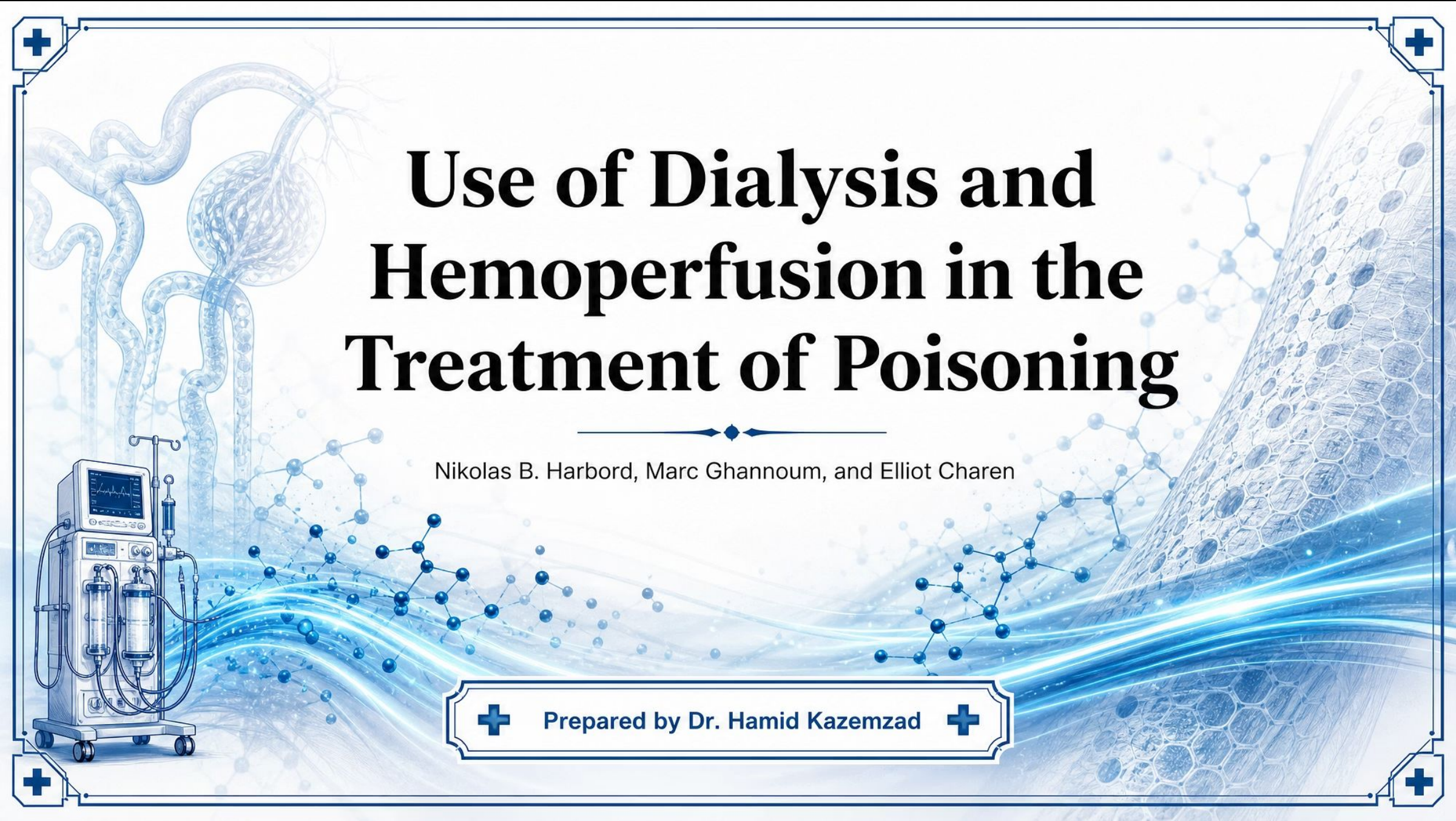


The background features a complex illustration. On the left, a dialysis machine is shown with its various components like filters and tubing. Behind it, a stylized human kidney is depicted. The right side of the image is dominated by a large, detailed illustration of a cell membrane or a similar biological structure, showing a hexagonal lattice pattern. Scattered throughout the background are blue molecular models, consisting of spheres connected by lines, representing chemical structures. The entire scene is set against a light blue gradient with subtle wavy lines.

