EXTRACORPOREAL ELIMINATION TECHNIQUES IN POISONING

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A long but not helpful list…

TABLE 7-5 Drugs and Chemicals Removed with Dialysis and Hemoperfusion*

Barbiturates
Amobarbital
Butabarbital
Hexabarbital
Pentobarbital
Phenobarbital†
Quinalbital
Secobarbital
Thiopental
Vinalbital

Analgesics
Acetaminophen
Acetylsalicylic acid
Colchicine
d-Propoxyphyene
Methylsalicylate
Phenylbutazone
Salicylic acid

Nonbarbiturate Hypnotics and Tranquilizers
Carbromal
Chloral hydrate
Chlorpromazine
(Diazepam)
Diphenhydramine
Ethchlorvynol
Meprobamate
Methaqualone
Valproate

Inorganics and Alcohols
Ethanol
Ethylene glycol
Isopropanol
Methanol
Polychlorinated biphenyls
Paraquat
Parathion

Antimicrobials and Anticancer Agents
Ampicillin
Carbenicillin
Tetracycline
Isoniazid
Chloramphenicol
Chloroquine
Clindamycin
Dapsone
(Doxorubicin)
Carmustine

Cardiovascular
β-Blockers
Captopril
(Digoxin)
Diltiazem
(Disopyramide)
Flecainide
Metoprolol
N-Acetyl-procainamide
Procainamide
Quinidine

Antidepressants
(Amitriptyline)
(Imipramine)
(Tricyclics)†

Metals and Others
(Aluminum)
Cimetidine
Diquat
(Lead)
Lithium
Methylmercury complex
Paraquat
Sodium chlorate
Theophylline
(Phencyclidine)
Phenols
(Podophyllin)
Herbicides
Solvents, gases
Insecticides
Carbon tetrachloride
Amanitin
Ethylene oxide

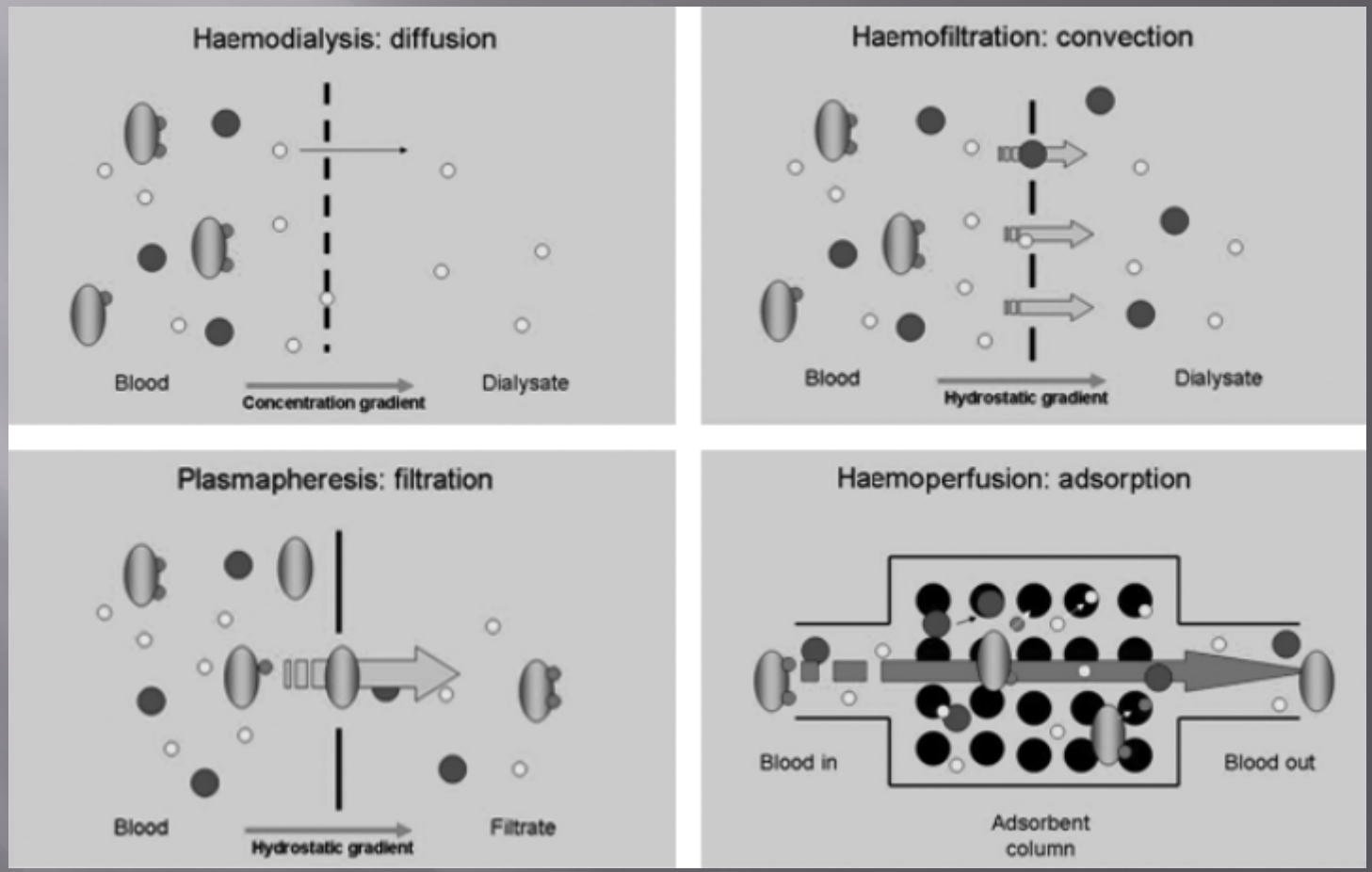
Note. Agents in parentheses are not well removed or required a chelating agent.
*For more detail, see Winchester and Kitiyakara.[31]
†More recent clinical success with highly efficient dialysis or hemoperfusion.

(Critical Care Toxicology, 2005)

Criteria

- Toxicokinetic efficiency : true increase of the toxin elimination that is validated by accurate sampling analysis (more than a shorter plasmatic half-life)
- Toxicodynamic effectiveness : shortening of the symptoms duration or decrease of the severity of poisoning
- Real benefit in comparison with the existing treatments (supportive, antidotes), risk/benefit ratio of the technique
- Enthusiasm for innovative techniques (MARS) but validation is still required

Physical principles of the different techniques



Albumin-based hemodialysis: MARS

Dia-Flux membrane

blood pump

adsorption columns

Bicarbonate buffered dialysate solution

albumin pump

MARS-Flux membrane

blood circuit

albumin circuit

single pass

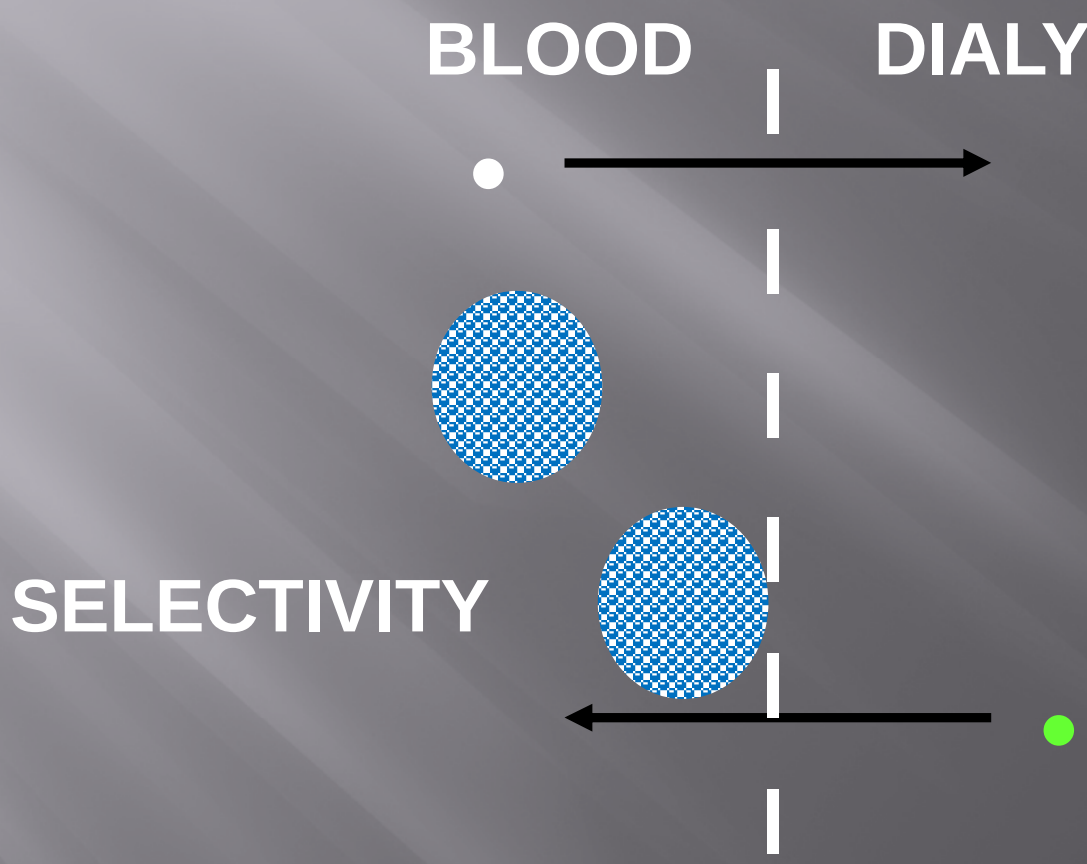
- Dialysis

(Laleman et al., Aliment Pharmacol Ther, 2006)

