ECMO and ECTR in poisonings

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Classification of treatments in medical toxicology

1- Supportive treatment

2- Prevention of absorption (GI decontamination)

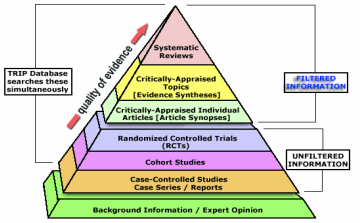
3- Enhancement of elimination

4- Antidotes

➡ With supportive treatment alone, spontaneous recovery usually occurs (98% of the poisonings in ICU).

Ellenhorn MJ. Ellenhorn's Medical Toxicology

What are the evidence to support the benefit of ECTR and ECMO and improve patient's outcome?



Low evidence data - no randomized prospective study

The poisoned patient requiring extracorporeal elimination

Only 0.04% of poisonings require renal extracorporeal support. When required, the technique should be available within a short time.

Goldfarb DS. Goldfrank's Toxicologic Emergencies

Intermittent HD

The patient in the nephrology department

Intermittent HD or CRRT

The poisoned patient in the ICU in the real life

Which poisonings to treat with extracorporeal elimination?

Decisions have to rely on:
- Knowledge of the technique principles and drug kinetics.
- Reports with removal kinetics (before, during, and after elimination)

⬇

Extracorporeal renal support should be considered

1- Poisoning with a drug which elimination could be enhanced.

AND

2- Severe features or toxicity

OR 3- Failure to respond to full supportive care

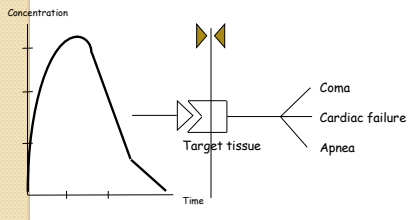
3- Impairment of the normal route of elimination

4- Raised blood concentrations with good PK/PD correlations

Goldfarb DS. Goldfrank 's Toxicologic Emergencies

When assessing efficacy, the clinical response must be considered in addition to the evidence of enhanced elimination

Toxicokinetics **Toxicodynamics**



With a better safety and a lower cost than other treatments

- To enhance elimination
- To reduce duration of poisoning

- To reduce severity or mortality
- To correct renal failure
- To correct electrolytic abnormalities

Hemodialysis is the extracorporeal method of choice to enhance the elimination of toxicants

Which drugs ?

Characteristics for removal by hemodialysis

- MW < 500 D
- Water solubility and low steric hindrance
- Poor binding to plasma proteins: <60%
- Small volume of distribution <1 l/kg
- Low endogenous clearance <4 ml/min
- Single - compartment kinetics

Goldfarb DS. Goldfrank 's Toxicologic Emergencies

How to anticipate the removal of toxin ?

% free drug / V_D	% drug removed by 6h-hemodialysis
> 80	20 - 50%
< 20	< 10%

Gwilt PR. *Clin Pharmacol Ther* 1978

Which drugs ?

Potential indications of dialysis in clinical toxicology

1- Salicylate
2- Lithium
3- Toxic alcohols (methanol, ethylene glycol)
4- Metformine

Others: amanita toxin, acetaminophen, aminoglycosides, atenolol, borate, bromide, carbamazepine, disopyramide, glyphosate, meprobamate, metformin, methotrexate, paraquat, phenobarbital, phenytoin, procainamide, sotalol, trichloroethanol, theophylline, valproic acid, …

In all these cases, the role of hemodialysis needs further demonstration

Goldfrank 's Toxicologic Emergencies

1 Hemodialysis in salicylate poisoning

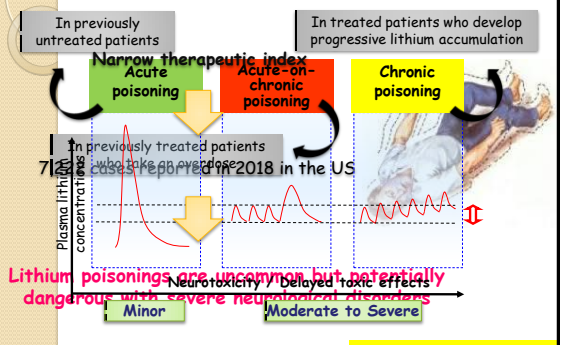
- The method of choice.
- HPF achieves marginally better clearance but cannot correct the acid-base, electrolyte and fluid balance, common in salicylate poisonings.