Use of Dialysis and Hemoperfusion in the Treatment of Poisoning

Nikolas B. Harbord, Marc Ghannoum, and Elliot Charen



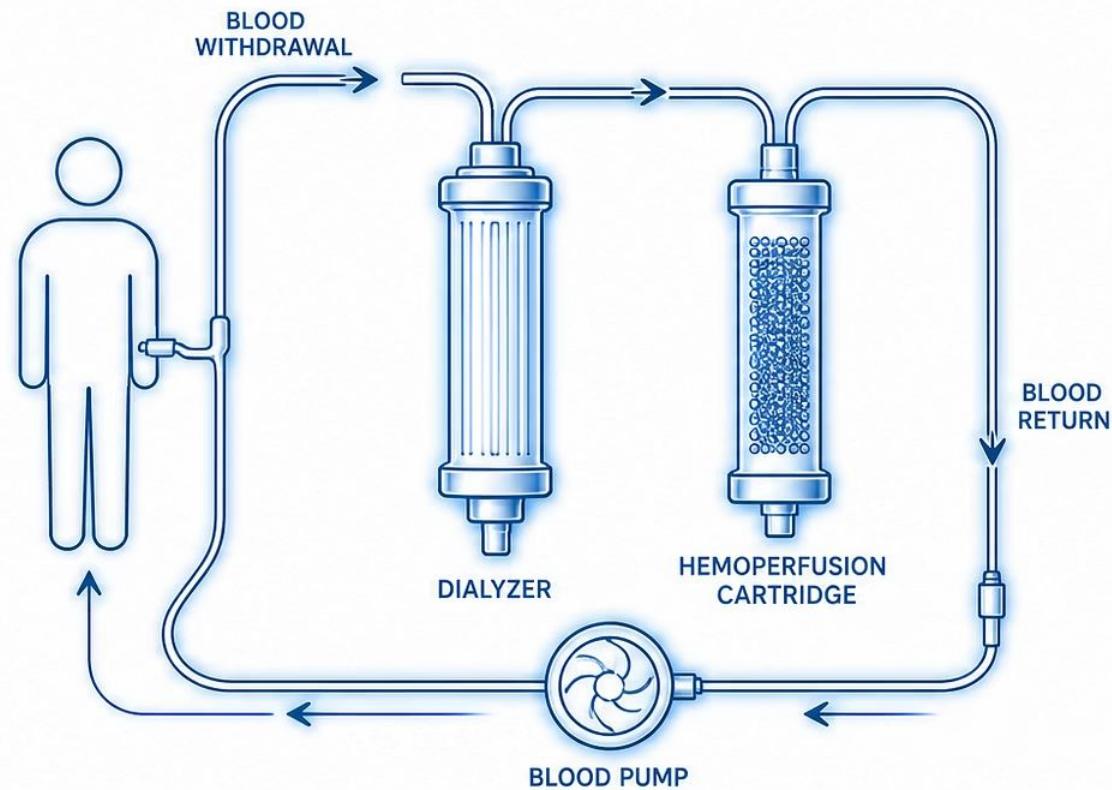
Prepared by Dr. Hamid Kazemzad



Clinical Framework for Extracorporeal Toxin Removal

Presentation Roadmap

-  1. Epidemiology of Poisoning
-  2. Indications for ECTR
-  3. Choice of Therapy
-  4. Pharmacokinetics of Dialyzability
-  5. Technical Considerations
-  6. Complications of ECTR
-  7. Drug-Specific Management (A–O)
-  8. Evidence Tables and Clinical Takeaways



The Poisoning Crisis in America

~100,000

Annual Overdose Deaths,
US & Canada Combined

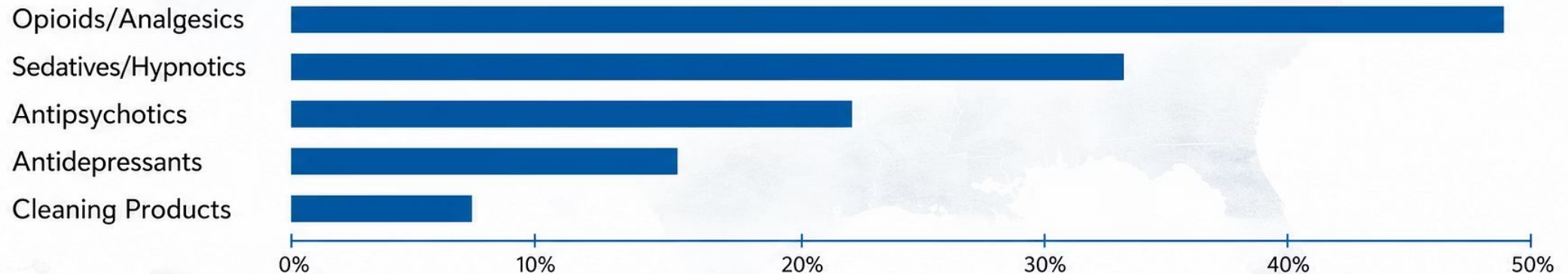
#1 Cause

Death in Americans Under
Age 44 — Unintentional Poisoning

Millions

Reported Toxic Exposures
Annually — Majority Unintentional

RELATIVE FREQUENCY OF EXPOSURE CATEGORIES (NPDS 2020)

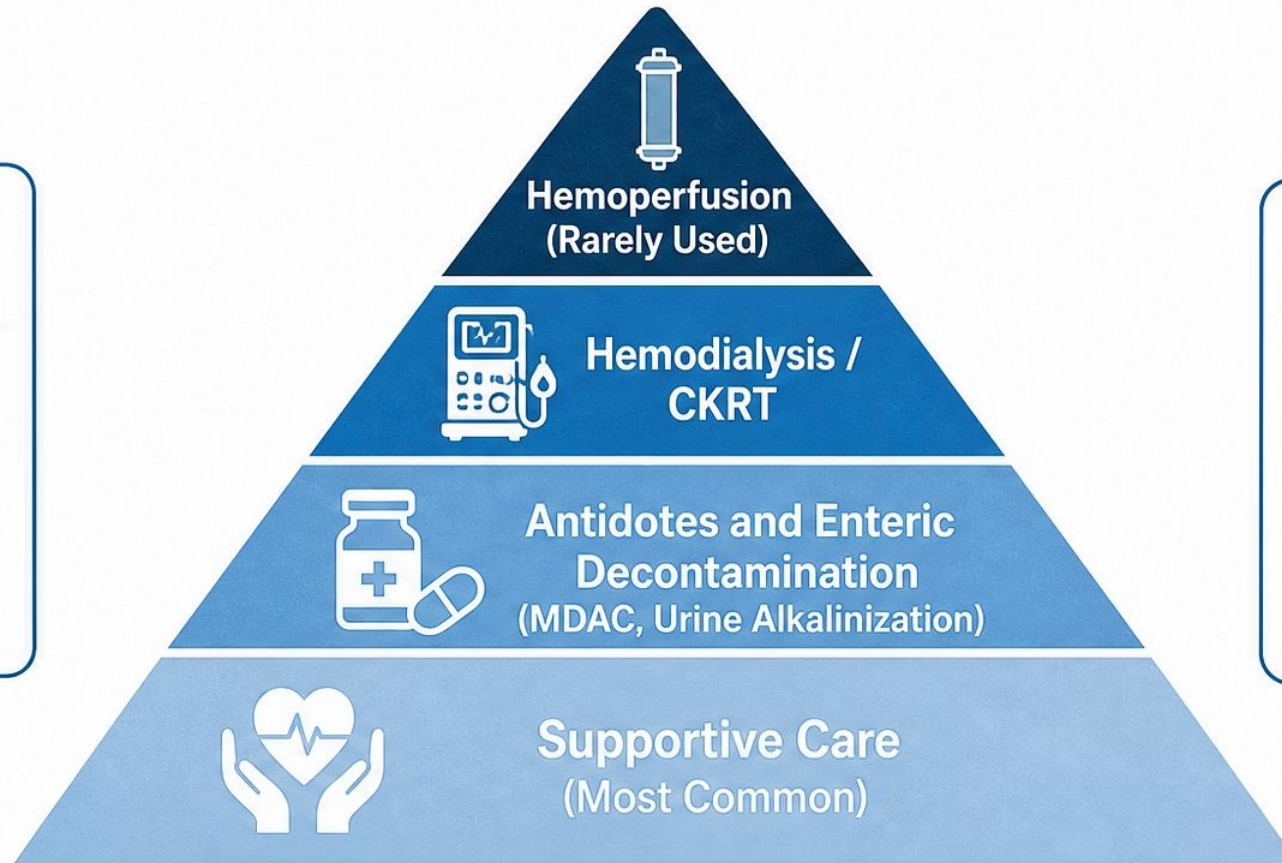


Data: NPDS 2020 Annual Report (Gummin, 2021).

