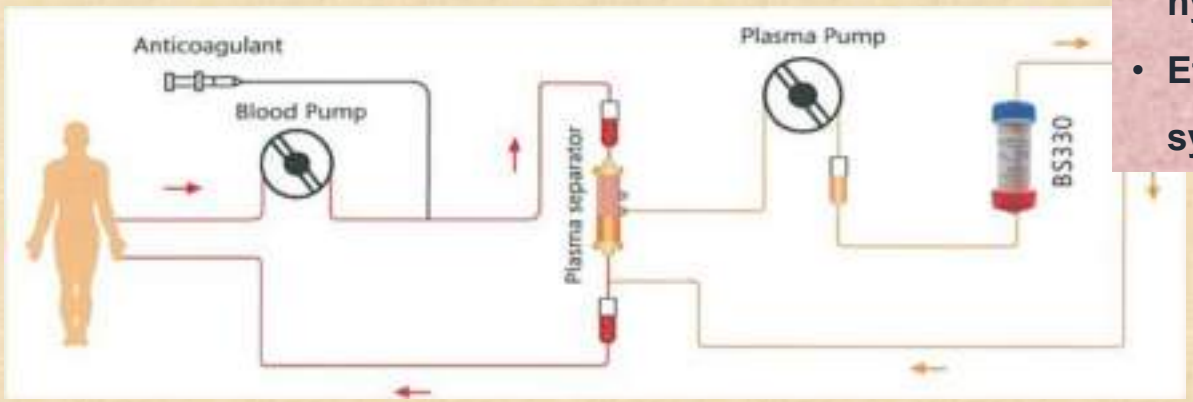
HA330-II broad-spectrum adsorbs toxins such as inflammatory mediators, ammonia, phenol mercaptan, etc

HA330-II Disposable Hemoperfusion Cartridge

Neutral-macroporous resin

DPMAS

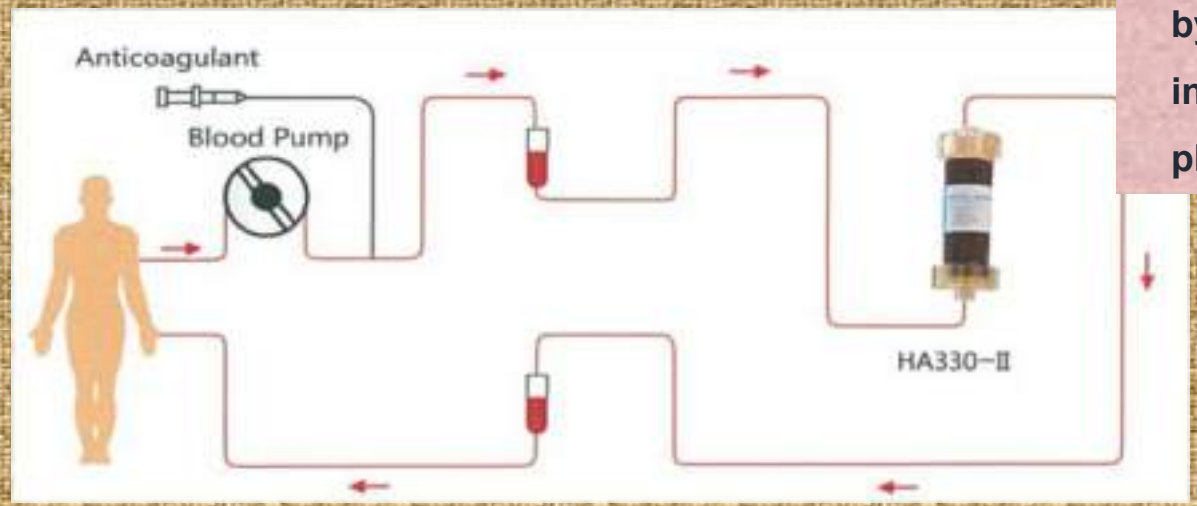
- BS330 plasma absorption



Plasma Adsorption

- For hyperbilirubinemia and hyperbileacidemia
- Effectively improve jaundice symptom