Principles related to the toxin

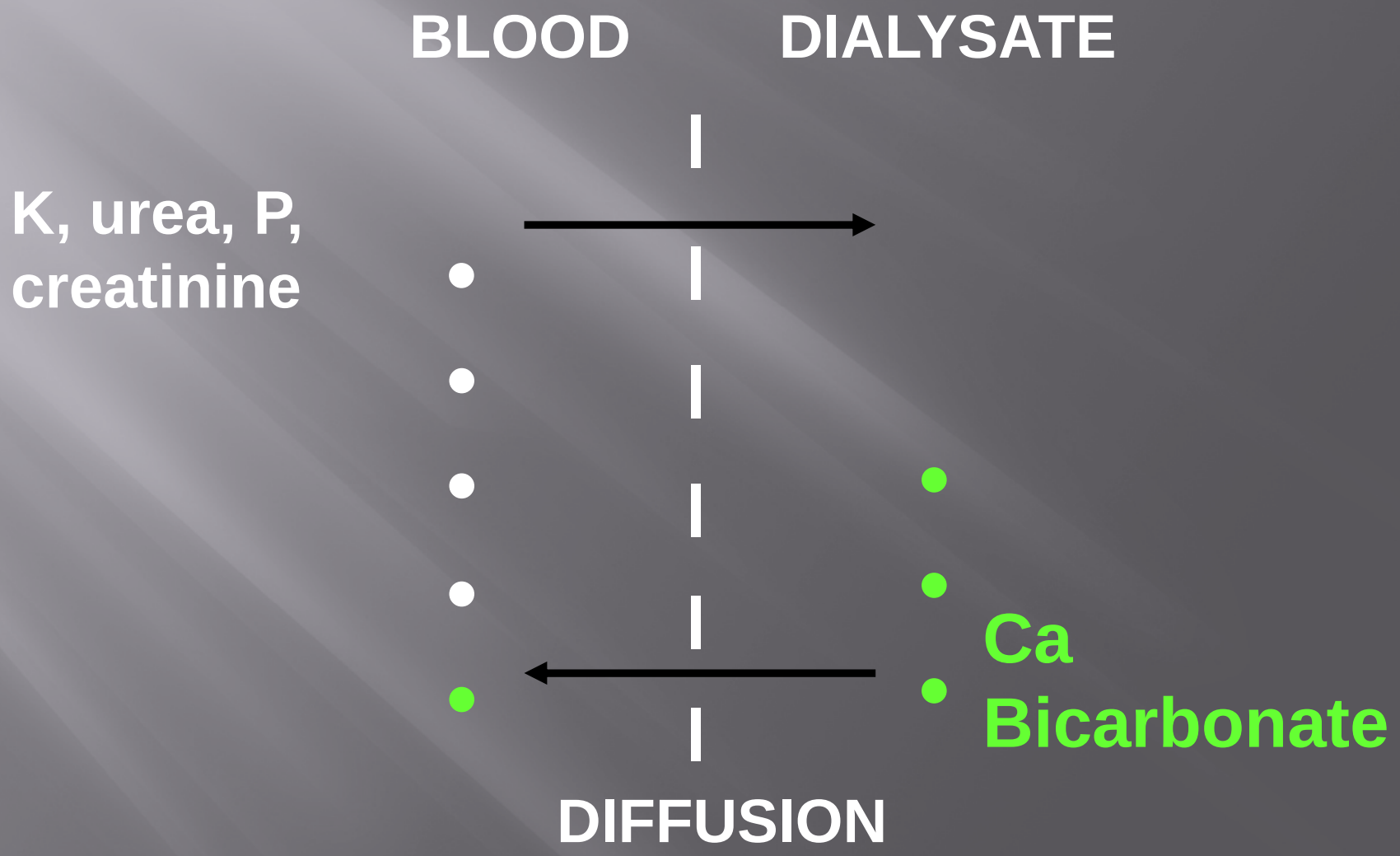
- Molecular weight
  - The size of the molecule must be small enough to fit through the pores of the filter
- Volume of distribution
  - Only the blood compartment gets filtered
    - 0.08 L/kg
  - A traditionally small Vd = 1 L/kg or less
  - Utility may improve for toxins with a large Vd if ECTR is performed before distribution
- Protein binding
  - As protein binding increases available free toxin decreases
  - Pharmacokinetic parameters are often misleading

Semi-permeable membrane (synthetic or peritoneal)

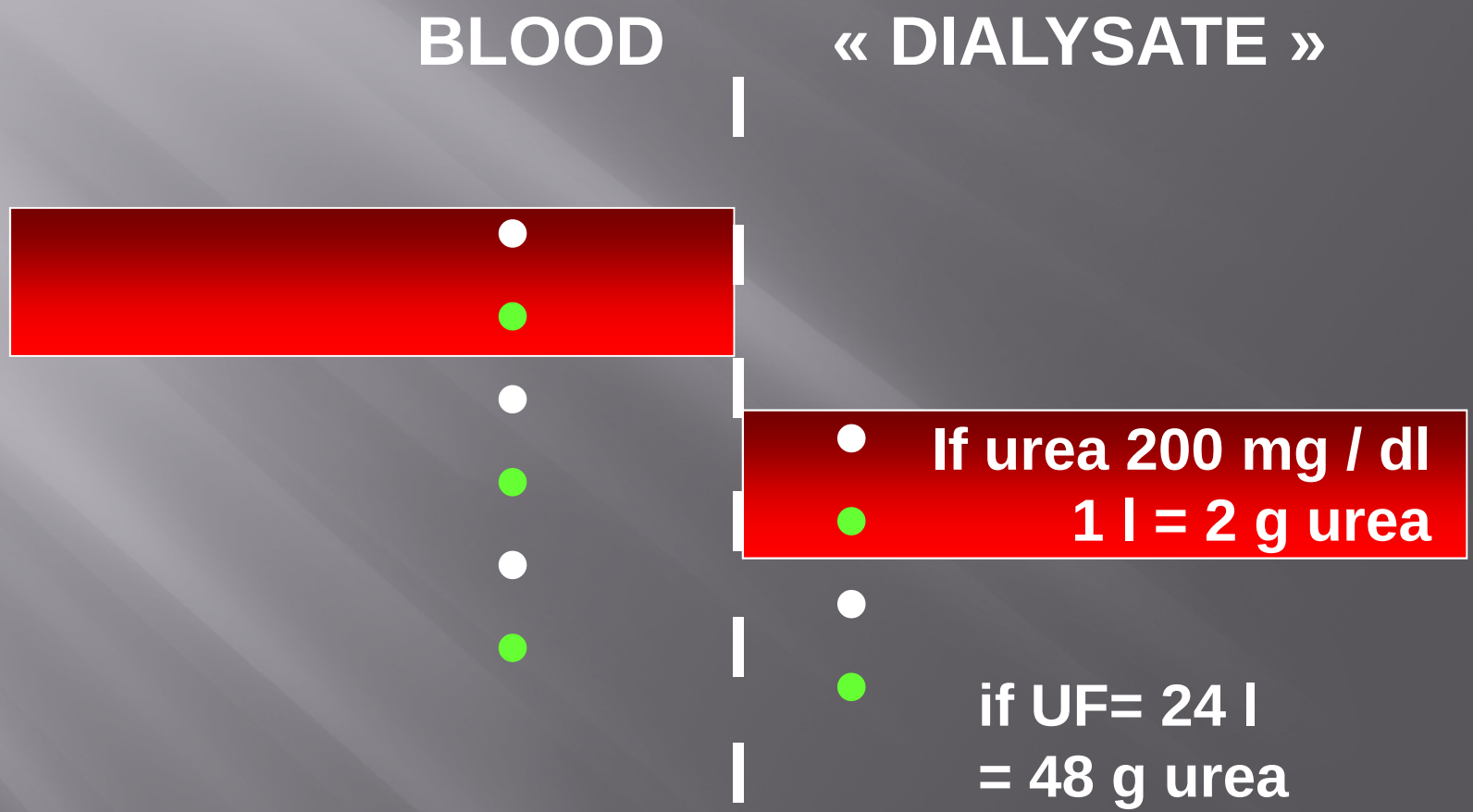


MW (molecular radius) and pores' size !

Gradient of [ ]

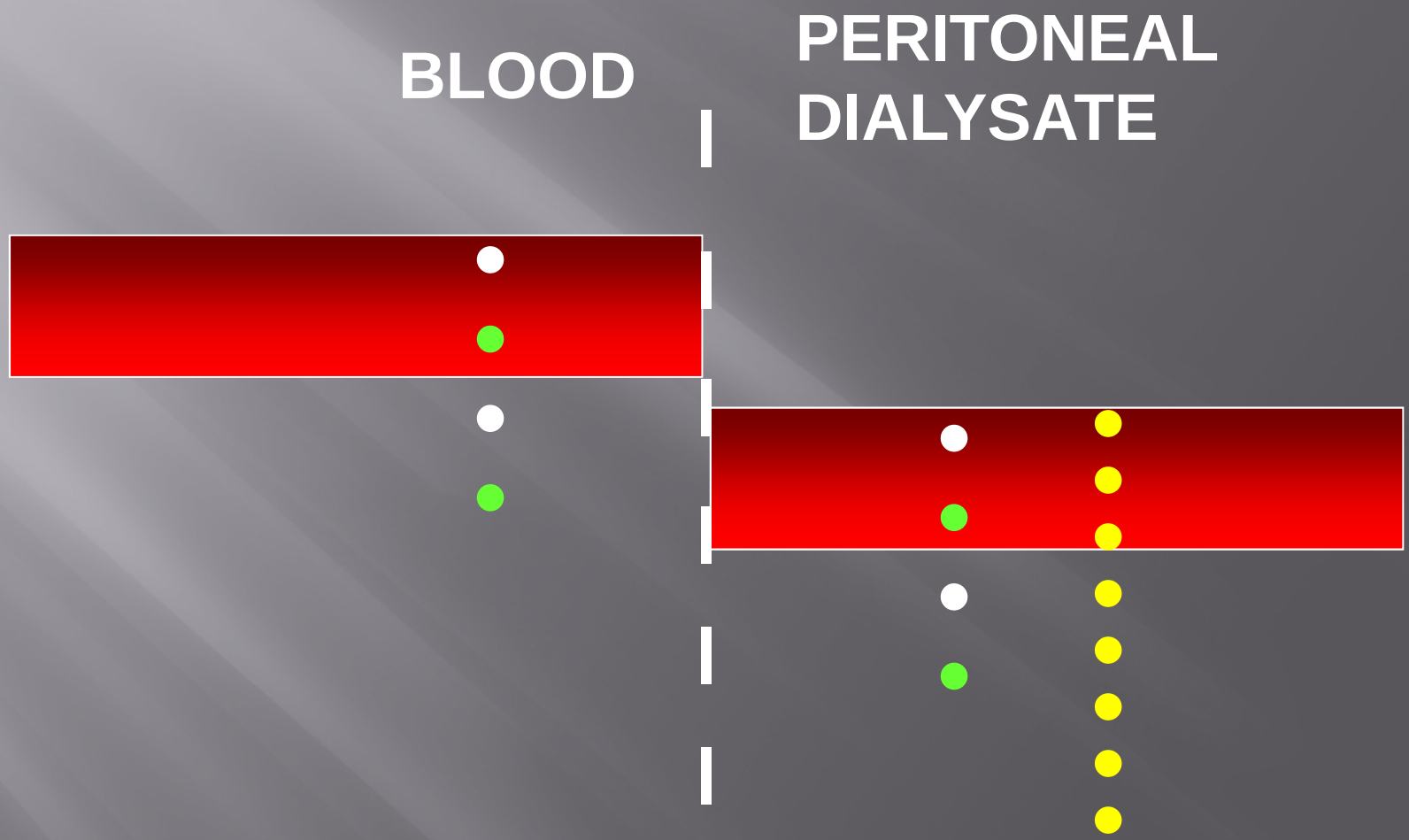

BLOOD
DIALYSATE
K, urea, P, creatinine
Ca
Bicarbonate
DIFFUSION

Pressure gradient



CONVECTION = ULTRAFILTRATION (UF)

Osmotic gradient



CONVECTION = ULTRAFILTRATION (UF)

Use of these principles

DIFFUSION	UF	DIFFUSION + UF
HD without UF	UF only	HD + UF
PD without UF	CAVH	CAVHD
	CVVH	CVVHD
	HF	PD + UF

Hemodialysis efficacy

enhanced by

- ↗ blood flow
- ↗ surface of dialyzer
- ↗ dialysate flow
- ↗ duration of session

reduced by

- clotting within HD circuit / filter
- recirculation of vascular access
- protein-coating of high-flux membranes
- saturation of (recirculating) dialysate
- high-protein binding of toxic agent
- (high molecular weight of toxic agent)

HD : efficacy or effectiveness ?

- A high volume of distribution of the toxic
  - limits effectiveness
  - increases rebound
- A high « spontaneous » (renal, …) clearance of the toxic also limits effectiveness ! (lithium, …)
- A long delay between intake and HD is another important factor

Hemofiltration efficacy

enhanced by

- (blood flow)
- (surface of dialyzer)
- (dialysate flow)
- ↗ duration of session
- higher volume of UF
- postdilution versus predilution

reduced by

- (clotting within HD circuit / filter)
- (recirculation of vascular access)
- (protein-coating of HF membrane)
- (saturation of (recirculating) dialysate)
- high-protein binding of toxic agent
- (high molecular weight of toxic agent)

Hemoperfusion or MARS efficacy ?