From Antidote to Extracorporeal: The Treatment Hierarchy



Most exposures involve children and are unintentional; adult exposures more often intentional and requiring hospitalization.



Opioid Epidemic Response:

Naloxone widely distributed to families, first responders, and community programs for intranasal administration.

When Is Extracorporeal Toxin Removal Warranted?

Table 18.1 — Criteria for ECTR Consideration in Poisoning

1.



Progressive clinical deterioration despite intensive supportive therapy.

2.



Severe intoxication with midbrain depression: hypoventilation, hypothermia, hypotension.

3.



Complications of coma (pneumonia, septicemia) or predisposing conditions (obstructive airway disease).

4.



Impaired drug excretion due to hepatic, cardiac, or renal insufficiency.

5.



Toxins with delayed/metabolic effects: methanol, ethylene glycol, paraquat.

6.



Drug removable at rate exceeding endogenous hepatic or renal elimination.



Clinical judgment is mandatory — these are frameworks, not absolute triggers.

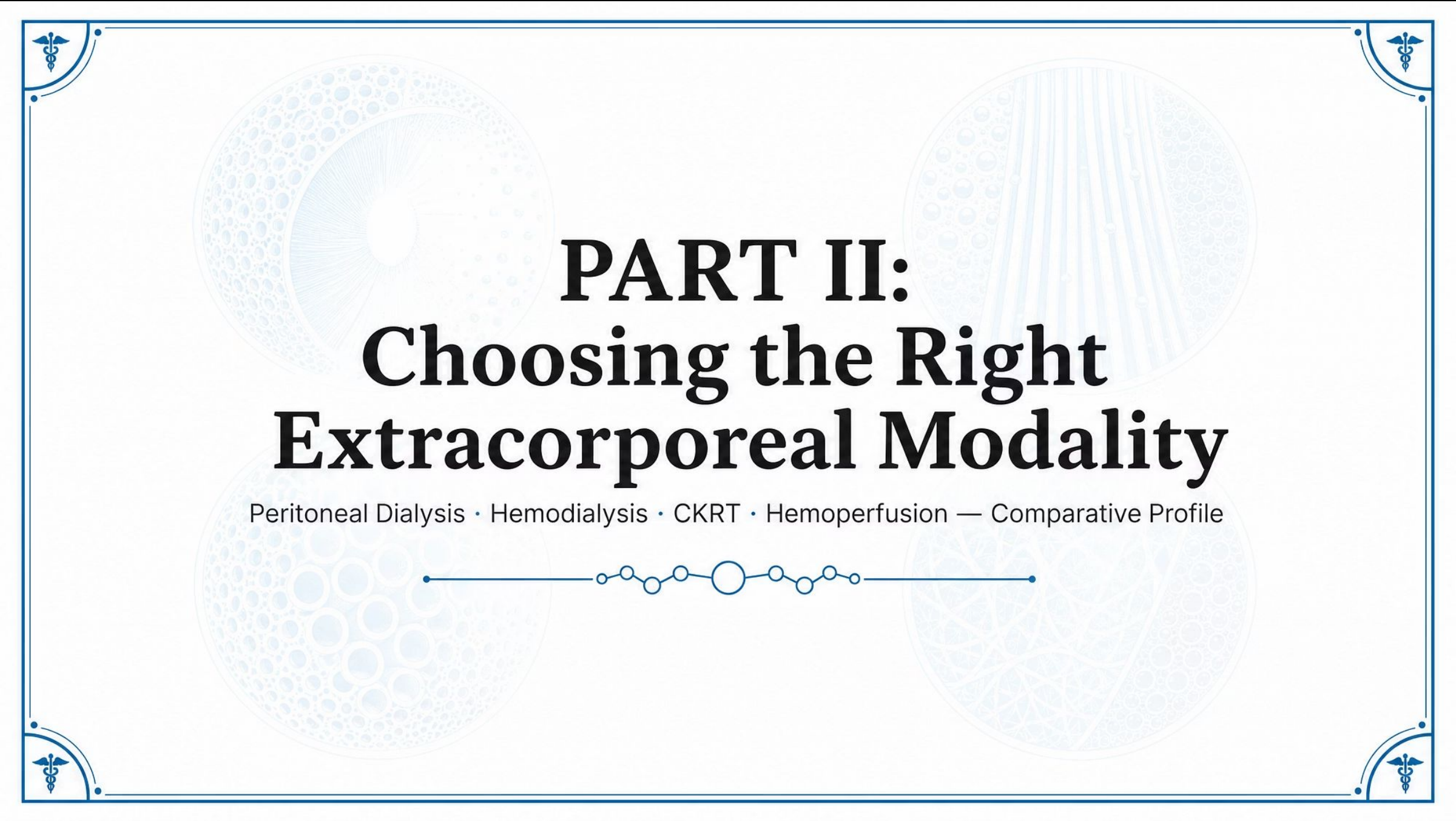
Table 18.2 — EXTRIP Evidence-Based ECTR Recommendations: Overview

Poison	Concentration Threshold	Clinical/Lab Trigger	Preferred ECTR Modality
Acetaminophen	>900 mg/L	acidosis/altered consciousness	HD
Baclofen	not specified	coma + MV + renal impairment	HD
Barbiturates	increasing levels	coma/shock/MV	HD>HP
Beta-blockers	not specified	refractory bradycardia + renal impairment	HD>CKRT
Carbamazepine	increasing levels	refractory seizures/dysrhythmia	HD>CKRT/HP
Chloroquine	none specified	—	none recommended

HD = Hemodialysis • **HP** = Hemoperfusion • **CKRT** = Continuous Kidney Replacement Therapy • **ECTR** = Extracorporeal Toxin Removal.