- HA330-II direct blood absorption

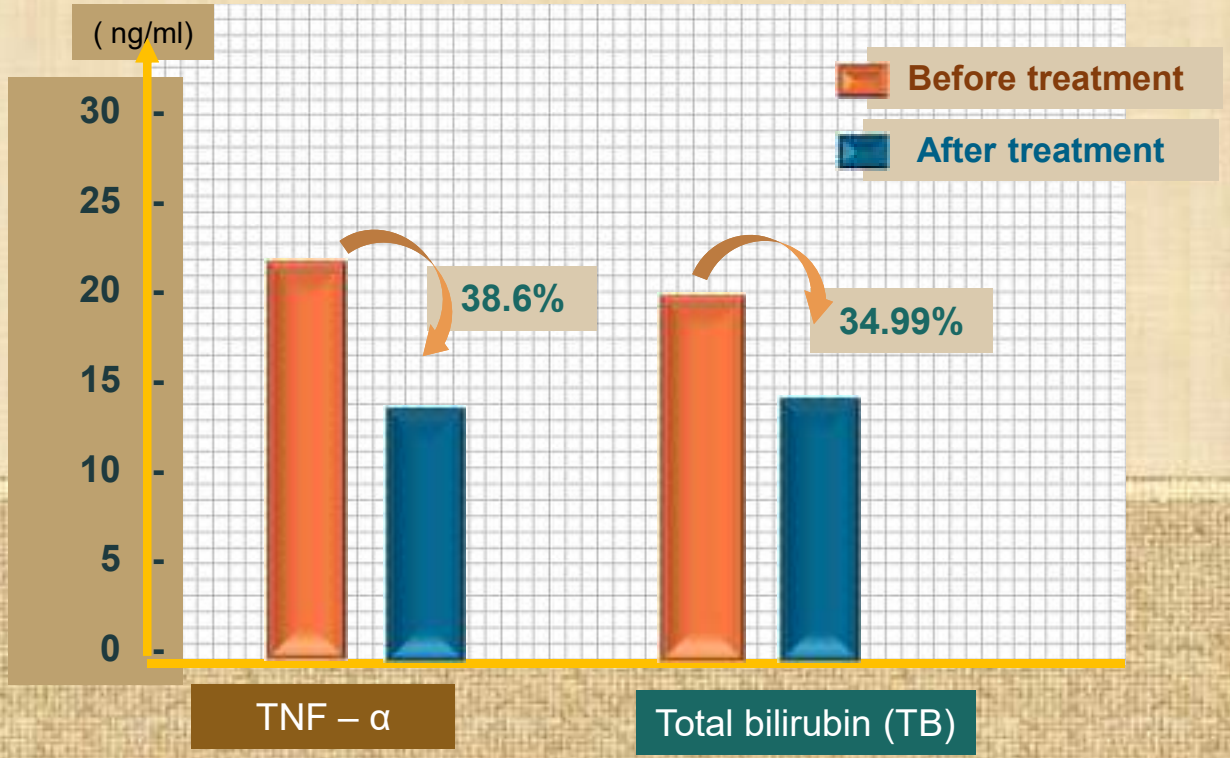


Direct Blood Perfusion

- For early hepatitis
- Extensively remove toxins induced by liver disorder such as inflammatory mediators, ammonia, phenol mercaptan, etc.

DPMAS

- Clinical Efficacy



Conclusion: DPMAS efficiently removes bilirubin while clearing inflammatory mediators

Clinical emergency treatment of 68 critical patients with severe organophosphorus poisoning and prognosis analysis after rescue. Hui Dong et al. Medicine 2017;96(25)

The frequency of both groups having organ failure (n [%])			
Groups	Renal failure	Heart failure	Respiratory failure
Control group (n=34)	4 (11.76)	1 (2.94)	6 (17.65)
Treatment group (n=34)	1 (2.94)	3 (8.82)	6 (17.65)

Comparison of rescue outcomes			
Groups	Renal failure	Heart failure	Respiratory failure
Control group (n=34)	**4 (11.76)**	**6 (17.65)**	**28 (82.35)**
Treatment group (n=34)	**1 (2.94)**	**1 (2.94)**	**33 (97.06)**
x^2	5.712	11.715	11.715
P	<.05	<.05	<.05

Comparison of the clinical effect and length of hospital stay						
Groups	Atropinization time (h)	Recovery time of cholinesterase activity (day)	Recovery time of consciousness (h)	Extubation time (day)	Total usage of atropine (mg)	Length of hospital stay (day)
Control group (n=34)	6.4±1.1	18.8±3.2	14.4±2.5	7.4±2.5	485.4±64.4	**18.3±3.5**
Treatment group (n=34)	2.8±.5	7.9±1.4	3.5±1.0	2.3±1.1	119.3±22.5	**11.2±1.4**
T	17.373	18.196	23.605	10.888	31.293	10.982
P	<.05	<.05	<.05	<.05	<.05	<.05