Indications:

- Severe features: acute renal failure (impaired elimination), coma, seizures or non-cardiogenic pulmonary edema
- Metabolic acidosis resistant to correction: pH < 7.2
- Contra-indications of urine alkalization: renal or cardiac insufficiency
- Elevated concentrations > 1.2 g/l or 1 g/l, 6 H post-ingestion
  Lower threshold for children or chronic salicylate poisoning (> 0.6 g/l)

Mokhlesi B, Chest 2003

Lithium poisoning – epidemiology and patterns



7126 cases reported in 2018 in the US

Lithium poisonings are uncommon but potentially dangerous with severe neurological disorders

El Gummin DD. *Clin Toxicol* 2018

Hemodialysis in lithium poisoning

- Dialysis ability to enhance Li elimination is well-documented.
  - ↘ $t_{1/2}$ from 12-27 to 3-6 h
  - ↗ clearance from 10-40 to 70-170 ml/min
- Rebound occurs following dialysis-induced rapid drop in Li plasma level.
  - Li concentration measurement should be repeated /6-12 h

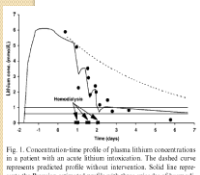
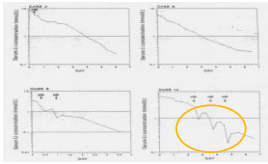


Fig. 1. Concentration-time profile of plasma lithium concentrations in a patient with an acute lithium intoxication. The dashed curve represents predicted profile without intervention. Solid line represents the Bayesian estimated profile with three episodes of haemodialysis. The horizontal lines represent the therapeutic range of lithium.

Kerbush. *Pharmacol Toxicol* 2002



Jaeger A. 1993
Okussa MD. 1994
Scharman EJ. 1997

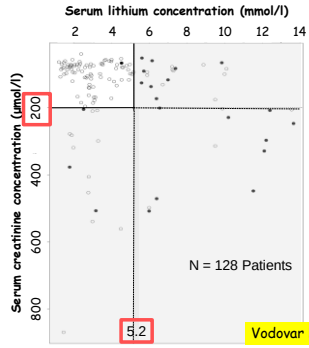
Indications of ECTR in lithium poisoning

- Primary treatment is based on supportive care + GI decontamination.
- Serum Li concentration is not sufficient to decide to undertake dialysis. This parameter should be taken with others, including type, severity, impaired renal excretion and spontaneous expected kinetics.
- Clearing plasma from Li is not a guarantee to obtain favorable outcome.

- **Severe poisoning** (coma, convulsions) + Renal failure
- **Elevated plasma concentration thresholds**
  6-8 mmol/l in acute overdose
  4 mmol/l in acute/chronic overdose
  2.5 mmol/l in chronic accumulation
- **Kinetic criteria:** amounts expected to be removed with 6h-dialysis > amounts spontaneously eliminated by kidneys within 24h

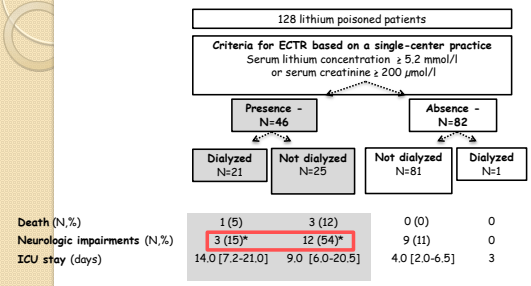
However, none of these criteria have been validated

Simple decision tree for dialysis indications (1)



Vodovar D. *Clin Tox* 2016

Simple decision tree for dialysis indications (2)



Death (N,%)	1 (5)	3 (12)	0 (0)	0
Neurologic impairments (N,%)	3 (15)*	12 (54)*	9 (11)	0
ICU stay (days)	14.0 [7.2-21.0]	9.0 [6.0-20.5]	4.0 [2.0-6.5]	3

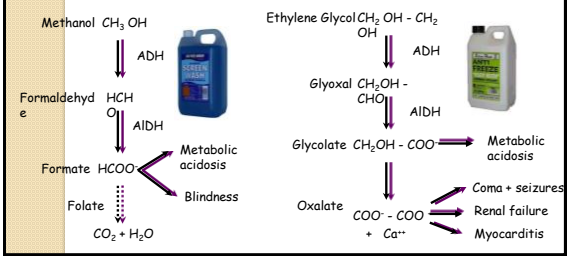
Vodovar D. *Clin Tox* 2016

3 Toxic alcohol poisonings

Offending chemicals in suicide, unintentional and epidemic poisonings
- Ethylene glycol: 4867 exposures /year (mortality: 0.09%)
- Methanol: 2418 exposure/year (mortality: 0.05%)