Table 18.2 (Continued) — EXTRIP Recommendations: Toxic Alcohols and CNS Agents

Agent	EXTRIP Recommendation (Biomarker Threshold)	Clinical Indications	Preferred Modality (Order of Preference)
Ethylene Glycol	>310 mg/dL with antidote / >62 mg/dL without	shock, coma, seizures, AG >24	HD > CKRT
Methanol	>70 mg/dL with fomepizole	coma, vision deficits, pH ≤ 7.15	HD > CKRT
Lithium	>5.0 mEq/L	decreased LOC, seizures, dysrhythmia	HD > CKRT
Metformin	not specified	lactate >20, shock, pH < 7.0	HD > CKRT
Valproic Acid	>1,300 mg/L	cerebral edema, coma, pH ≤ 7.10	HD > CKRT/HP
Theophylline	>100 mg/L acute / >60 mg/L chronic	seizures, shock, dysrhythmia	HD > HP > CKRT

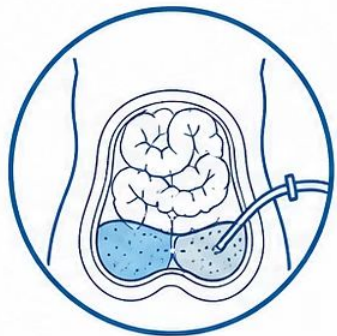


PART II: **Choosing the Right** **Extracorporeal Modality**

Peritoneal Dialysis • Hemodialysis • CKRT • Hemoperfusion — Comparative Profile



Peritoneal Dialysis vs. Hemodialysis in Poisoning



Peritoneal Dialysis

- Maximal clearance rarely >15 mL/min ($\approx 1/10$ of hemodialysis).
- Valuable when HD is delayed or technically difficult (e.g., small children).
- Useful for core rewarming in hypothermic-poisoned patients.
- Limited role — generally inferior.



Hemodialysis

- Therapy of choice for water-soluble, low-MW, low-protein-bound drugs.
- Well-dialyzed toxins: methanol, ethanol, ethylene glycol, lithium, salicylates.
- High-flux membranes and hemodiafiltration extend larger solute removal.
- Not efficient for high-Vd, lipid-soluble, or highly protein-bound agents.

CKRT vs. Hemoperfusion in Poisoning



Continuous Kidney Replacement Therapy (CKRT)

- Combines diffusion and/or convection at lower blood/effluent flows.
- Preferred in hemodynamically unstable patients unable to tolerate HD.
- Prolonged treatment limits posttherapy drug rebound from tissue stores.
- Substantially lower poison clearance than intermittent HD — a key limitation.
- HD for initial removal → CKRT for sustained removal and rebound prevention.



Hemoperfusion

- Blood passed through activated charcoal or resin sorbent cartridge.
- Historically removed large protein-bound drugs better than HD.
- Now largely supplanted by modern high-flux dialysis.
- US availability limited — cartridges expensive, largely discontinued (Shalkham, 2006).
- Remaining indication: paraquat/diquat within first 4 hours of ingestion.
- Complications: thrombocytopenia, leukopenia, cartridge saturation.

Clearance Hierarchy Across ECTR Modalities

Hemodialysis (HD):



Hemodiafiltration (HDF):



Hemoperfusion (HP):



CKRT:



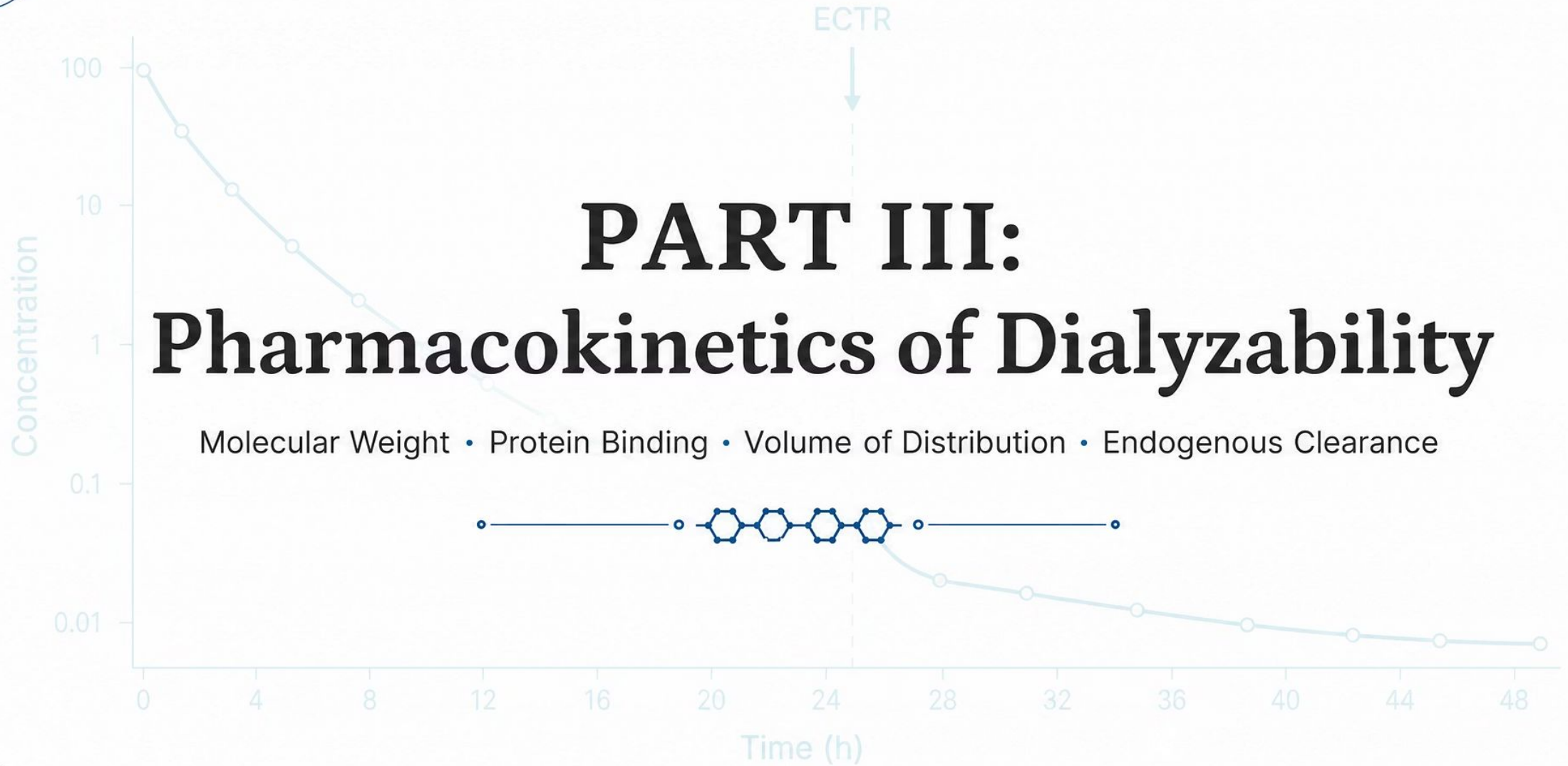
Peritoneal Dialysis:	max ~15 mL/min.
HD:	typically 150–300 mL/min.
HP:	variable, affected by cartridge saturation.
CKRT:	20–45 mL/min — lowest but sustained.