Early hemoperfusion for emergency treatment of carbamazepine poisoning. Yang Xet al .Am J Emerg Med 2018 Jun;36(6):926-930

104 patients with acute CBZ poisoning
Group (HP in Emergency Department)=51
Group (HP in the blood purification room)=34
Control group (No HP)=19

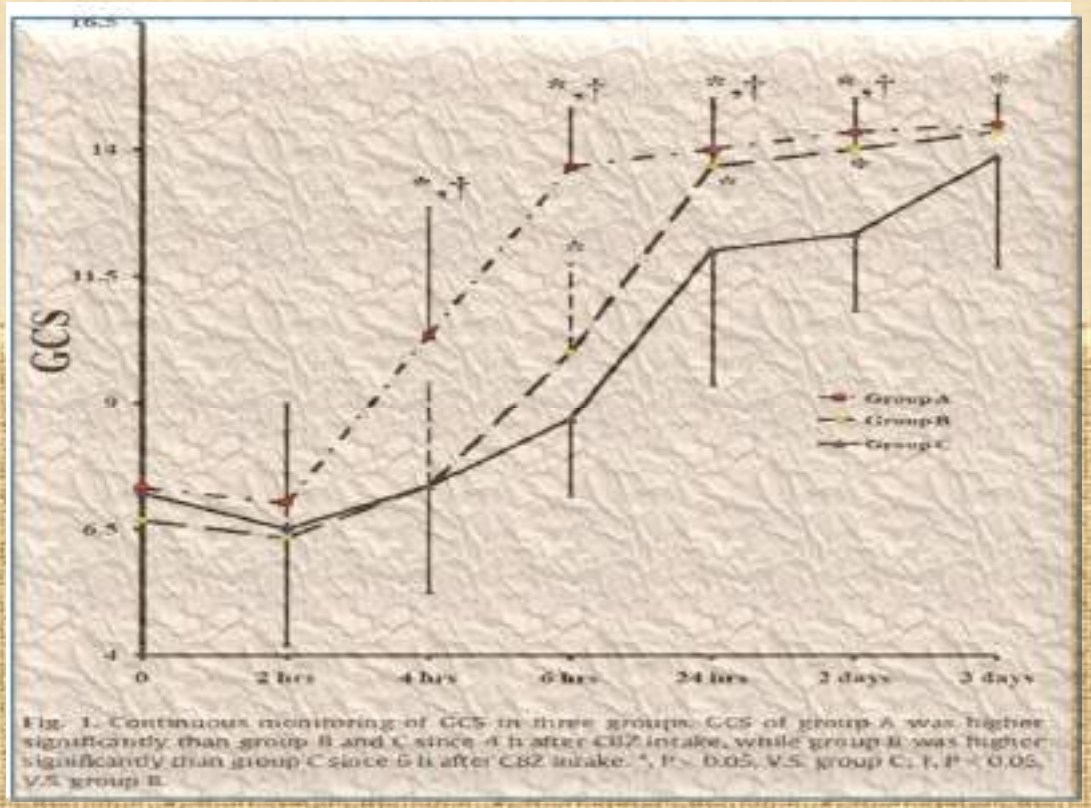


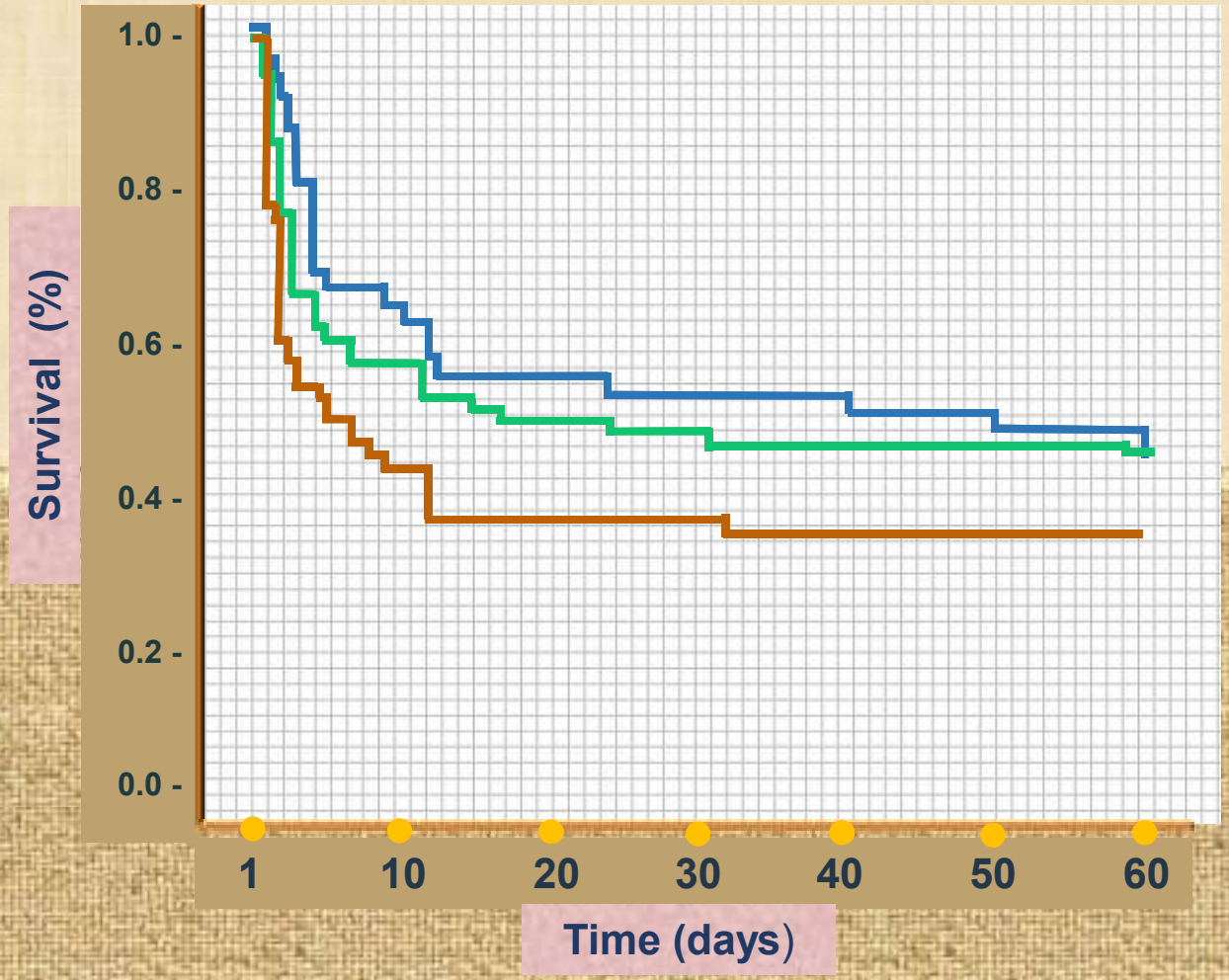
Fig. 1. Continuous monitoring of GCS in three groups. GCS of group A was higher significantly than group B and C since 4 h after CBZ intake, while group B was higher significantly than group C since 6 h after CBZ intake. *, P < 0.05, V.S. group C; †, P < 0.05, V.S. group B.

	HP IN EMERGENCY DEPARTMENT	HP IN BLOOD PURIFICATION ROOM	NO HP
MORTALITY	0	0	10.5 %
HOSPITALISATION DAYS	3.12+/-0.98	4.16+/-0.74	5.85 +/- 1.32

Improve the consciousness recovery & survival and shorten the hospitalization

Early Stage Blood Purification for Paraquat Poisoning: A Multicenter Retrospective Study. An Li et al. Blood Purif 2016;42:93-99

HA330



HP + CVVH-	46.5
HP	43.1
Conservative	21.3

Sixty-day survival according to treatment after acute PQ poisoning.