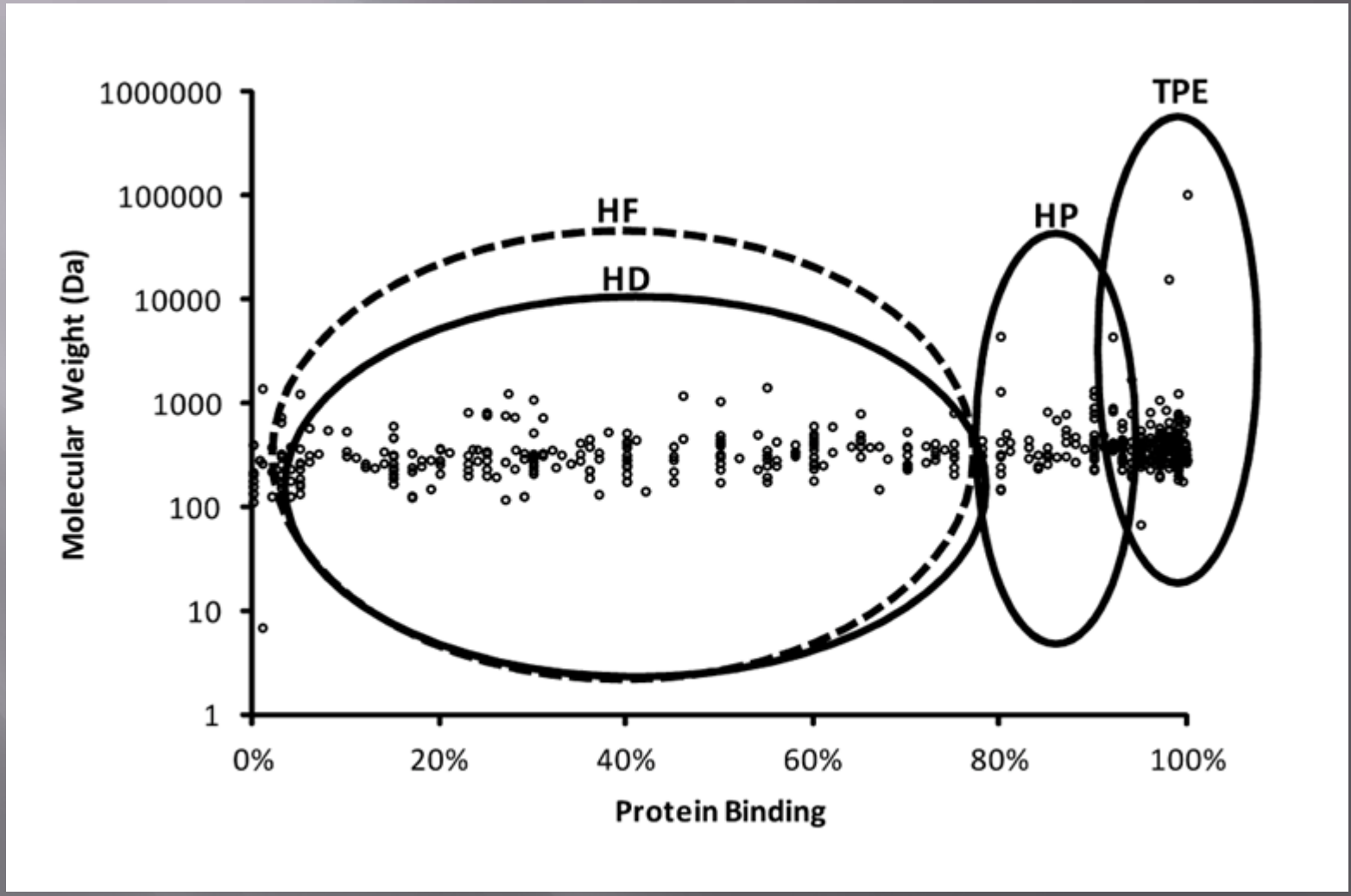
enhanced by

- **↗ blood flow**
- **↗ duration of session**

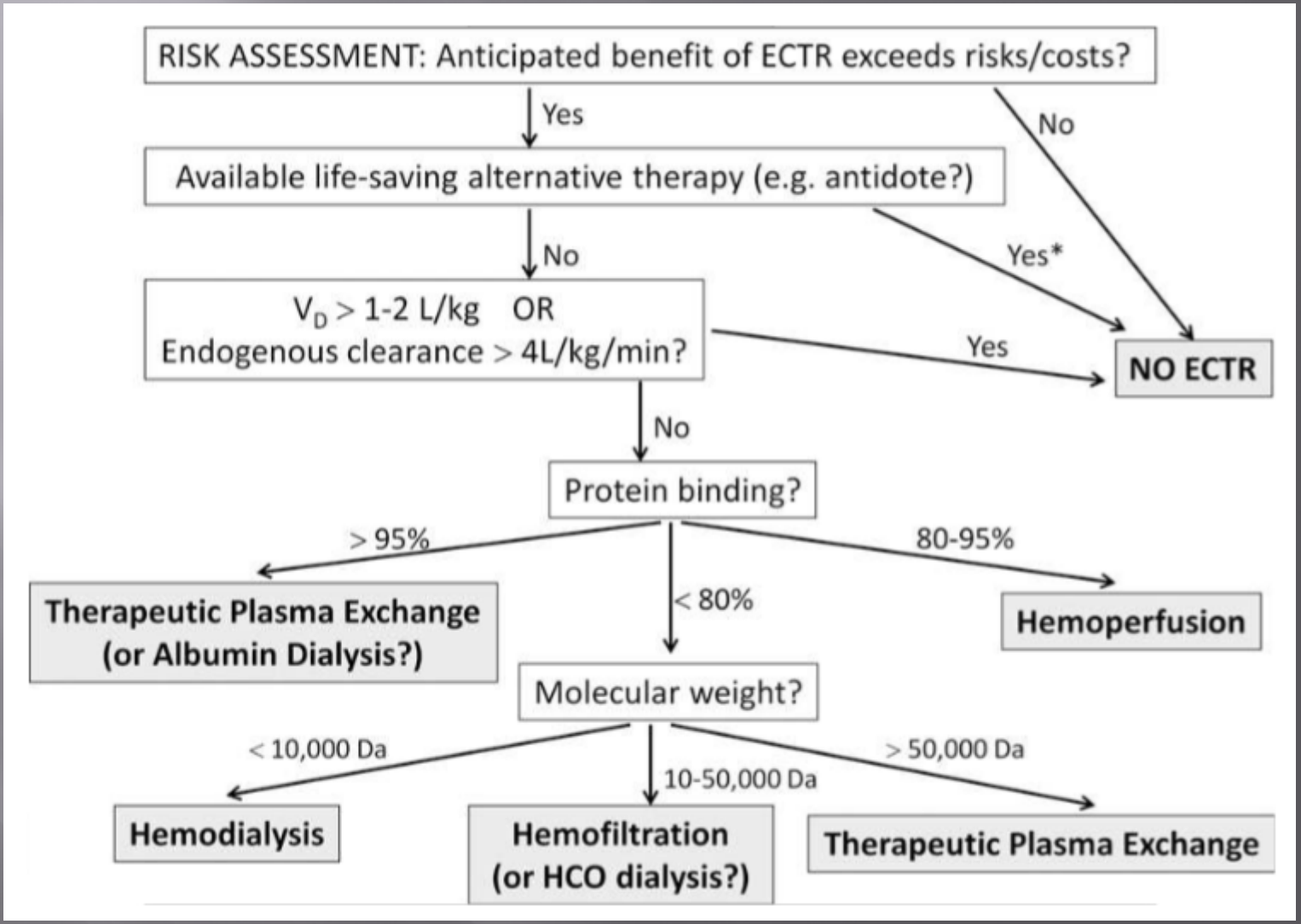
reduced by

- **saturation of charcoal/resin**
- **clotting within circuit/sorbent**

Which is the most appropiate technique for a single substance?



Some theoretical flow chart



Maximal clearance & techniques

ECTR	Conditions	Max CL (mL/min)
PD	2L exchange every hour, 50% equilibration of dialysate compared to plasma	16
TPE	QB = 140 mL/min and a plasma removal rate 50 mL/min	50
IHD/HF/HP	QB = 400 mL/min, HCT = 40%, ER = 100%	240
CRRT	QB = 180 mL/min, high volume CRRT (effluent flow = 45 mL/hr/kg), weight = 70 kg	52
ET	1L whole blood exchanged/hour, HCT = 40%	10

Methanol poisoning

Recommendations for the Role of Extracorporeal Treatments in the Management of Acute Methanol Poisoning: A Systematic Review and Consensus Statement

Roberts, Darren M. PhD, FRACP[1,2]; Yates, Christopher MD[3]; Megarbane, Bruno MD[4]; Winchester, James F. MD[5]; Maclaren, Robert PharmD[6]; Gosselin, Sophie MD[7]; Nolin, Thomas D. PharmD, PhD[8,9]; Lavergne, Valéry MD[10]; Hoffman, Robert S. MD[11]; Ghannoum, Marc MD[12]; on behalf of the Extracorporeal Treatments in Poisoning Workgroup

Weak level of evidence D!

- In the presence of at least one of the following criteria: coma, seizures, visual disorders, metabolic acidosis with pH<7.15, persisting metabolic acidosis despite optimal support and antidotal therapy, anion gap >24 mmol/L;
  - Or (relative criteria): MetOH blood concentration > 700 mg/L and treatment by fomepizole, MetOH blood concentration > 600 mg/L and treatment by ethanol, MetOH blood concentration > 500 mg/L in the absence of therapy blocking ADH
- Epuration may be stopped when MetOH < 200 mg/L
- The absolute priority is to block the activity of ADH, before considering the indication for extracorporeal epuration
- Extrarenal epuration may contribute to the correction of metabolic acidosis and to the elimination of both MetOH and formic acid, but no study was able to demonstrate that it could improve either the vital or functional (visual) prognosis

Methanol poisoning

Does IHD clear formate?

- Retrospective review of the medical records of the methanol poisoned patients treated in the ICU
- Inclusion criteria: history of deliberate methanol ingestion, with a blood methanol concentration greater than 6.2 mmol/L or a high anion gap metabolic acidosis
- Data extracted and analyzed independently by two physicians; analyzable data obtained for 25 patients
  - Mean initial blood methanol 71.4 mmol/L (range 8.7-321.4 mmol/L)
  - Mean initial plasma formate 12.6 mmol/L (range 0.33-22.4 mmol/L)
  - Good correlation between plasma formate and bicarbonate (r^2=0.52)
  - Mean duration time of HD 10.2±6.6 hr
  - Formate half-life before HD or in the absence of HD 6.03±3.25 hr
  - Formate half-life elimination during HD 1.80±0.77 hr (p=.004)
  - Formate half-life elimination after HD 3.89±1.97 hr (similar to the values observed before or in the absence of HD)

(Hantson, Hum Exp Toxicol, 2005)

Intermittent hemodialysis versus CVVHD(F)

- 24 patients intoxicated by methanol during the last mass poisoning in 2012 in Czech Republic
  - 11 treated byHDI, 13 by CVVHD or CVVHDF

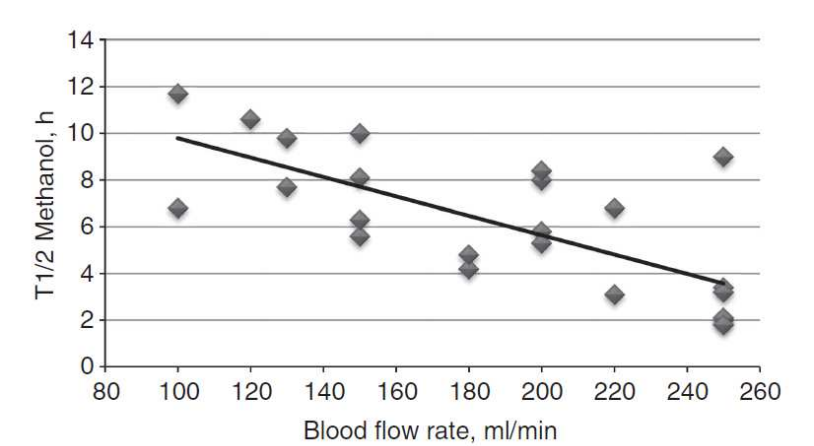


Figure 1 | Elimination half-life of methanol versus blood flow rate ($y = -0.04x + 13.9$, $R^2 = 0.52$).