PCCTESS, USA, 2005

Toxicity is due to enzymatic degradation by alcohol dehydrogenase



Treatment of toxic alcohol poisonings

Recommended treatments include:
- **Supportive treatments:** intravenous fluids, anticonvulsive medications
- **Sodium bicarbonate :**
  to correct metabolic acidosis
  to increase renal elimination of glycolate and formate
  to inhibit precipitation of calcium oxalate crystals
- Folinic acid supplementation , thiamine and multivitamins (ethanol ingestion)
- **Antidotes** (competitive ADH substrate or inhibitor): fomepizole and ethanol
- **Intermittent dialysis:** routinely used to correct acidosis, to remove toxic metabolites and to shorten the course of hospitalization (methanol).

Jacobsen D. *Clin Toxico*l 1997
Mégarbane B. *Intensive Care Med* 2006
Brent J. *NEJM* 2009

Advantages of fomepizole over ethanol to treat toxic alcohol poisonings

Ease of administration
- Fixed loading dose independent of baseline ethanol concentration
- Intermittent bolus dosing every 12 hours (every 4 hours during hemodialysis)
- No need for monitoring serum antidote concentrations or continuous infusion

Wide therapeutic margin
Absence of central nervous system depression and inebriation
Absence of metabolic and biochemical adverse effects
Reduced intensity of nursing care
Simplification of interfacility transfer
Ability to forgo hemodialysis in selected patients
Safety of patient and of medical personnel

+ Possibility to obviate the need of hemodialysis in selected cases

Sivilotti ML. *Ann Emerg Med* 2009

Hemodialysis in toxic alcohol poisoning

Indications:

- Significant metabolic acidosis (pH < 7.25)
- Renal failure or electrolyte imbalance unresponsive
- Deteriorating vital signs despite intensive supportive care
- Neurological (EG/methanol) and Visual impairments (methanol)

Barceloux DG. *Clin Toxicol* 1999, 2002

EG ➔ Patients receiving fomepizole prior to significant acidosis do not require dialysis. EG ≥ 50 mg/dL should not remain an independent criterion

Borron SW. *Lancet* 1999

Methanol ➔ In poisonings without severe acidosis or visual impairment, patients may be treated with repeated fomepizole without dialysis. However, methanol ≥ 50 mg/dL is a debated indication

Mégarbane B. *Intensive Care Med* 2001

4 Metformin poisoning

Metformin-associated lactic acidosis is rare (0.08 /1000 patients /yr) but severe complication in type-II diabetes.

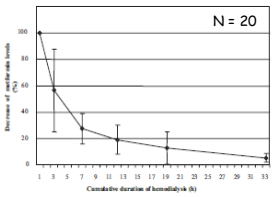
Metformine inhibits neoglucogenosis and reduces hepatic clearance of lactates in the presence of a trigger increasing lactate production.

Two categories of poisonings:

- Metformin-dependent toxic mechanism: elevated serum metformin concentrations, better prognosis in relation to metformin elimination
- Metformin-independent anoxic mechanism: lower serum metformin concentrations, worse outcome dependent on the underlying cause

Baily, Diabetes Care, 1992

Role of hemodialysis in metformin-associated lactic acidosis



Indications: - Severe lactic acidosis with acute renal failure
- Lactate > 5 mmmol/L with increasing kinetics

Duration: 16h

Seidowsky A. CCM 2009

Are there alternative extracorporeal renal support techniques with potential interest in toxicology?

Why CRRT could be attractive?