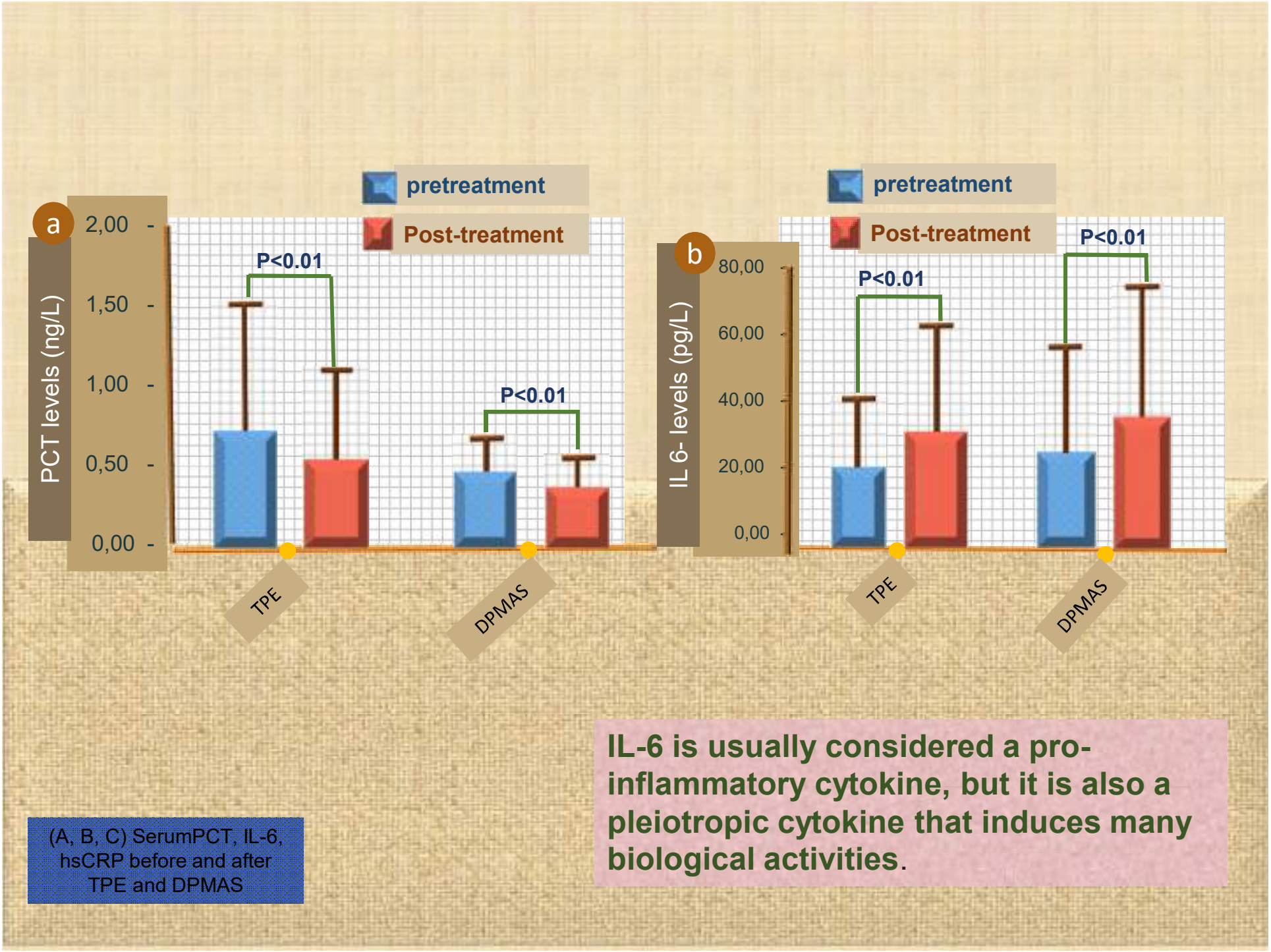
Early Stage Blood Purification for Paraquat Poisoning: A Multicenter Retrospective Study. An Li et al. Blood Purif 2016;42:93-99

Blood levels of PQ comparison at baseline and during treatment						
Group	n	Baseline	24 h	48h	72h	p value
Conservative	75	21.56±11.17	16.71±8.35[a]	10.33±6.67[a, b]	6.02±3.29[a–c]	<0.001
HP	65	22.95±10.41	7.84±3.63[*, a]	4.54±2.58[*, a, b]	2.50±1.34[a–c]	<0.001
HP + CVVH	43	20.82±9.26	4.95±2.81[*, #, a]	3.91±1.89[*, a, b]	2.11±1.67[a–c]	<0.001
p value	-	0.553	<0.001	<0.001	<0.001	
All data are presented as mean ± SD, μg/ml.						
* p < 0.05 vs. conservative treatment; # p < 0.05 vs. HP; a p < 0.05 vs. before baseline; b p < 0.05 vs. 24 h; c p <0.05 vs. 48 h.						