Note: Choose modality based on hemodynamic stability, urgency of removal, and drug characteristics.

PART III:

Pharmacokinetics of Dialyzability

Molecular Weight • Protein Binding • Volume of Distribution • Endogenous Clearance



Key Determinants of Poison Dialyzability



Molecular Weight:

Small MW toxins diffuse quickly through membranes. High-flux membranes pass compounds up to ~20–25 kDa. Larger (25–50 kDa) require convection (HDF). Adsorption via HP or plasmapheresis for very large MW compounds.



Protein Binding:

Only free (unbound) fraction is removable. In overdose, binding may saturate → higher free fraction available for ECTR. Future strategy: drug displacers to increase dialyzability of protein-bound toxins.



Volume of Distribution (Vd):

High Vd = drug stored in tissues → little in blood. Even efficient HD removes small fraction of total body burden. However, transient blood level lowering may still mitigate toxicity.



Endogenous Clearance:

ECTR unwarranted if hepatic/renal CL exceeds ECTR rate. In organ impairment, ECTR provides meaningful supplemental clearance.

Vd and Protein Binding: Clinical Examples

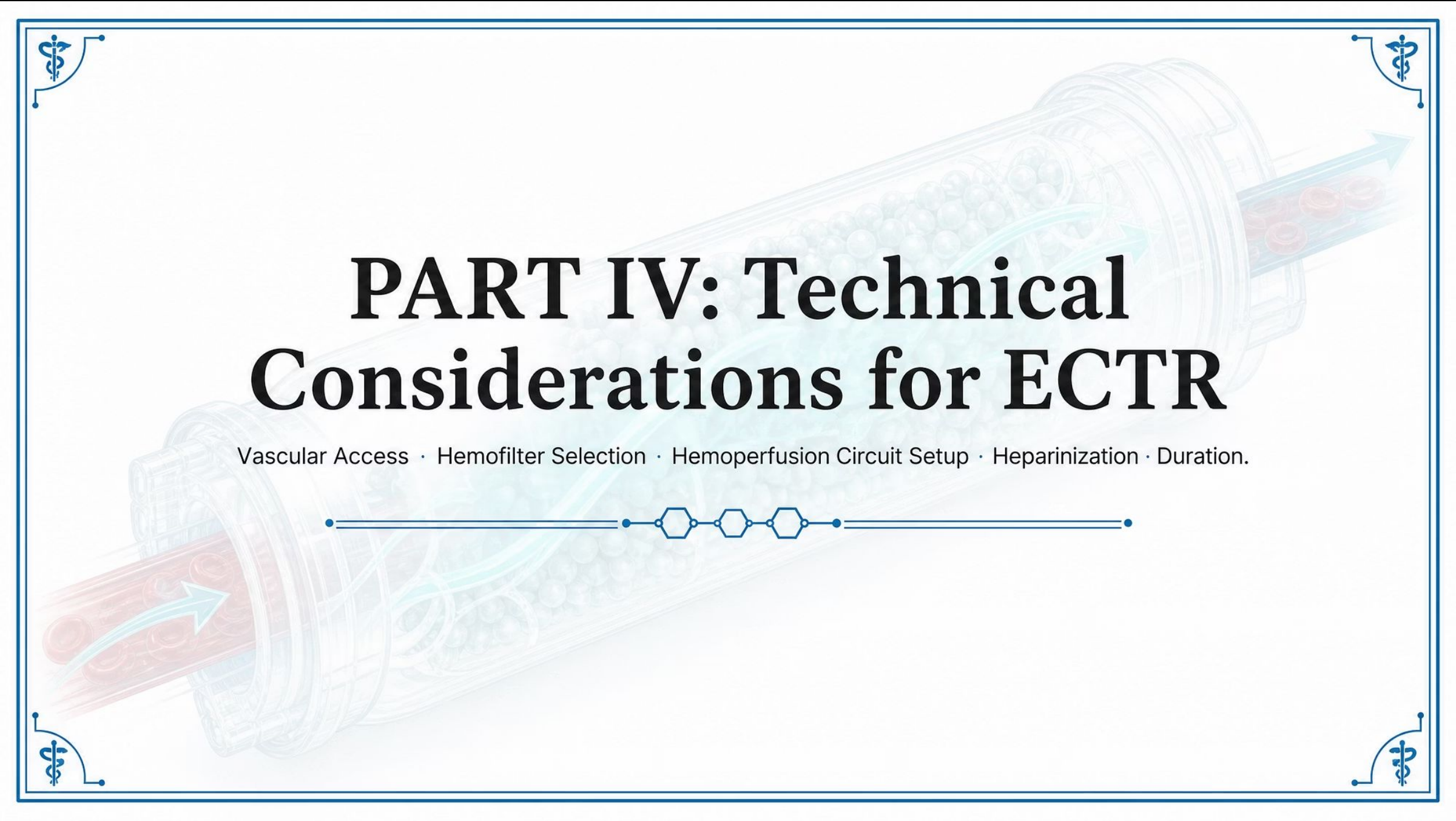
Drug	Vd (L/kg)	Protein Binding	ECTR Utility
Heparin	0.06	endogenous	not applicable
Salicylate	0.15–0.2	50%	well removed — binding saturates in OD
Lithium	0.8	0%	excellent HD candidate
Phenobarbital	0.5	50%	well removed HD/HP
Digoxin	8.0	25%	poor — Vd too large, use Fab
Amitriptyline	14–21	>90%	not recommended — Vd and PB both prohibitive
Valproic Acid	0.3	90%	removed in OD — binding saturates

**Extraction Ratio
(ER):**

$$\frac{A - V}{A}$$

where
A = inflow concentration
V = outflow concentration.