Advantages:

- Availability in most ICUs
- Suitability in hemodynamically unstable patients
- Easy to regulate fluid volume
- ↗ Clearance of mid-MW solutes (aminosides, iron-DFO, digoxin-Fab)
- Usefulness to remove solutes with larger Vd or extensive tissue binding
- Tendency to ↘ rebounds

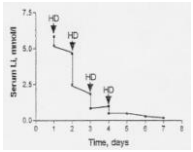
Inconveniences

- Lower clearance: Postdilutional HF clearance = UF flow rate (~ 67 mL/min) << HD clearance (up to 500 mL/min)
- Anticoagulation to prevent filter and extracorporeal circuit from clotting (duration, lower flow, hemoconcentration)

CRRT in lithium poisoning

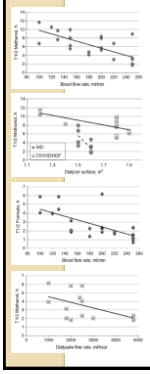
CVVHDF, CAVHDF	Bellomo 1991 - Leblanc 1996
CVVHF	Menghini 2000 - Meyer 2001
CCHVF + CVVHDF	Hazouard 1999
HV-CVVH	Van Bommel 2000 - Peces 2001

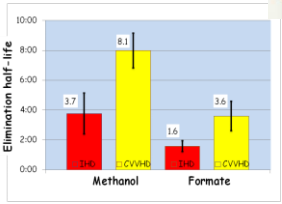
➔ Improved tolerance
➔ Absence of rebound due to better intracellular compartment clearance (CRRT couple a longer running time to an acceptable clearance)



HD remains the method of choice in severe Li poisonings. However, CVVHDF may be suitable alternative (if HD not available) or adjunctive (6-12h later, to avoid a second HD session).

CVVHD/HDF in methanol poisoning





- IHD is superior to CVVHD/HDF for more rapid methanol and formate elimination
- ↗ blood and dialysate flow increase elimination.
- If only CVVHD/HDF is available then elimination is greater with greater blood and dialysate flow rates.

Zakharov S. *Kidney Int* 2013

Charcoal hemoperfusion

Limited indications to exceptional cases of severe poisonings, when repeated-dose activate charcoal decontamination is unavailable or unfeasible:

Carbamazepine Phenobarbital Phenytoin
Theophylline Paraquat

Advantages:
- Uses same vascular access ar
- Can be used in series wit
- Not dependent on d olubility or protein binding - as long as drug binds to ch

Inconvenienc
- Greater antic n required
- Saturation of ch coal limits cartridge duration
- Worse tolerance

The ability of hemoperfusion to improve outcome has never been proven.

I do not use it

Plasmapheresis and Exchange blood transfusions

Plasmapheresis:
- Most useful for highly protein bound agents
- Reports with chemotherapy, antiinfect nts, antiepileptics, cardiovascular agents, and immunosu
- No role in enhancing toxicant

Exchange Blood Trans
- Pediatric e
- Over ole in poisoning.
- patients with intravascular hemolysis or severe obinemia unresponsive to symptomatic treatments or methylene

Ibrahim RB. *Pharmacotherapy* 2007

I exceptionally use them

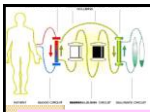
Molecular adsorbent regenerating system (MARS) dialysis

MARS® albumin treatment method

- No clearly asse ancing the elimination of toxicants
- Potential i ove liver function in poisoned patients waiting plantation.

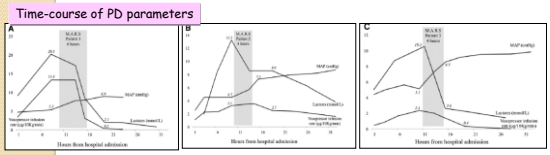
Schmidt LE. Liver Transpl 2003
Wu BF. *Hepatobiliary Pancreat Dis Int* 2004
Pugliese F. *Transplant Proc* 2007

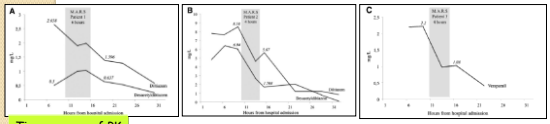
I am interested to investigate its usefulness in some well-defined poisonings



MARS usefulness in diltiazem and verapamil poisonings with refractory vasoplegic shock

Time-course of PD parameters





Time-course of PK

Pichon N. *Ann Emerg Med* 2011

What is the exact place of elimination techniques in the management of poisonings?

EXTRIP recommendations

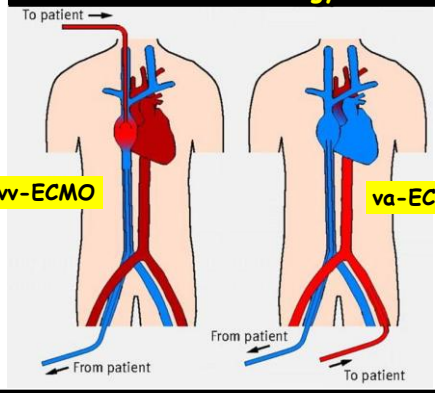
Take home messages (1)

- For most severely poisoned patients, supportive care and antidotes are all that is necessary; extracorporeal renal support is indicated in limited cases.
- In practice, hemodialysis should be considered in severe poisonings with : salicylates, lithium, methanol, ethylene glycol and metformin.