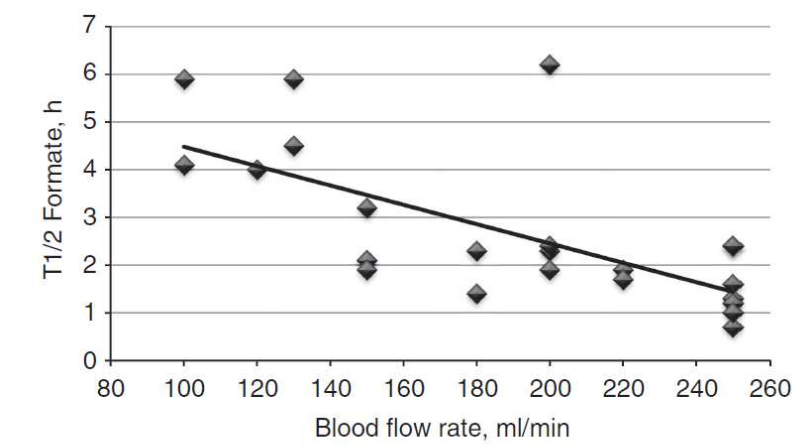


Figure 2 | Elimination half-life of formate versus blood flow rate ($y = -0.02x + 6.5$, $R^2 = 0.44$).

(Zakharov et al., Kidney Int, 2014)

Intermittent hemodialysis versus CVVHD(F)

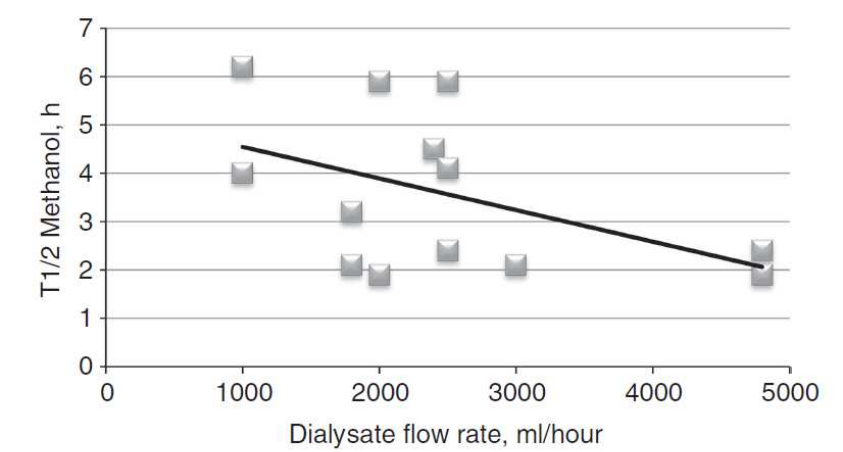


Figure 3 | Elimination half-life of methanol versus dialysate flow rate on CVVHD/HDF ($y = -0.0011x + 10.91$, $R^2 = 0.12$).

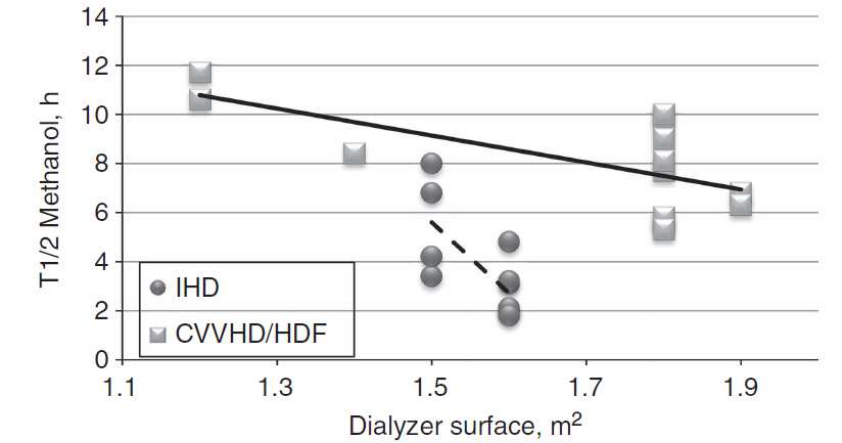


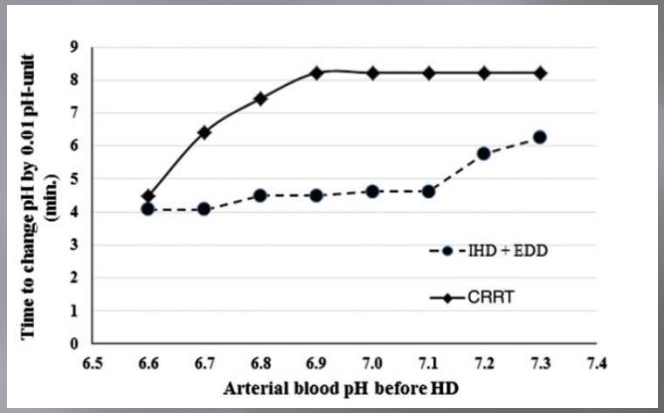
Figure 4 | Elimination half-life of methanol versus dialyzer membrane surface ($y = -5.49x + 17.37$, $R^2 = 0.44$).

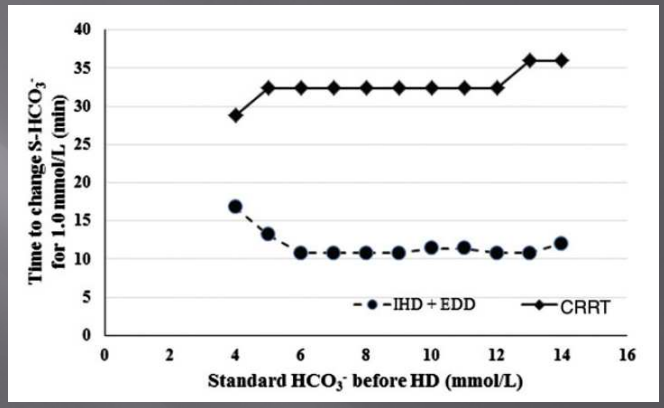
- Clear superiority of intermittent HD over CVVHD(F) for the elimination of both methanol and formic acid
- How to optimize dialysis?: by increasing blood flow during intermittent HD and blood flow and dialysis rate during CVVHD(F)
- Which is the optimal duration for epuration? At least 8 h for intermittent HD and 18 h for CVVHD(F)
- Better to continue antidotal treatment for at least 12-24 h after the end of dialysis

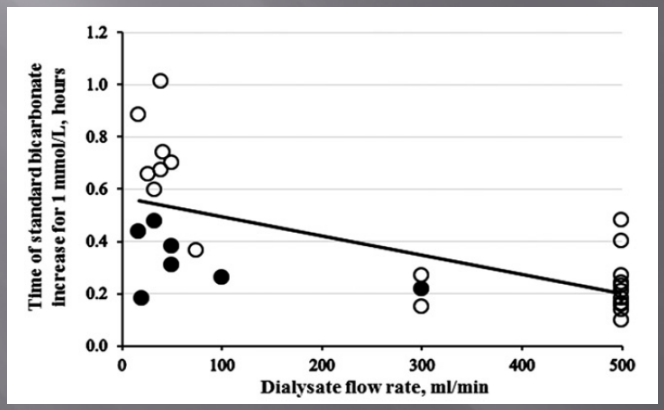
(Zakharov et al., Kidney Int, 2014)

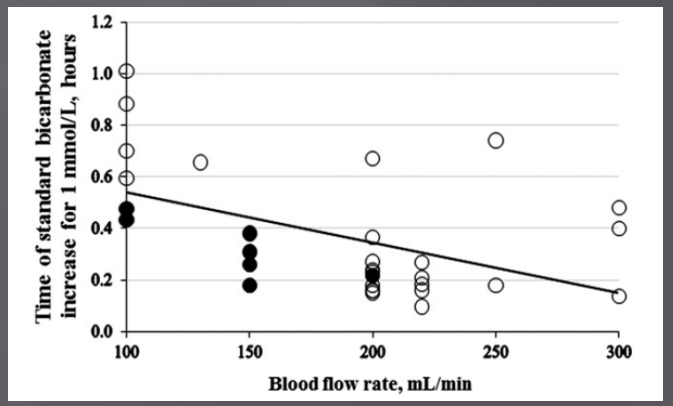
Efficiency of acidemia correction on IHD versus CRRT

- Observational cohort study (Czech), 18 pts treated with IHD and 13 pts treated with CRRT









(Zakharov et al., Clin Tox, 2017)

Intermittent hemodialysis & methanol: precautions

- What about antidotal treatment during extrarenal epuration?
  - 26 patients admitted to the ICU for acute methanol poisoning (Hantson et al., 2002)
    - 2 treated by 4-MP (+ 2 partially)
    - Ethanol used as antidote in 24 patients
    - Intermittent HD used in 19 patients (17 patients receiving ethanol)
      - Blood ethanol level < 1 g/l in 2 consecutive blood samples during intermittent HD = 12 patients (70.6%)
  - Isolated observations of 4-MP kinetics during intermittent HD or CVVH:
    - Mean clearance 4-MP: 216 ml/min during intermittent HD and 51 ml/min during CVVHD
  - 4-MP: empiric recommendations
    - Intermittent HDI 1 - 1.5 mg/kg/h, or interval dose reduction of 4 h instead of 12 h, but limited observations suggest that the concentrations remain well above the therapeutic range, no monitoring required
    - CVVHD: dose interval of 8 h, 4-MP blood concentrations well above the therapeutic range