★ High Vd and high protein binding are the two most common barriers to effective ECTR. ★



PART IV: Technical Considerations for ECTR

Vascular Access · Hemofilter Selection · Hemoperfusion Circuit Setup · Heparinization · Duration.





Vascular Access and Hemofilter Selection

Vascular Access

- Temporary nontunneled dual-chamber large-caliber central venous catheter required when no AV fistula/graft present.
- Preferred site: internal jugular vein under ultrasound guidance.
- Risks: bloodstream infection, thrombosis, occlusion.
- Anticoagulants increase bleeding risk from access site.

Hemofilter Selection

- Use high-flux, high-efficiency dialyzers with high urea clearances.
 - High-cutoff membranes (pore 8–10 nm): allow clearance of toxins up to 50–60 kDa (e.g., albumin-bound toxins).
 - AN69 membrane: adsorptive capacity for many compounds — useful for selected overdoses.
 - Standard high-flux membranes efficiently clear compounds <20–25 kDa.
- 
- 

Hemoperfusion Cartridges: Types and Brands

Manufacturer	Device	Sorbent Type	Amount	Coating
Asahi	Hemosorba	Spherical charcoal	170 g	Polyhema
Gambro	Adsorba	Norit charcoal	100 or 300 g	Cellulose Acetate
Cytosorbents	CytoSorb*	Polystyrene divinylbenzene	300 g	None
Jafron Biomedical	HA 130–380*	Polystyrene divinylbenzene	Various	None
ExThera	Seraph-100*	Polyethylene	Embedded	None
Baxter	Oxiris*	AN69 polyethyleneimine	N/A	Heparin

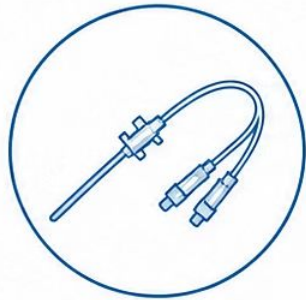
Charcoal: greater affinity for water-soluble drugs.

Resin: greater affinity for lipophilic drugs.

*Available in Europe/Japan; compassionate or emergency use only in the US.

Hemoperfusion: Circuit Setup, Priming, and Heparinization

STEP 1



Establish central venous access — temporary nontunneled catheter preferred in internal jugular vein.

STEP 2



Prime cartridge vertically, arterial (inlet) side facing DOWN. Follow manufacturer instructions — saline or dextrose priming.

STEP 3



Administer heparin bolus 2,000–3,000 units into arterial line before blood flow starts.

STEP 4

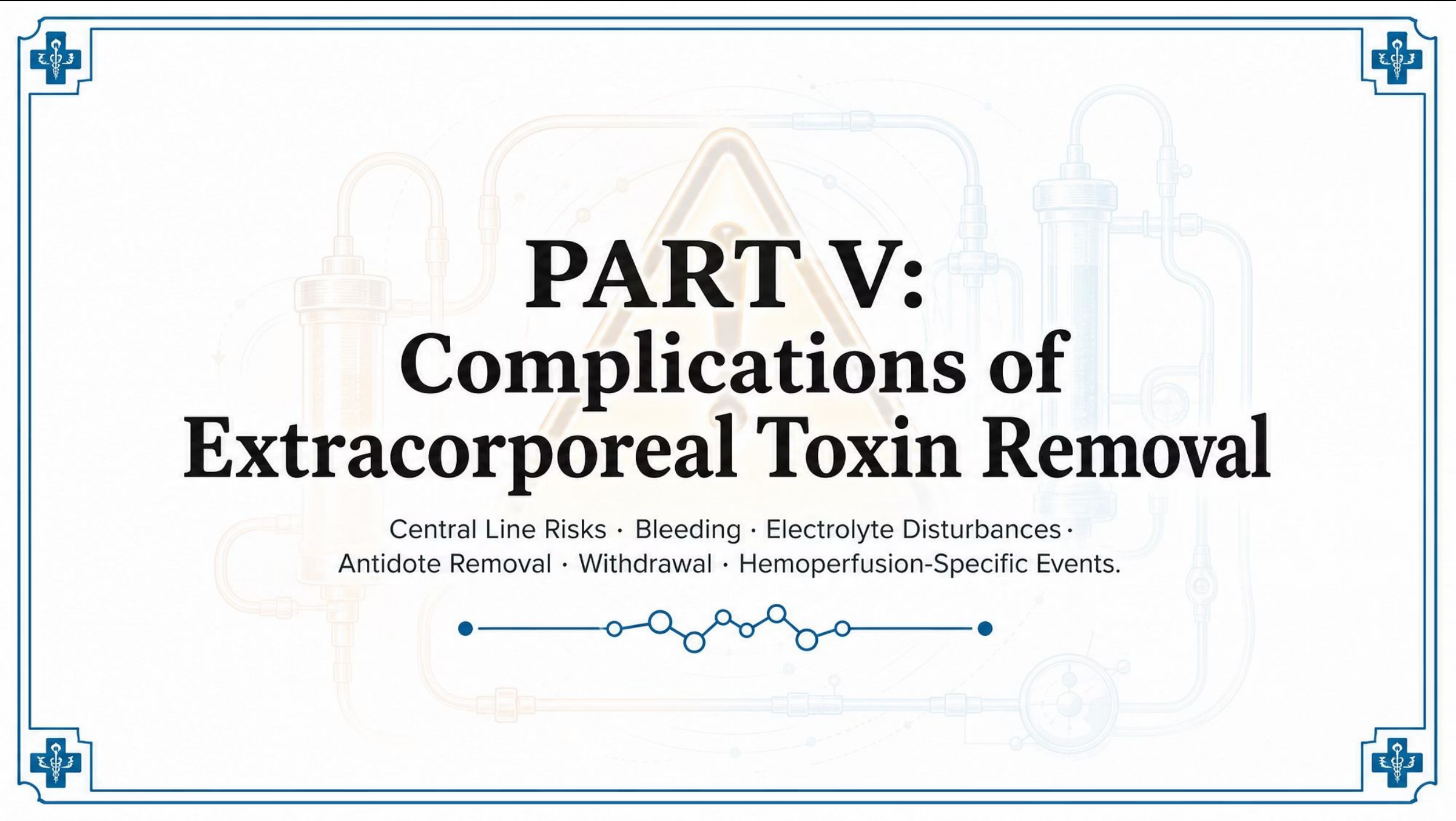


Begin blood flow through cartridge using standard HD blood pump and machine (no dialysis solution used).