Further randomized studies are needed to evaluate hemodialysis benefit.

Further experience is needed to evaluate continuous techniques.

ECMO in toxicology



Two options to bring ECMO to the patient

To transfer the patient to Cardiac Surgery Department

To implement ECMO by mobile TCS team

To develop an ECMO program in the ICU in our hospital devoid of cardiac surgery

Specialized team in ICU

Patient with severe drug-induced cardiac/respiratory failure is announced

Warning

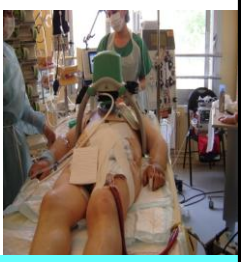
Perfusionist | Surgeons | ICU Physician | Cardiologists | Nurses

DISPONIBILITY

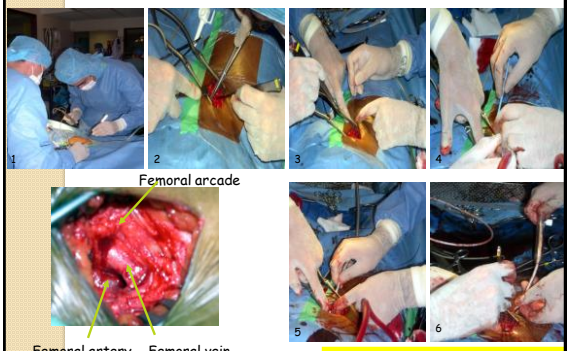
morning | night

working days | week ends

Adequate cardiac massage and ACLS are the keys for good prognosis in patients with cardiac arrest before VA-ECMO implementation

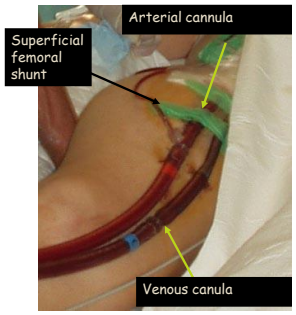


Cannulation of femoral vessels in the medical ICU



Mégarbane B. *Intensive Care Med* 2007

Preparation of ECMO device in the medical ICU

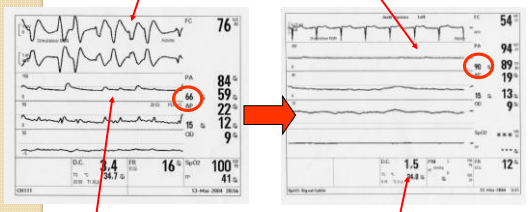


7F/9F catheter connected with luer of the arterial cannula

va-ECMO monitoring in the ICU

Spontaneous cardiac rhythm

ECLS completely dependent cardiac flow (around 5-6 l/min)

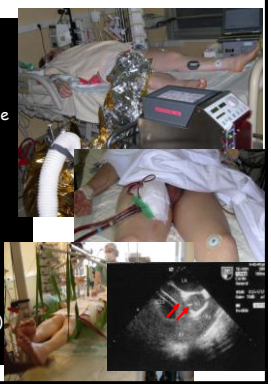


Severe hypotension despite high dose catecholamine

Spontaneous cardiac flow

Monitoring of VA-ECMO-treated patients in the ICU

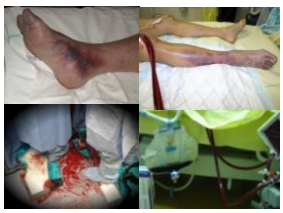
- Efficient anticoagulation: heparin to obtain ACT = 2N
- Catecholamines for mean BP = 60-70 mmHg + dobutamine to facilitate LV discharge
- Adequate transfusions
- Adapted Mechanical ventilation ABG monitoring by radial catheter
- Temperature control
- Canulated lower limb monitoring
- Echocardiography: weaning criteria
- Neurological evaluation (EEG, clinical)
- Care, nursing



Initial ECMO complications

Local complications

- Acute limb ischemia 10%
- Scarpa hemorrhage 9%
- Sub-acute ischemia 5%
- Infected lymphocele 5%
- Arterial dissection 2%



General complications: hemorrhage, thrombosis, systemic infection, pulmonary edema, thrombocytopenia

When to perform ECMO in the poisoned patient?