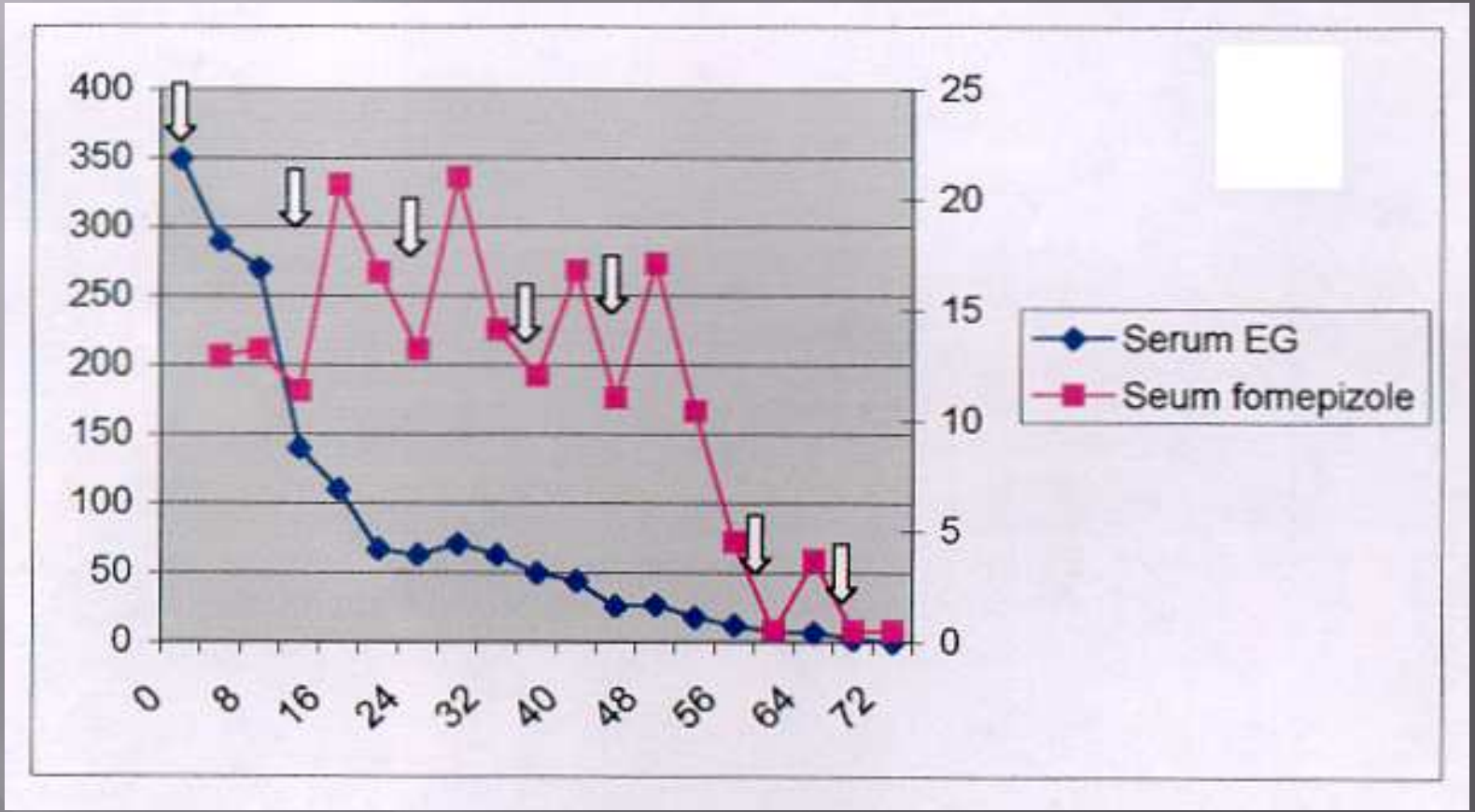
Intermittent hemodialysis & ethylene glycol

- Favourable toxicokinetic profile:
  - PM 62 Da, Vd 0.7 l/kg, no protein binding
  - Clearance EG by HD: 145 - 210 ml/min vs 17 - 39 ml/min by the kidney
  - Clearance glycolate HD: 167 ml/min
- Criteria for HD:
  - Severe metabolic acosis and CNS disorders
  - Acute renal failure, oliguria
  - Ethylene glycol > 0.5 - 1 g/l: relative indication!
- However, they are numerous publications of EG poisoning treated by antidote alone without hemodialysis
  - According to the clinical severity at presentation (patient poorly symptomatic or asymptomatic, absence of significant metabolic acidosis)
  - Availability of the different epuration techniques
  - Choice of the antidote with the most secure profile

Ethylene glycol: can we treat without HD?

- 5-month child (7 kg): accidental adminsitration by the mother of two feeding bottles prepared with an antifreeze solution that was stored in the kitchen !
- Lethargia, polypnea 45/min. Admitted within 6 h after ingestion
- Increased anion gap (31 mmol/l) and osmol gap (91 mmol/l). Blood EG concentration on admission: 350 mg/dl.
- Preserved renal function: creatinine 0.2 mg/dl
- Fomepizole 15 mg/kg iv and bicarbonate 3 mEq/kg, then 10 mg/kg every 12 h for a total of7 doses.
- Full correction of metabolic acidosis < 6 h
- No need for intermittent HD, normal renal function
- Full recovery and discharge at day 4

Ethylene glycol: can we treat without HD?



(Detaille et al., Pediatr Crit Care Med, 2004)

Salicylate poisoning

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Darren M. Roberts, PhD, FRACP[1,2]; Christopher Yates, MD[3]; Bruno Megarbane, MD[4]; James F. Winchester, MD[5]; Robert Maclaren, PharmD[6]; Sophie Gosselin, MD[7]; Thomas D. Nolin, PharmD, PhD[8,9]; Valéry Lavergne, MD[10]; Robert S. Hoffman, MD[11]; Marc Ghannoum, MD[12]; on behalf of the Extracorporeal Treatments in Poisoning Workgroup

Weak level of evidence D!

- Epuration recommended in the presence of the following criteria :
  - Salicylates > 100 mg/dL
  - Salicylates > 90 mg/dL and renal dysfunction
  - Alteration of consciousness
  - Gas exchanges impairment needing correction
- Epuration suggested, after the failure of supportive therapy (bicarbonate,…) in the presence of one of the following criteria :
  - Salicylates > 90 mg/dL
  - Salicylates > 80 mg/dL and renal dysfunction
  - Arterial pH < 7,20
- When to stop ?
  - Following clinical improvement and salicylates < 20 mg/dL or duration of epuration of at least 4-6 h if blood concentration not available
- Which technique ?
  - Intermittent HD rather than hemoperfusion or CVVH
- Follow supportive therapy with sodium bicarbonate infusion

Metformin poisoning

Extracorporeal Treatment for Metformin Poisoning: Systematic Review and Recommendations From the Extracorporeal Treatments in Poisoning Workgroup

Calello, Diane P. MD[1]; Liu, Kathleen D. MD, PhD[2]; Wiegand, Timothy J. MD[3]; Roberts, Darren M. PhD, FRACP[4]; Lavergne, Valéry MD[5]; Gosselin, Sophie MD[6]; Hoffman, Robert S. MD[7]; Nolin, Thomas D. PharmD, PhD[8]; Ghannoum, Marc MDCM[9]; on behalf of the Extracorporeal Treatments in Poisoning Workgroup

Weak level of evidence D!

- Epuration recommended when :
  - Lactate > 20 mmol/l
  - Arterial pH < 7,0
  - Failure of supportive therapy (with all the required therapy, including mechanical ventilation, vasopressors, bicarbonate…)
- Epuration suggested when :
  - Lactate between 15 and 20 mmol/l
  - Arterial pH 7,0-7,1
- Situations suggesting strongly epuration:
  - Acute renal failure, shock, alteration of consciousness, acute hepatic failure
- When to stop ?
  - Lactate < 3 mmol/l and pH > 7,35
- Which technique ?
  - Start ASAP with intermittent DI rather than CVVH, follow by intermittent HD or CVVH

Theophyllin poisoning

Extracorporeal treatment for theophylline poisoning: Systematic review and recommendations from the EXTRIP workgroup

MARC GHANNOUM,[1] TIMOTHY J. WIEGAND,[2] KATHLEEN D. LIU,[3] DIANE P. CALELLO,[4] MELANIE GODIN,[5] VALERY LAVERGNE,[6] SOPHIE GOSSELIN,[7] THOMAS D. NOLIN,[8] and ROBERT S. HOFFMAN[9]; ON BEHALF OF THE EXTRIP WORKGROUP

Weak level of evidence D!

- Epuration recommended when :
  - [Theophyllin] > 100 mg/L in case of acute exposure (1C)
  - Convulsions
  - Life-threatening cardiac arrhythmias
  - Shock
  - Increasing blood concentrations despite optimal therapy
  - Clinical worsening despite optimal therapy
- Epuration suggested when :
  - [Théophylline] > 60 mg/L in case of chronic exposure
  - Age < 6 months or > 60 years and [theophyllin] > 50 mg/L in case of chronic exposure
  - Impossibility to perform gastrointestinal epuration
- When to stop ?
  - Clinical improvement or [theophyllin] < 15 mg/L
- Which technique ?
  - Preferably intermittent HD rather than hemoperfusion or CVVH

Valproate poisoning

Extracorporeal treatment for valproic acid poisoning: Systematic review and recommendations from the EXTRIP workgroup

MARC GHANNOUM,[1] MARTIN LALIBERTÉ,[2] THOMAS D. NOLIN,[3] ROBERT MACTIER,[4] VALERY LAVERGNE,[5] ROBERT S. HOFFMAN,[6] and SOPHIE GOSSELIN[7]; ON BEHALF OF THE EXTRIP WORKGROUP*

Weak level of evidence D!

- Epuration recommended in the presence of one of the following criteria :
  - Blood concentration > 1300 mg/L
  - Brain edema or shock clearly in relationship with VPA
- Epuration suggested in the presence of one of the following criteria:
  - Blood concentration > 900 mg/L
  - Coma or respiratory depression requiring mechanical ventilation
  - Acute hyperammonemia
  - Arterial pH < 7,10
- When to stop ?
  - Clinical improvement or blood concentration between 50 and 100 mg/L
- Which technique ?
  - Preferably intermittent HD, alternatively hemoperfusion or CVVH

Lithium poisoning

Extracorporeal Treatment for Lithium Poisoning: Systematic Review and Recommendations from the EXTRIP Workgroup

Weak level of evidence D!

- Epuration recommended when :
  - Acute renal dysfunction and [Li(+)] > 4 mEq/L
  - Or presence of altered consciousness, seizures, life-threatening cardiac arrhythmias, independently of [Li(+)]
- Epuration suggested in the presence of one of the following criteria :
  - [Li(+)] > 5,0 mEq/L
  - Presence of major mental confusion
  - Estimated delay to achieve [Li(+)] < 1,0 mEq/L more > 36 h
- When to stop ?
  - After evidence of clinical improvement or [Li(+)] < 1,0 mEq/L, duration of epuration at least 6 h if [Li(+)] not available
- Which technique ?
  - Preferably intermittent HDI rather than CVVHD

Lithium poisoning

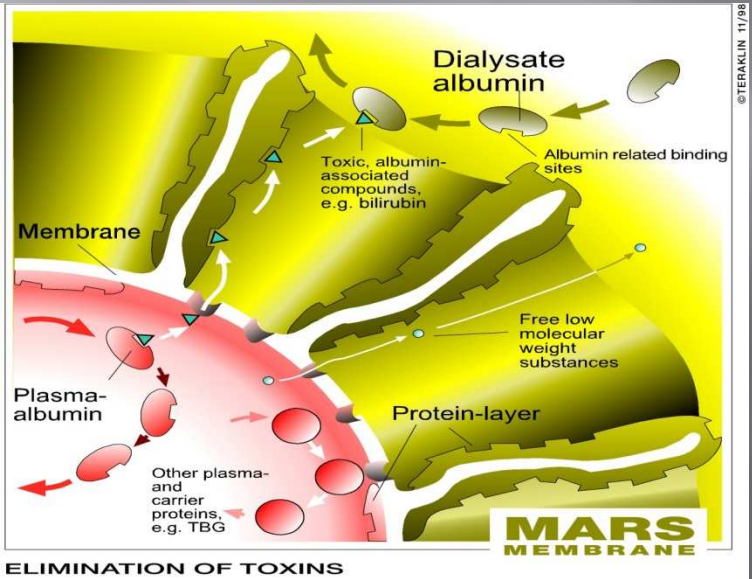
- Retrospective cohort study of 128 lithium-poisoned patients (10% acute, 63% acute-on-chronic, 27% chronic)
- Severity defined according to Hansen's criteria: severe= seizures or catecholamine infusion or mechanical ventilation or fatality in the ICU
- Univariate analysis of predictive factors of poisoning severity:
  - GCS < 10
  - Serum lithium ≥ 5,2 mmol/L
- Univariate analysis of predictive factors for ECTR use:
  - Serum lithium ≥ 5,2 mmol/L
  - Serum creatinine ≥ 200 µmol/L
- No difference in mortality
- Only 21/46 with potential ECTR criteria were actually treated by ECTR
  - No change in ICU stay, more prolonged neurological symptoms