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 et al.Journal of Clinical Apheresis

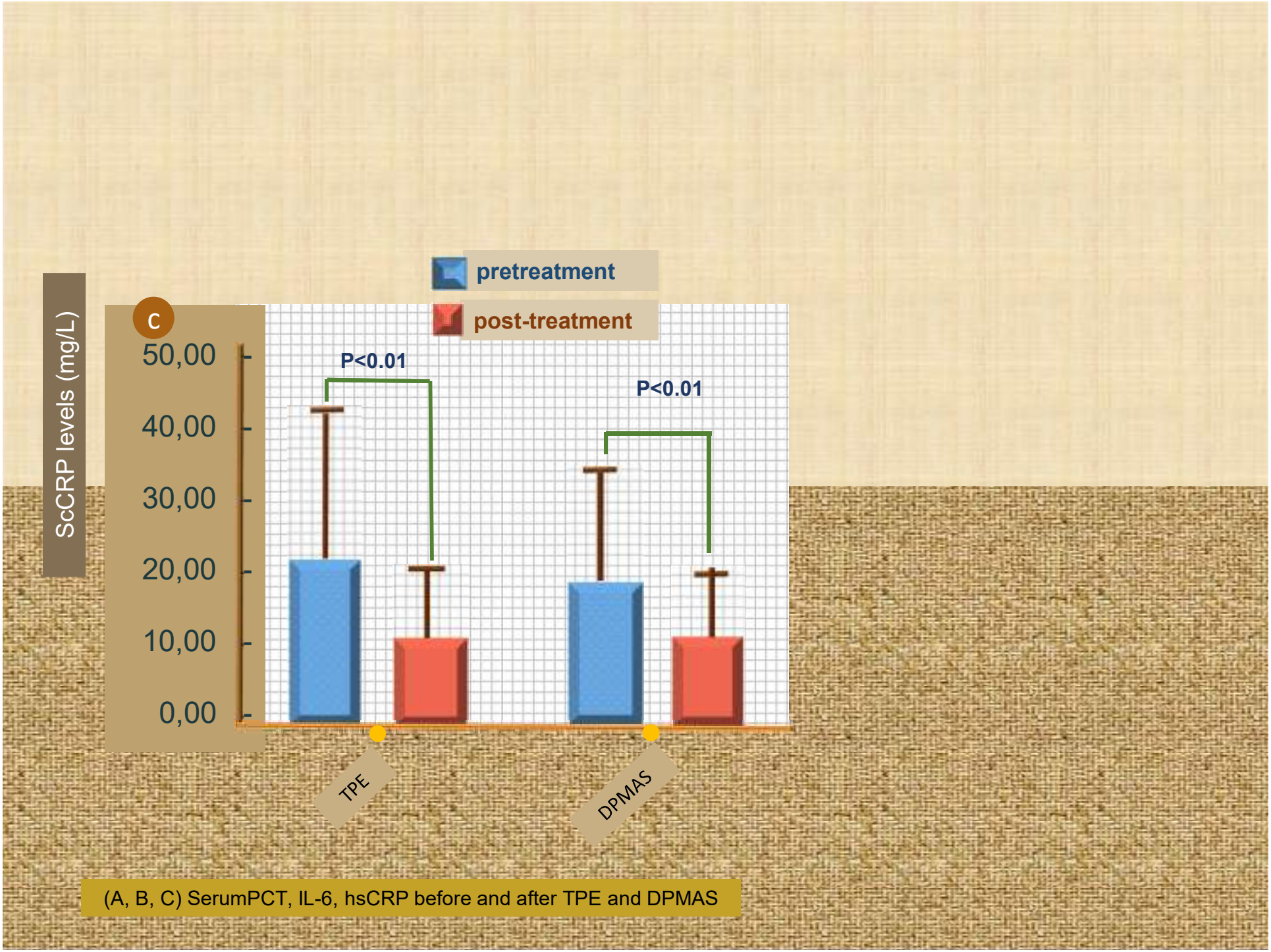
Design : A single center prospective controlled pilot study. Study
Subject: Acute-on-chronic liver failure (ACLF)
Regimens:
TPE Group (N=33): standard medical therapy + TPE (2-3 times/week, 2-3h/session) plasma exchange rate: 20-30ml/min.
DPMAS Group (N=27): standard medical therapy +DPMAS (2-3 times/week, 2-3h/session) blood flow rate: 100-150ml/min, plasma flow rate: 25-50ml/min.

Purpose: compare the efficacy of TPE and DPMAS on acute on-chronic liver failure (ACLF) caused by hepatitis B virus (HBV-ACLF).