Strategy of management of drug-induced cardiovascular failure

Diagnosis of shock

↓

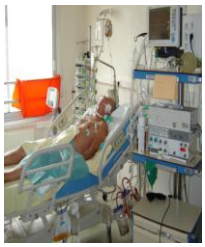
Determination of the mechanism of shock

↓

Definition of the optimal treatment

↓

Diagnosis of the refractoriness of shock



Refractoriness requires failure of optimal supportive treatments in the ICU

- **Intubation and mechanical ventilation :**
  - Severe arrhythmias and associated collapse
  - Coma, convulsions, respiratory failure
- **Treatment of collapse/shock**
  - Fluids + adequate catecholamines
- **Treatment of torsade-de-pointes**
  - Defibrillation, $MgSO_4$, titrated isoproterenol, cardiac pacing
  - Correction of electrolyte imbalance (K^+, Mg^{2+})
- **Treatment of monomorphic ventricular tachycardia**
  - Defibrillation, $MgSO_4$, lidocaine infusion
- **Cardiac pacing**
  - High degree AV block with preserved inotropism

Refractoriness requires failure of the optimal administration of antidotes in the ICU (1)

Beta-blockers

Dobutamine 5-20 µg/kg/min
Isoprenaline 1-5 mg/h (Sotalol)

↓

Glucagon 2-5 mg IV bolus
2-10 mg/h continuous infusion
Or
Insulin 1 IU/kg IV bolus
1 IU/kg/h continuous infusion

↓

Epinephrine 0.5-10 mg/h

± **Cardiac Pacing**

Calcium channel blockers

Calcium chloride 1 g IV bolus /15 min
4 doses, 20-50 mg/kg/h infusion

↓

Insulin 1 IU/kg IV bolus
1-10 IU/kg/h continuous infusion

↓

Epinephrine 0.5-10 mg/h
Norepinephrine 0.5-10 mg/h

↓

Methylene blue 2 mg/kg bolus
1 mg/kg/h infusion

Refractoriness requires failure of the optimal administration of antidotes in the ICU (2)

Sodium channel blockers

Sodium bicarbonates 8.4%
250 ml to be repeated 3 times
+ 2g KCl / 250 ml
(cocaine: **Lidocaine** IV)

↓

Epinephrine 0.5-10 mg/h
Norepinephrine 0.5-10 mg/h

Cardioglycosides

Atropine 0.5-1 mg to be repeated

↓

Anti-digoxin Fab fragments
Semi-molar or molar dose
(if not available: ventricular pacing)

Evidence-based recommendations on the use of intravenous lipid emulsion therapy in poisoning

For the management of cardiac arrest:
We recommend using ILE with bupivacaine toxicity, while our recommendations are neutral regarding its use for all other toxins.

For the management of life-threatening toxicity:
- We suggest using ILE as a part of treatment in bupivacaine toxicity and we recommend its use if other therapies fail;
- We suggest using ILE if other therapies fail for toxicity due to other local anesthetics, amitriptyline, and bupropion;
- Our recommendations are neutral for all other toxins.

In the treatment of non-life-threatening toxicity, recommendations varied according to the balance of expected risk/benefit for each toxin

Gosselin S. *Clin Tox* 2016

Refractoriness to the conventional therapies (supportive care + catecholamine + antidotes)

F, 17 years, severe propranolol poisoning

Sedation + mechanical ventilation + FiO_2 100%

		Epinephrine 1.5 mg/h	Dobutamine 15 µg/kg/min	
BP	S	93	56	mmHg
	D	64	33	mmHg
	M	75	43	mmHg
P_{RA}		7	6	cmH_2O
P_{AP}	S	27	19	cmH_2O
	D	19	11	cmH_2O
	M	23	15	cmH_2O
P_{cw}		17	13	cmH_2O
Cardiac Index		1.4	1.8	$l/min/m^2$
Systemic resistances		50.3	20.3	UI

30 min later

Dramatic decrease in BP ...

ECMO indications in acute poisonings

Which patients to treat with ECMO ?

↓

Numerous risks

Too late : To result in anoxic brain injury or multiorgan failure

Undiscriminated use: to treat patients who would spontaneously have had favorable outcome with pharmacological treatments

Is ECMO efficient to improve outcome in the poisoned patient?

↓

Level of evidence still limited !