(Megarbane et al., Clin Tox, 2016)

MARS for poisoning with or without hepatic failure

Use of the molecular adsorbent recirculating system (MARS^{TM}) for the management of acute poisoning with or without liver failure

XAVIER WITTEBOLE and PHILIPPE HANTSON

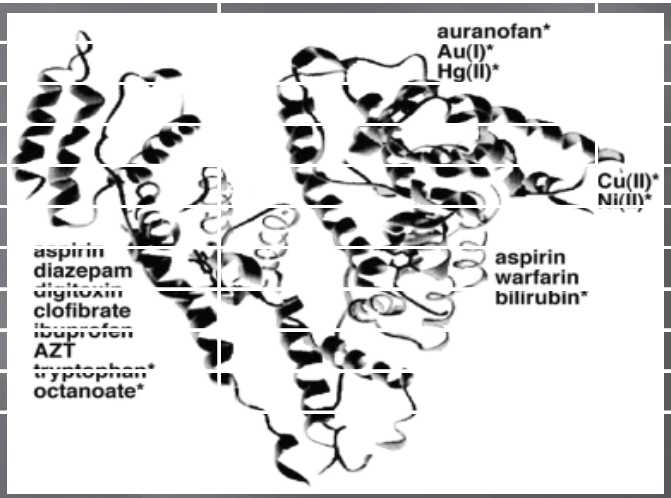


- Different situations according to the presence or not of acute hepatic failure
  - MARS and acute hepatic failure following paracetamol or amanita poisoning
    - Does not modify toxicokinetics
    - Does not influence mortality, no RCT
    - Trend to an improvement of biochemical, hemodynamic or neurological parameters

- MARS as an epuration technique without concomitant acute hepatic failure
  - Some experimental toxicokinetic data and isolated clinical data with toxins highly bound either to albumin or α1-glycoprotein acid
  - No strong evidence for improvement of toxicodynamics

Drugs protein binding

Albumin	Albumin & AAG	Albumin & lipoproteins	Albumin, AAG and lipoproteins
Ceftriaxone (A)	Alprenolol (B)	Cyclosporine (N)	Amitryptilline (B)
Clindamycine (A)	Carbamazepine (N)	Probucol (N)	Bupivacaine (B)
Clofibrate (A)	Disopyramide (B)		Chlorpromazine (B)
Dexamethazone (N)	Erythromycine (B)		Diltiazem (B)
Diazepam (B)	Lidocaine (B)		Imipramine (B)
Diazoxide (A)	Meperidine (B)		Nortryptilline (B)
Dicloxacilline (A)	Methadone (B)		Propanolol (B)
Digitoxine (N)	Verapamil (B)		Quinidine (B)
Ibuprofen (A)	Tacrolimus (N)		
Indomethacine (A)			
Naproxene (A)			
Oxacillin (A)			
Phenylbutazone (A)			
Phenytoïne (A)			
Probenecide (A)			
Salicylate (A)			
Thiopental (A)			
Tolbutamide (A)			
Acide valproïque (A)			
Warfarine (A)			



A= acid
B= base
N=neutral

Does MARS effectively clear toxins ?

- 3 severe cases of CCB poisoning (8,4 g SR diltiazem, 4,2 g SR diltiazem, 14,4 g SR verapamil)
- Cardiovascular failure and cardiac conduction disturbances unresponsive to fluid resuscitation, calcium salts, glucagon, HIET, and increasing doses of adrenergic agonists
- MARS therapy initiated after respectively 11 and 12 h
- Outcome: weaning of adrenergic agonists agents, decrease of serum lactate, recovery of hemodynamic conditions
- Decrease of serum [drug] during MARS, but does not mean that MARS effectively improved drug clearance
- Is the apparent benefit of MARS related to drug removal or to other factors (removal of NO, pro-inflammatory cytokines,…)

(Pichon et al., Ann Emerg Med, 2012)

Does MARS effectively clear toxins ?

	Admission	+8h	+13h	+15h	+19h	+23h
Blood lactates (mmol/L)	9	20.1	17.3	8.5	2.1	2.0
Norepinephrine and epinephrine (µg/kg/min)	0.34	1.34	1.34	0.32	0.03	0
Plasma levels of diltiazem and desacetyldiltiazem (nmol/L)	- -	6421 1388	4631 2724	4825 2898	3371 1769	3133 1509
Blood pressure (systolic/diastolic) (mmHg)	70/36	79/41	109/63	135/53	143/62	132/65

+10h +16h MARS®

- 55-yr-old woman, admitted 4 h after ingestion of 28*300 mg extended release diltiazem
- Shock, bradycardia, oliguria
- Lactic acidosis, acute kidney injury
- Refractory to max supportive therapy
- MARS started 8 h after admission
- Early improvement of hemodynamic conditions, weaning from vasopressors

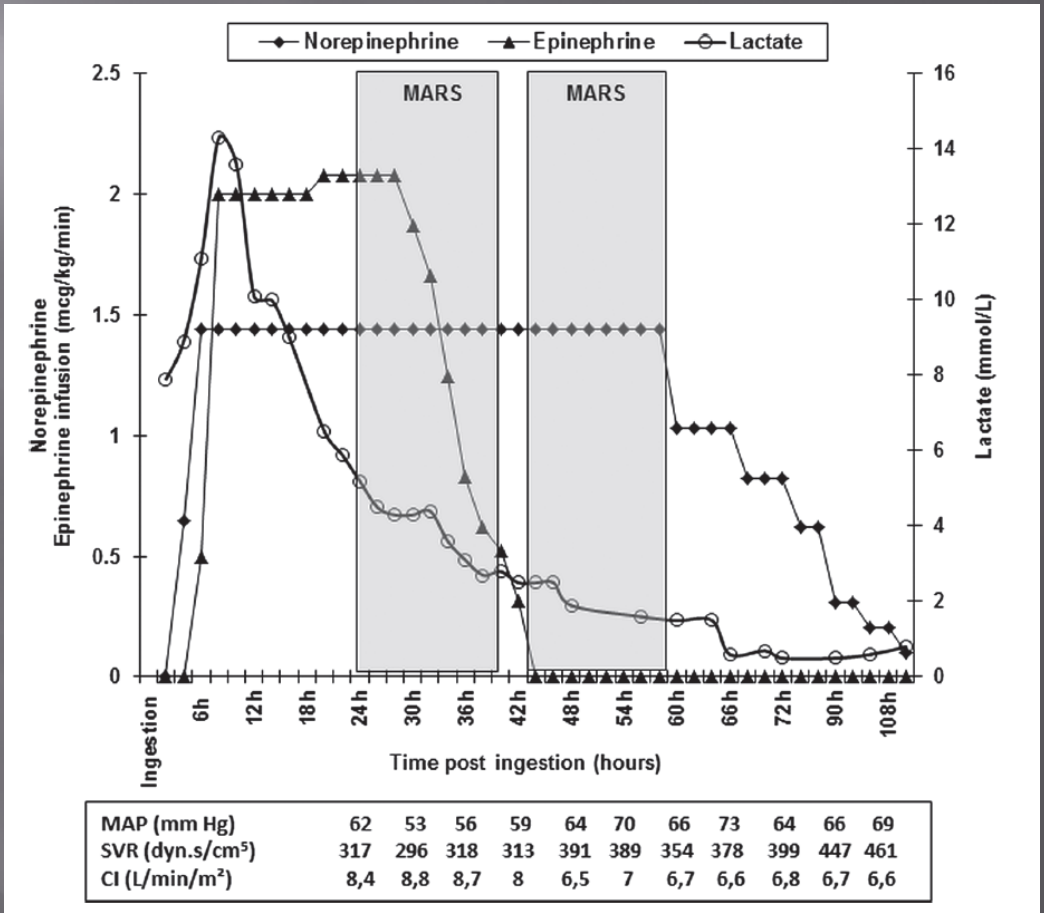
(Pichon et al., Clin Tox, 2006)

Does MARS effectively clear toxins ?

Mixed amlodipine/valsartan overdose treated by the molecular adsorbent recirculating system (MARS™)

Ludovic Gérard[a], Anne-Cécile Galloy[b], Arnaud Capron[c] & Philippe Hantson[ad]

- Severe poisoning by amlodipine-valsartan with refractory vasoplegia
- Amount ingested by history : 480 mg amlodipine et 3680 mg valsartan
- Both drugs are highly protein-bound (>90%)



MAP (mm Hg)	62	53	56	59	64	70	66	73	64	66	69
SVR (dyn.s/cm⁵)	317	296	318	313	391	389	354	378	399	447	461
CI (L/min/m²)	8,4	8,8	8,7	8	6,5	7	6,7	6,6	6,8	6,7	6,6

Does MARS effectively clear toxins ?

Mixed amlodipine/valsartan overdose treated by the molecular adsorbent recirculating system (MARS™)

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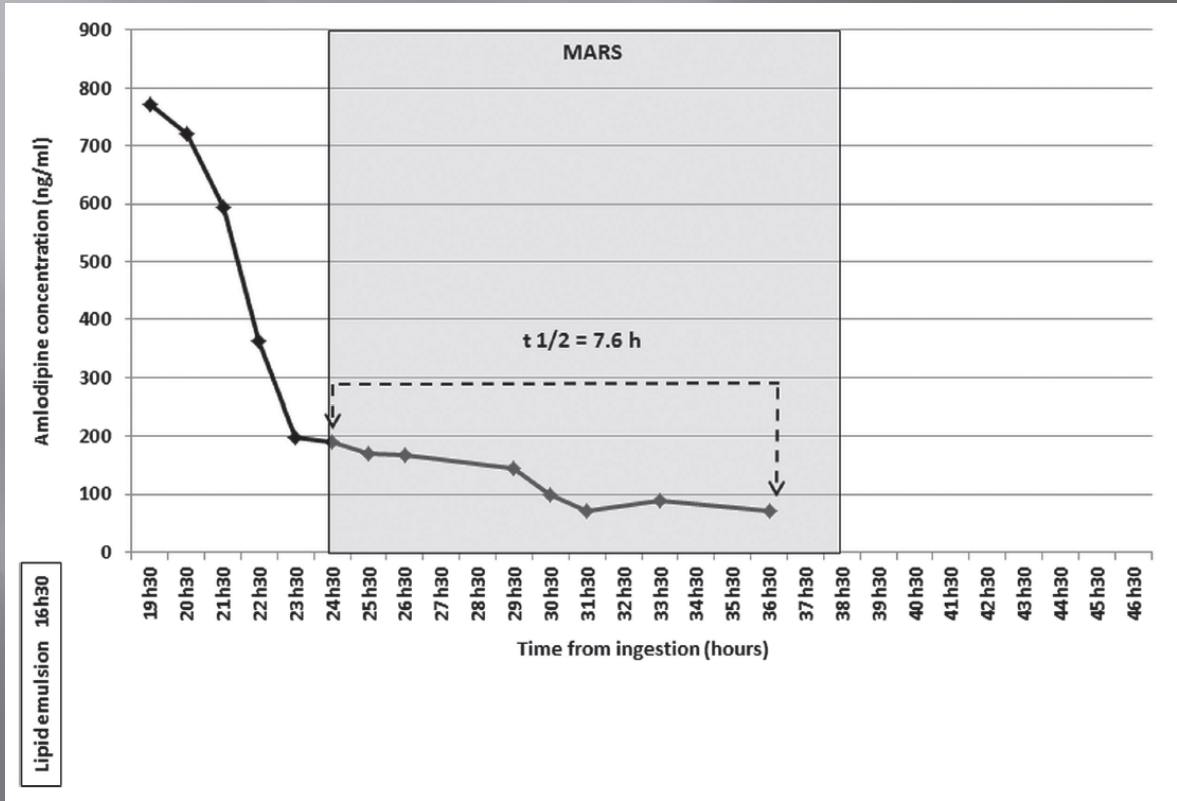