STEP 5



Maintain aPTT or ACT $\approx 2\times$ normal.
Charcoal: $\sim 6,000$ units/session.
Resin: $\sim 10,000$ units/session.
Single treatment: 3 hours — longer use leads to sorbent saturation.



PART V: Complications of Extracorporeal Toxin Removal

Central Line Risks • Bleeding • Electrolyte Disturbances •
Antidote Removal • Withdrawal • Hemoperfusion-Specific Events.



Complications of ECTR: Systematic Review



1. Central Line Complications

Infection, thrombosis, occlusion;
use ultrasound guidance;
anticoagulation increases bleeding risk.



2. Bleeding

Exsanguination risk from extracorporeal circuit;
monitor lines continuously;
arterial pressure alarms mandatory.



3. Hypophosphatemia

Dialysis removes phosphate;
can cause respiratory insufficiency;
supplement dialysis solution with phosphate to prevent.



4. Alkalemia

Standard HD solutions contain high bicarbonate;
reduce bicarbonate concentration if patient
has metabolic or respiratory alkalosis.



5. Disequilibrium Syndrome

In severe uremia + poisoning; avoid prolonged
high-clearance HD; consider urea-enriched dialysate,
SLED, or CKRT; reduces clearance but safer.



6. Antidote Removal

NAC removed by HD/CKRT → increase NAC dose
to >12.5 mg/kg/h. Ethanol and fomepizole also
removed — adjust per Table 18.4.



7. Withdrawal

Baclofen removal may precipitate delirium,
spasms, seizures; manage with baclofen
reintroduction and GABA-A agonists.

Table 18.4 — Antidote Dosing for Toxic Alcohols: Adjustments During ECTR

Antidote	Loading Dose	Maintenance (Nondrinker)	Maintenance (Chronic Drinker)	HD Dose (Nondrinker)	HD Dose (Drinker)
Ethanol 43% oral	1.8 mL/kg	0.2 mL/kg/h	0.5 mL/kg/h	0.5 mL/kg/h	0.8 mL/kg/h
Ethanol 10% IV	7.5 mL/kg	0.8 mL/kg/h	2.0 mL/kg/h	2.1 mL/kg/h	3.3 mL/kg/h
Ethanol dialysate	300 mL of 95% ethanol added to 4.5 L acid concentrate; ultrafiltrate flow 500 mL/min.				
Fomepizole	15 mg/kg loading	10 mg/kg q12h ×4 doses then 10–15 mg/kg q12h	10 mg/kg q4h (q8h in CKRT) or 1 mg/kg/h during HD		

★ **Fomepizole preferred:** predictable PK, ease of administration, fewer adverse effects.

01

151 Da

Acetaminophen

02

180 Da

Salicylates

03

232 Da

Barbiturates

PART VI:

Drug-Specific Management – A to E

Acetaminophen • Salicylates • Barbiturates • Digoxin • Toxic Alcohols

04

781 Da

Digoxin

05

62 DaToxic Alcohols
(Methanol)

06

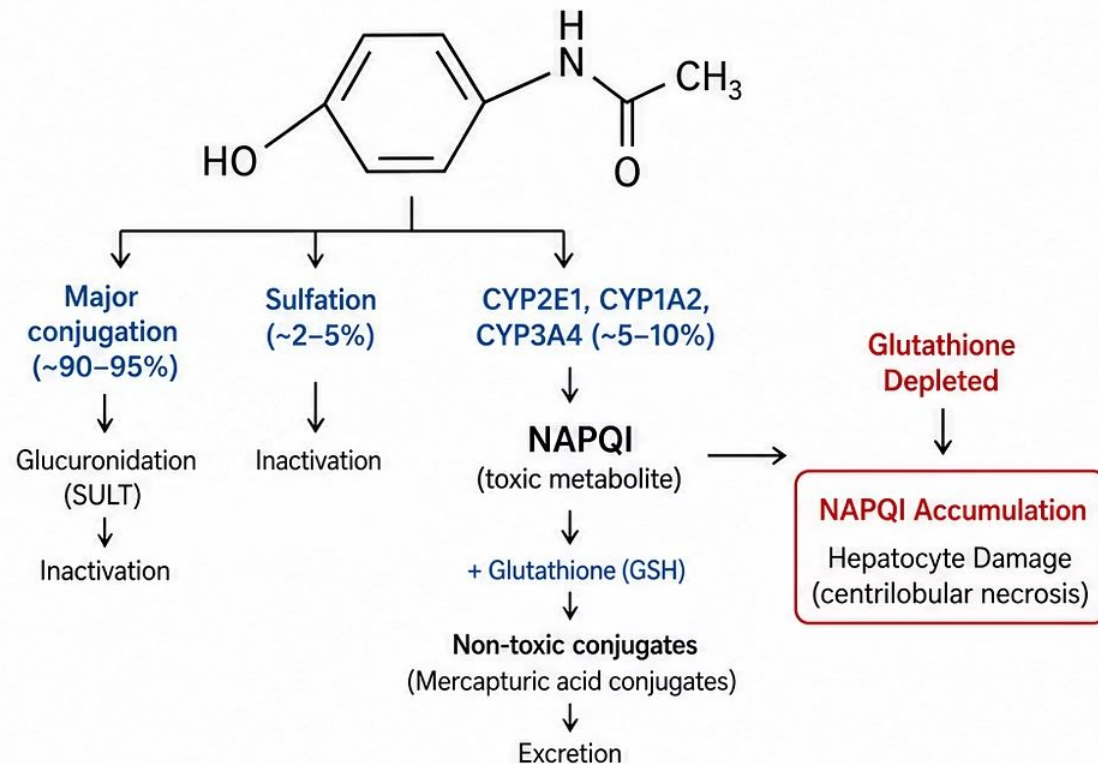
32 DaToxic Alcohols
(Ethylene Glycol)

A. Acetaminophen (MW 151 Da) — Management and ECTR

CLINICAL PATHWAY

- 1 MDAC within 4 hours of ingestion.
- 2 Rumack-Matthew nomogram: plot serum level at 4h.
- 3 If level >150 mg/L (1.0 mmol/L) at 4h → start NAC (PO or IV).
- 4 NAC increases glutathione, prevents toxic metabolite accumulation.
- 5 Efficacy declines >10h post-ingestion but still recommended even after 24h.
- 6 HD indication: acetaminophen >900 mg/L (5.9 mmol/L) + acidosis or altered consciousness.
- 7 During HD: IV NAC dose must exceed 12.5 mg/kg/h (NAC is dialyzed out).