Case report (1)

Severe propafenone poisoning

F 50 years
H0 : ingestion of 9 g propafenone (RYTHMOL®, 30 pills)
H1 : GCS 4 + HR 50/min + non-measurable SBP + complete AV block Intubation + isoprenaline + 11.2% lactate (250 ml) + 1.4% bicarbonates (1,000 ml)

In ICU :
Hypotonic coma then seizures (clonazepam + pentobarbital)
SBP 90/50 mmHg , HR 79 /min
ECG : AV block I, QRS 140 ms, RBBB, Brugada syndrome
Bio : Metabolic alcalosis (pH = 7.66 ; HCO_3^- = 42 mM)
PaO_2/FiO_2 : 246 mmHg, lactate : 3 mM, creatinine : 57 µM,
Propafenone concentration : 2.9 mg/l (N < 1 mg/l)

Cardiac failure (LVEF : 35%, cardiac output : 2.2 l/min)
despite epinephrine up to 5 mg/h and 8.4% bicarbonates

Case report (2)

Outcome in a severe propafenone poisoning

H3 : Renal failure : oliguria and creatinine of 107µM
Respiratory failure : PaO_2/FiO_2 ratio of 134 mmHg

H7 : ECMO with femoral cannulation
Anticoagulation with heparin
Assistance flow of 3.5 l/min with 2,800 turns/min.
Dobutamine : 10 µg/kg/min

H12 : Dissociation between electrical and mechanical activities
H48 : ECLS weaning

D4 : *P. aeruginosa* hospital-acquired pneumonia
D8 : Extubation
D22 : Return back home

M6: Normal life quality

Non-reactive mydriasis is not a sufficient reason to refuse ECLS

Initial non-reactive mydriasis | Photo-reactive pupils

On ICU admission | After ECMO

Case report (3)

Assessment of ECLS benefit in propafenone poisoning

	H3	H4	H12	H24	D2	D3
Spontaneous Q (l/min)	1.9	1.9	0	2.5	4.5	5.7
LVEF (%)	35	35	0	45	50	50
Assistance Q (l/min)	-	-	3.5	3.5	3	0
SvO_2 (%)	45	60	73	79	79	-
Plasma lactate (mmol/l)	8.3	-	4.6	1.8	0.9	0.9
Epinephrine (mg/h)	5	5	5	0.1	0	0
Dobutamine(µ/kg/min)	0	0	10	10	10	5

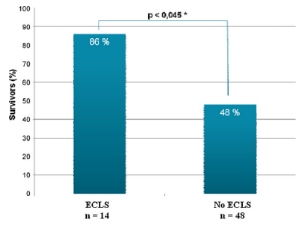
Published cases of va-ECMO-treated acute poisonings:

- Beta-blockers
- CCB
- Sodium channel blockers

Agent	References
Acebutalol	29,37
Amiodarone	38
Antidepressants (tricyclic)	15,29,39–41
Arsenic	42
Atenolol	29
Bisoprolol	29
Bupropion	43
Calcium Channel Blockers	1,44–49
Carbamazepine	29,50
Carbon monoxide	51
Chloroquine	15,52
Cibenzoline	29,53
Citalopram	29
Cocaine	54
Disopyramide	29,55
Diltiazem	29
Flecainide	29,56–58
Hydrocarbon products	59–63
Ibuprofen	64
Lidocaine	65
Mepivacaine	66
Methadone	67
Metoprolol	29
Opioids	67–69
Organophosphates	70
Paraquat	31,32
Paroxetine	29
Phosphine	71
Propafenone	15,29
Propranolol	29,72–74
Quetiapine	75
Quinidine	76
Radiocontrast material (intravenous)	77
Sotalol	29,78
Taxus	79
Venlafaxine	29
Verapamil	29
Zinc chloride	80
Zotepine	81

De Lange DW. *Clin Tox* 2013

A comparison of survival with and without ECMO support treatment for severe poisoning due to drug intoxication



Masson R. *Resuscitation* 2012

Outcome of poisoned patients treated with ECLS

	Total (N=112)	Cardiac failure (N=41)	Refractory arrest (N = 71)
Survival	35 (31%)	22 (54%)	13 (18%)
Neurological sequellae	4	3	1
Hemorrhagic accidents	18	4	14
Thombo-embolic complications	6	4	2
Lower limb ischemia	8	6	2

Outcome of patients supported by ECMO for aluminum phosphide poisoning: An observational study