- Short elimination half-life (but reflecting total clearance = renal + extracorporeal + metabolic)
- Plasmatic clearance of the circuit: 32,3 ml/min
- Mean extraction coefficient 24,9%
- Elimination in the hemodialysis tank: 1636.2 µg! Cf. ingested dose

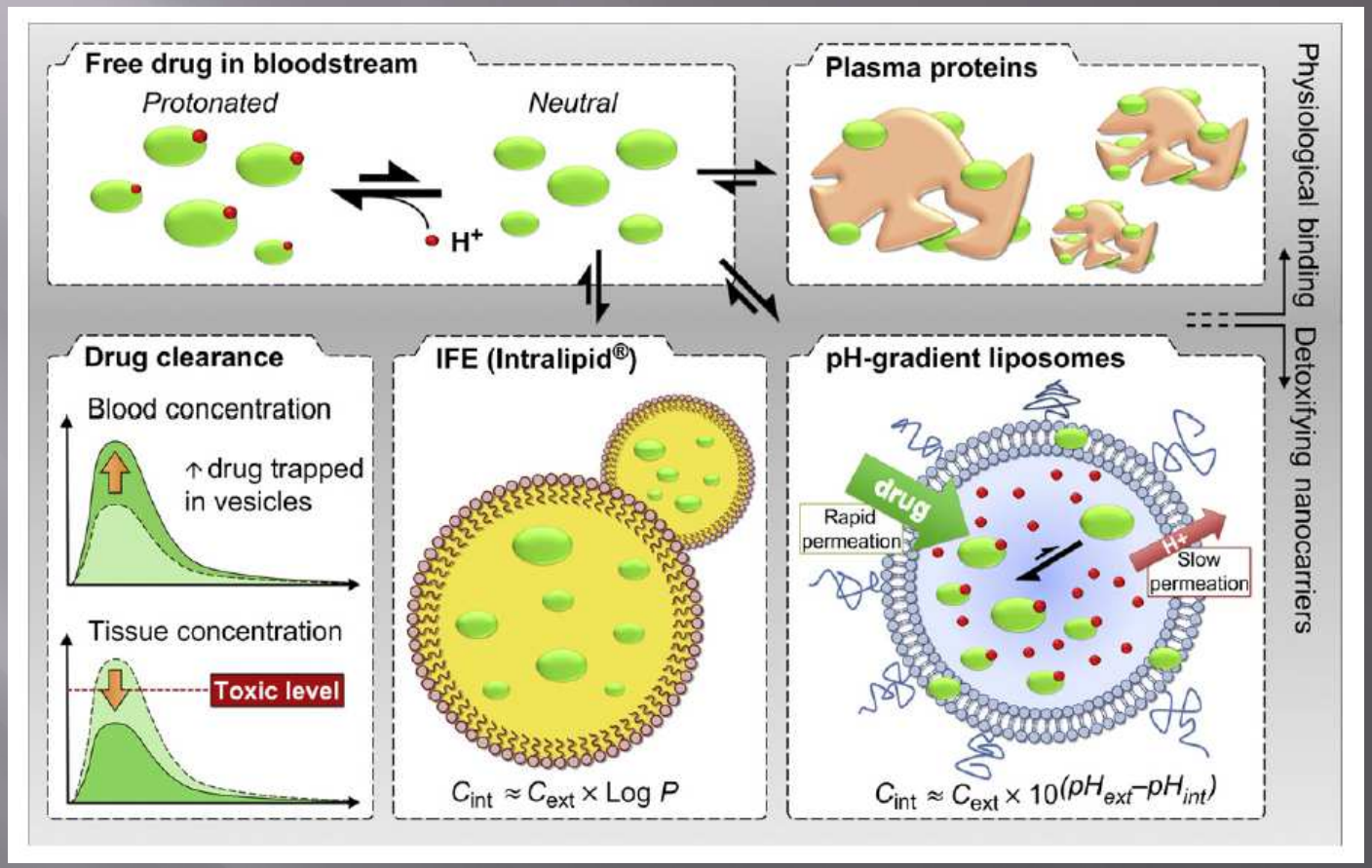
MARS and Amanita poisoning

- Isolated case reports dealing with a potential benefit of MARS
  - Great variation in the delay for MARS therapy
  - Great variation in the duration of MARS sessions
  - MARS as a prophylactic therapy to prevent the development of multiple organ failure?
  - MARS as a rescue therapy for the patients fulfilling the criteria for liver transplantation? (bridge to transplantation)?
  - To date, no evidence that MARS could influence mortality in ALF (some data suggest an improvement of neurological or hemodynamic condition while awaiting for LTx)
  - MARS is probably safe, but certainly expensive

Drug scavenging liposomes

- Liposomes are hollow, spherical, self-closed structures formed by concentric lipid bilayers surrounding an aqueous core
- Size from nanometers to micrometers
- Liposomes can be prepared with a transmembrane pH-gradient. With an acidic internal compartment in the liposomal core, it would be possible to enhance the sequestration of basic substances
- pH-gradient liposomes can sequester virtually any low-molecular weight, weakly-basic agent, with a possible sequestration of a broad range of drugs including CCB, antipsychotics, antidepressants and opioids
- Experimental data suggest that scavenging liposomes can be safely administered either intravenously or by peritoneal dialysis

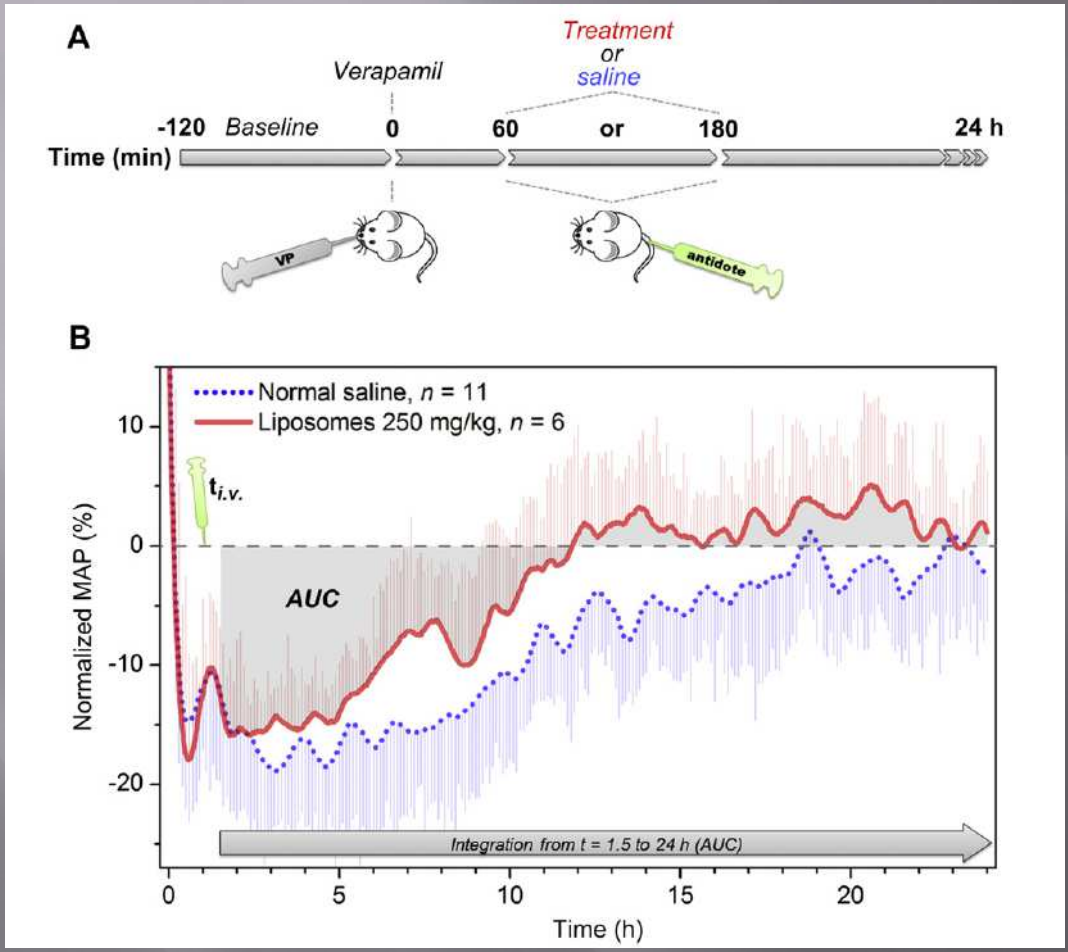
Drug scavenging liposomes



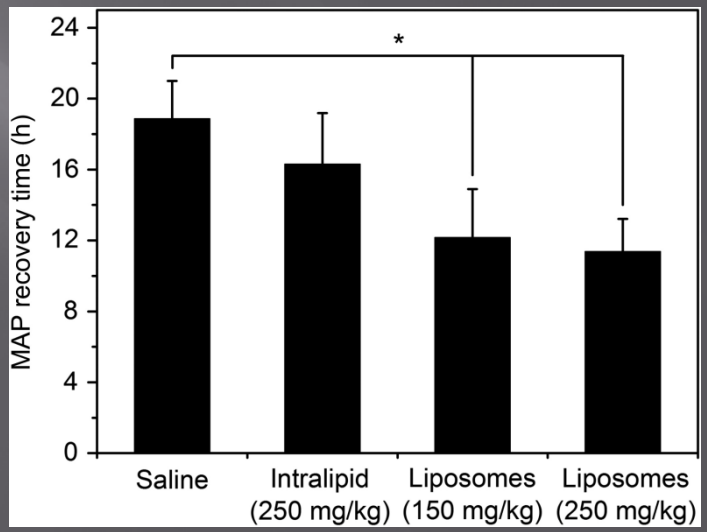
Strategies with nanocarriers, based either on lipid emulsion or on a pH difference driving force

(Forster et al., Biomaterials, 2012)