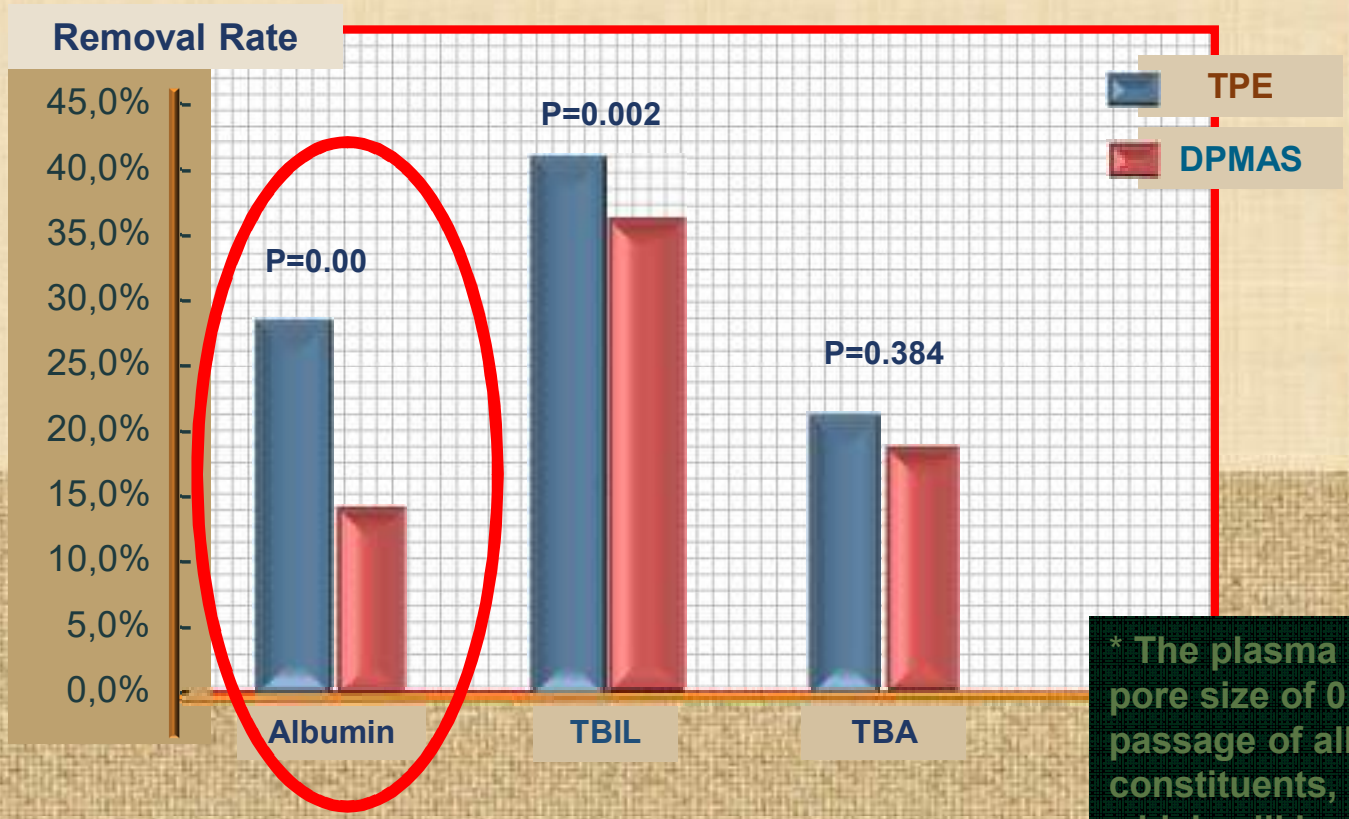


(A, B, C) SerumPCT, IL-6, hsCRP before and after TPE and DPMAS

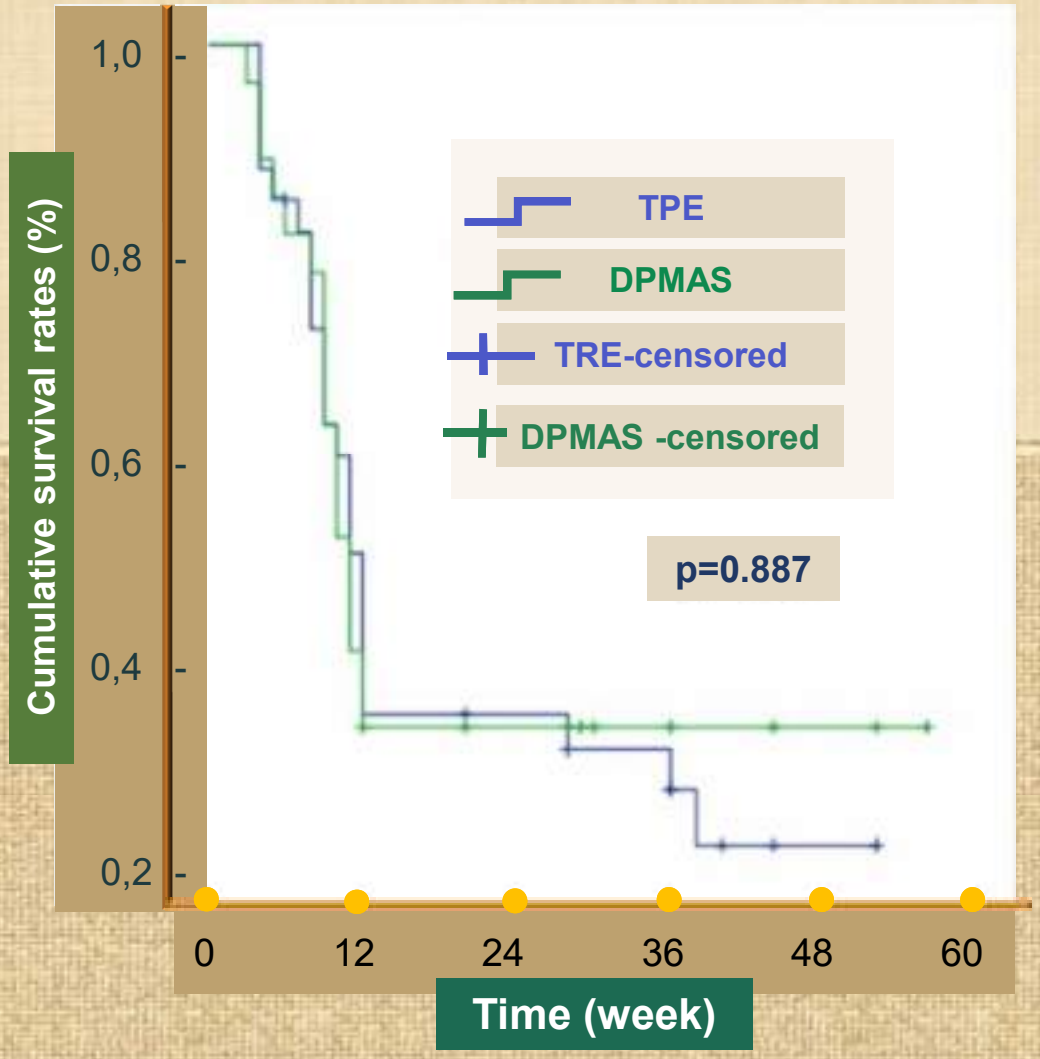
IL-6 is usually considered a pro-inflammatory cytokine, but it is also a pleiotropic cytokine that induces many biological activities.



(A, B, C) SerumPCT, IL-6, hsCRP before and after TPE and DPMAS



* The plasma separator with a pore size of 0.2-0.6 mm allows passage of all plasma constituents, including albumin, which will be either discarded in TPE or perfused over absorptive materials. The albumin then will be recycled into the patients in DPMAS.



Cumulative survival rates after treatment by TPE and DPMAS (P5.887, log-rank test)

High dynamic blood circulation is common in patients with liver failure, the circulation time is shortened, the ability to reserve the heart is diminished, hypotension is easy to occur.

The plasma adsorption column and extracorporeal circulation pipeline have a certain volume, After establishing the extracorporeal circulation, more blood is left in vitro, the effective circulating blood volume is reduced.

	Drugs	HD	HP (NMR)
Sedative-hypnotics	Barbiturates Glutethimide Methaqualone diazepam	+~++ -~+ +/-~+++	+++ ++~+++ ++++ ++++
anodyne	salicylate	+++	++~++++
Cardiovascular drugs	digitoxin quinidine procainamide	+ +/-~+ +~+++	++~+++ ++ ++++
Organophosphorous pesticide	Dimethoate DDVP	++	+++ ++++
Other drugs	paraquat		+++

	Resin	Activated carbon
adsorbent	Neutral microporous adsorption resin	Medical activated carbon
Pore size	Averaged 13-15mm	Not averaged
Absorption spectum	Relative specific adsorption	Not selective
adsorbate	Middle and big molecular and high fat soluble substances	Middle and small molecular substances
Application scope	Detoxification, uremia, hepatology ,criticall illness and so on	detoxification
safety	Produced by polymer material Uniform pore size, smooth surface Good blood compatibility	Natural materials temperature firing Uneven surface The damage of platelet