Comparison according to ECMO

Parameters	Conventional group (n = 30)	ECMO group (n = 15)	p Value
Average hospital stay (in days)	6.8 ± 10	16.1 ± 12.9	<0.0001
pH <7.0	8 (26.7%)	15 (100%)	–
LVEF (%)	27.2 ± 4.0	27.1 ± 2.9	0.7
Systolic blood pressure (<90 mmHg)	22	15 (100%)	–
In-hospital mortality	86.7% (26)	33.3% (5)	0.001

Comparison according to survival

	Survivors (n = 10)	Non-survivors (n = 5)	p Value
LVEF at admission (%)	26.2 ± 4.8	19.6 ± 1.7	0.01
Delay in presentation (hours)	7.3 ± 2.6	12.0 ± 2.6	0.01
Hospital stay (days)	22.8 ± 10.3	2.6 ± 0.5	0.002
Poison exposure to ECMO (hours)	10.8 ± 4.2	15.8 ± 3.1	0.01
Admission to ECMO (hours)	3.5 ± 3.2	3.8 ± 0.8	0.2
Duration of ECMO (hours)	60 ± 35	62.4 ± 13.1	0.1

Mohan B. *Indian Heart J* 2016

Clinical utility of VA-ECMO in patients with drug-induced cardiogenic shock - The ELSO case registry (N=104)

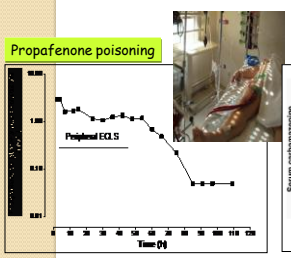
55 Survivors (53%)
VA-ECMO duration: 68 h [48-113]
Significant improvement of hemodynamics (MAP, BP), acidosis (pH, HCO_3) and ventilatory parameters (PaO_2, SpO_2, and SvO_2).

Variables	OR [95% CI]
Demographic	
Age	1.02 [0.99–1.05]
Male gender	1.96 [0.88–4.33]
Pre-ECMO variables	
CV agent vs. non-CV agent	0.64 [0.29–1.40]
pH at cannulation	0.38 [0.03–5.44]
HCO_3 at cannulation	1.01 [0.97–1.05]
MAP at cannulation	0.99 [0.96–1.02]
Pre-ECMO arrest	1.47 [0.64–3.34]
Intra-aortic balloon pump	13.72 [0.74–254.84]
Pacemaker insertion	3.01 [0.56–16.29]
Organ failures during ECMO	
Renal replacement therapy	0.57 [0.24–1.37]
Hyperbilirubinemia	3.92 [0.43–35.71]

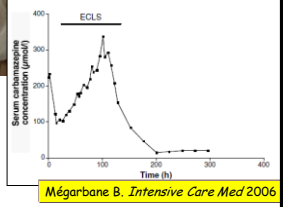
Weiner L. *Clin Tox*2019

Toxicokinetics in severe poisonings requiring ECMO

Propafenone poisoning



Carbamazepine poisoning



Mégarbane B. *Intensive Care Med* 2006

- $T_{1/2}$: 30 h (pharmacology: 4 h)
- Vd: 151 l/kg
- Clearance: 262 l/h

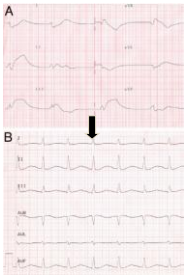
- Concentration on admission: 224 µmol/l
- Peak concentration: 338 µmol/l at 101 h
- Prolonged absorption despite MDAC
- $T_{1/2}$: 22.6 h (pharmacology: 12-20 h)

Death of ECLS-treated poisoned patients

- Death resulted from multiorgan failure, anoxic encephalopathy or capillary leak syndrome if ECLS was performed under cardiac massage.

- Four patients presented documented brain death, allowing organ donation in 2 cases.

- The heart of one flecainide-poisoned patient was successfully transplanted, after normalization of ECG and myocardial function as well as toxicant elimination under ECLS.



Vivien B. Ann Emerg Med 2010

Take home messages (2)

- Shock and arrhythmias following poisonings with cardiotoxicants may lead to life-threatening symptoms and death.
- Conventional treatment including supportive care and antidotes is generally life-saving.
- In a limited subset of patients admitted for severe poisonings with non-responding cardiovascular failure, arrhythmias or cardiac arrest, VA-ECMO may represent the unique solution. However, its definitive benefit should still be prospectively evaluated on larger cohorts.