Drug scavenging liposomes

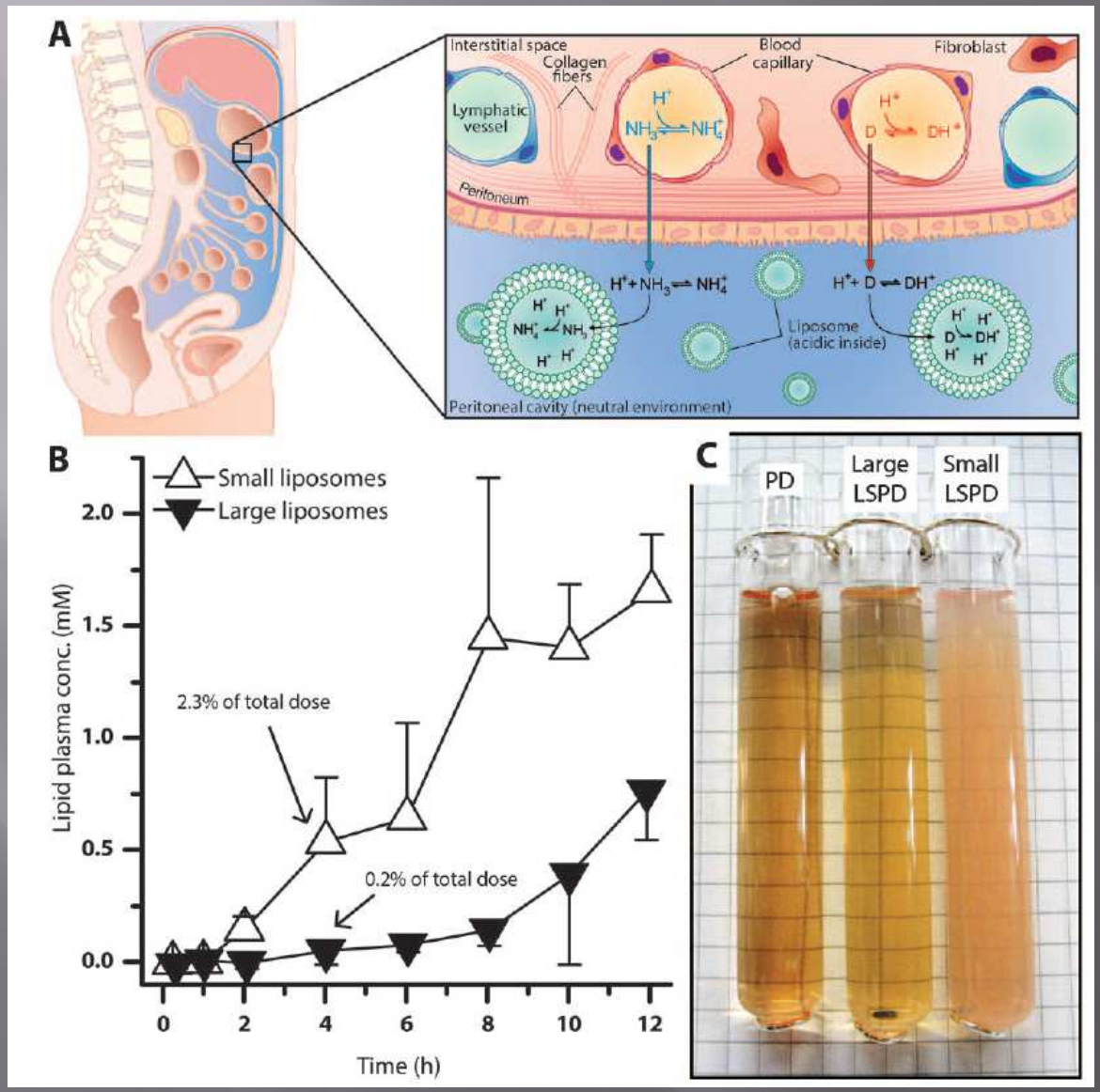


Experimental rat model of VP poisoning
Treated by intravenous ILE, liposomes or NS



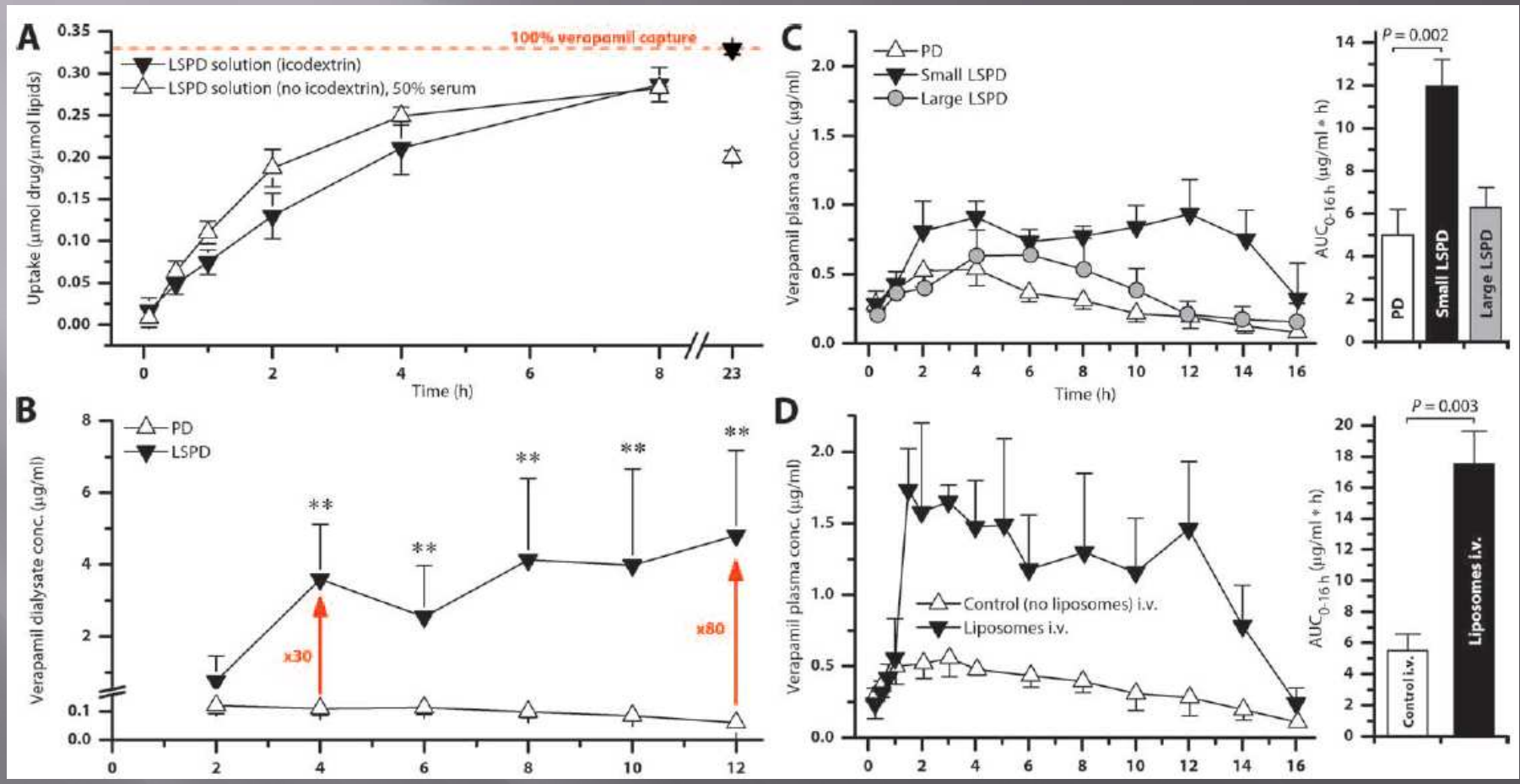
(Forster et al., Biomaterials, 2012)

Drug scavenging liposomes



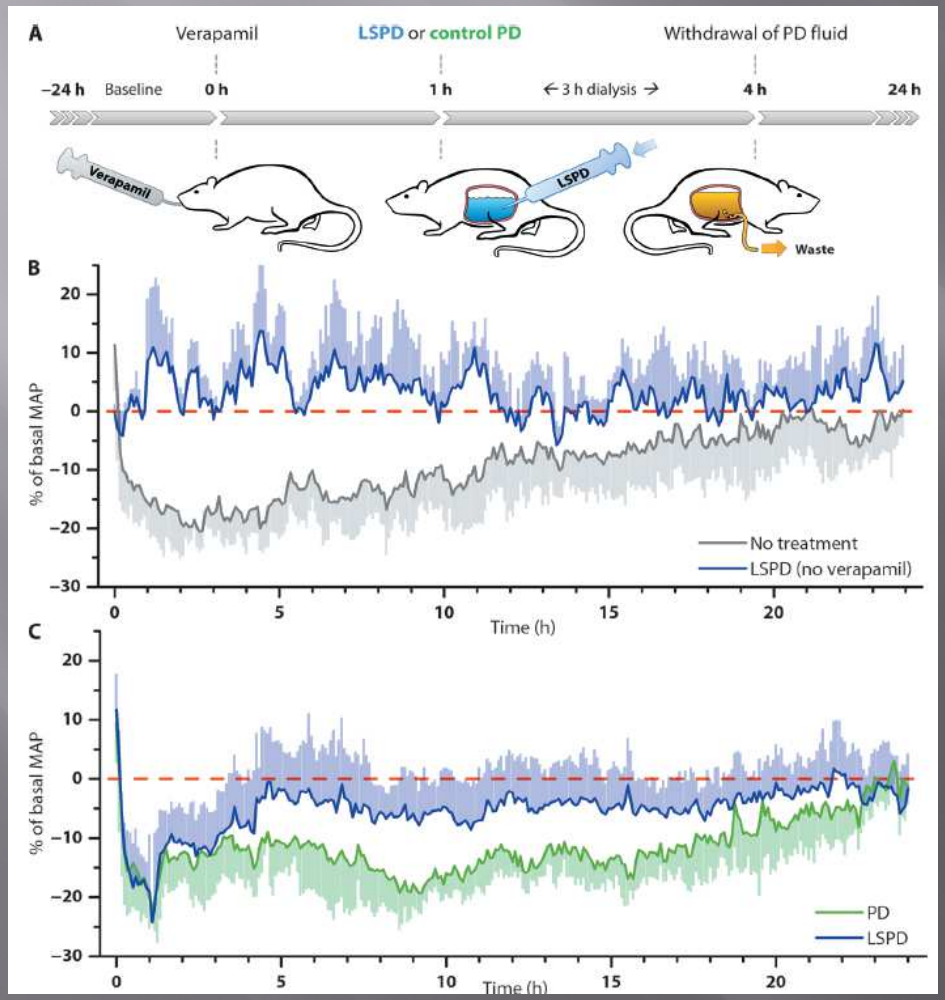
Development of a liposome-supported peritoneal dialysis

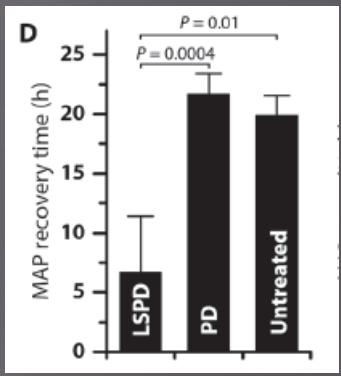
Drug scavenging liposomes

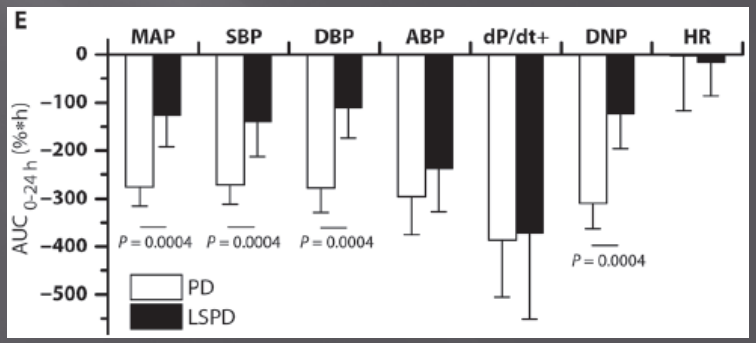


Drug scavenging liposomes

- Experimental model of verapamil poisoning in rats, treated with liposome-supported peritoneal dialysis







Conclusions

- The levels of evidence supporting the extracorporeal elimination techniques remain weak
- Some recommendations have emerged for a limited number of toxic substances with a very high toxic potential (mortality). In most instances, the indications are based on the severity of clinical criteria
- Recent techniques are still under investigation (MARS, scavenging liposomes,…) but further validation is needed
- With rare etiologies of poisoning, with very limited toxicokinetic data, clinicians are strongly encouraged to collect high-quality kinetic data in order to improve the interpretation of PK-PD relationships