Acetaminophen (Paracetamol)

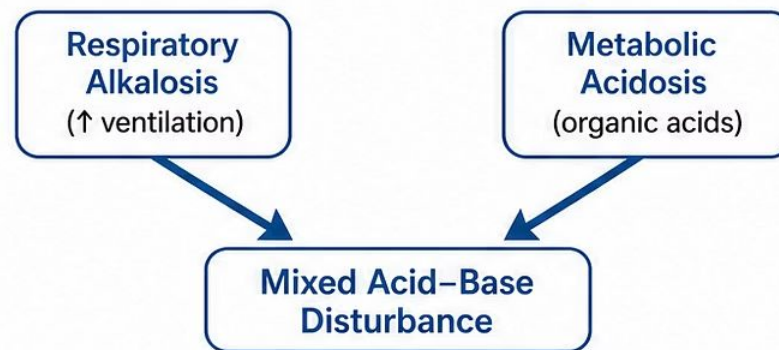


Concomitant moderate ethanol use markedly increases hepatotoxicity risk.

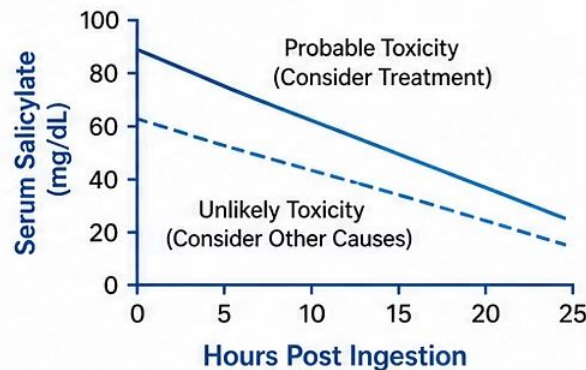
B. Salicylates (MW 138–180 Da) – Management and ECTR

- Adults: metabolic acidosis + respiratory alkalosis; children: isolated metabolic acidosis.
- CNS symptoms = severe poisoning marker.
- Initiate MDAC; urine alkalinization if urine output adequate and salicylate >50 mg/dL (2.8 mmol/L).
- Aspirin $V_d = 0.15 \text{ L/kg}$; ~50% protein bound but well removed by HD (binding saturates in OD).
- HD indications: salicylate >100 mg/dL (5.6 mmol/L); neurologic symptoms; ARDS; kidney impairment; $\text{pH} \leq 7.20$.
- Cessation: clinical improvement and salicylate <20 mg/dL (1.4 mmol/L).

Acid-Base Effects of Salicylates



Done Nomogram (Children)

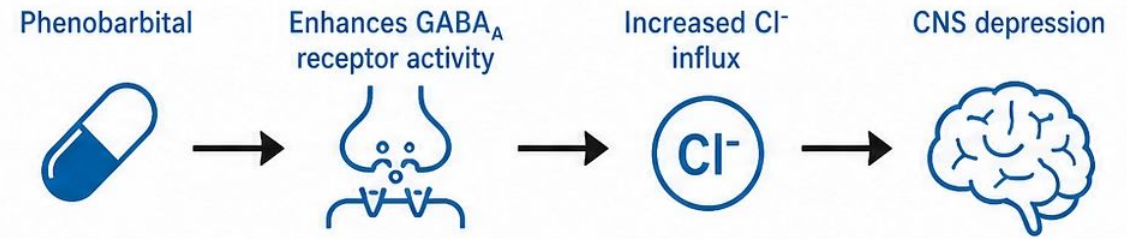


 **HD > HP > CKRT**
in order of preference.

C. Barbiturates (Phenobarbital, MW 232 Da) – Management and ECTR

- **Toxic serum level:** >3 mg/dL (130 $\mu\text{mol/L}$).
- **Coma onset:** ~6 mg/dL (260 $\mu\text{mol/L}$).
- **First-line:** MDAC + urine alkalization for long-acting barbiturates.
- **Phenobarbital:** 50% protein bound, $V_d = 0.5 \text{ L/kg}$ — well removed by HD or HP.
- **HD = HP** in removal efficacy with synthetic membrane dialyzer (Palmer, 2000).
- **HD indications:** coma, shock, or requirement for mechanical ventilation.
- **Cessation:** clinical improvement.

NEUROLOGICAL DEPRESSION PATHWAY



SERUM LEVEL AND CLINICAL EFFECTS



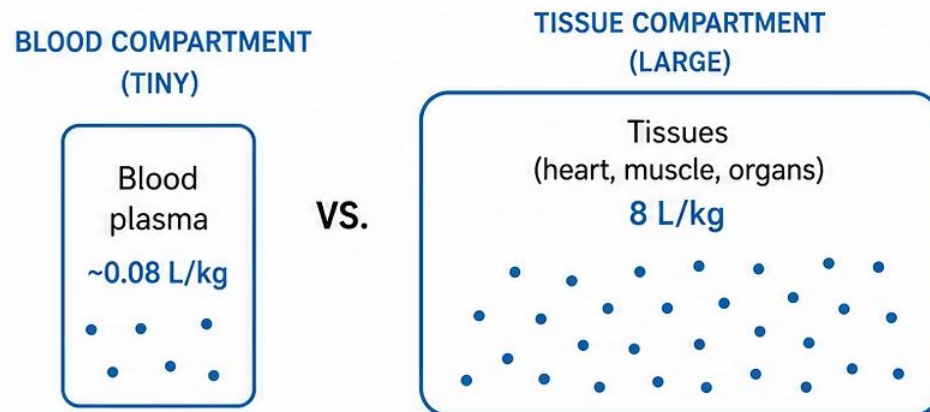
HD > HP preferred;

MDAC should be coadministered throughout ECTR.

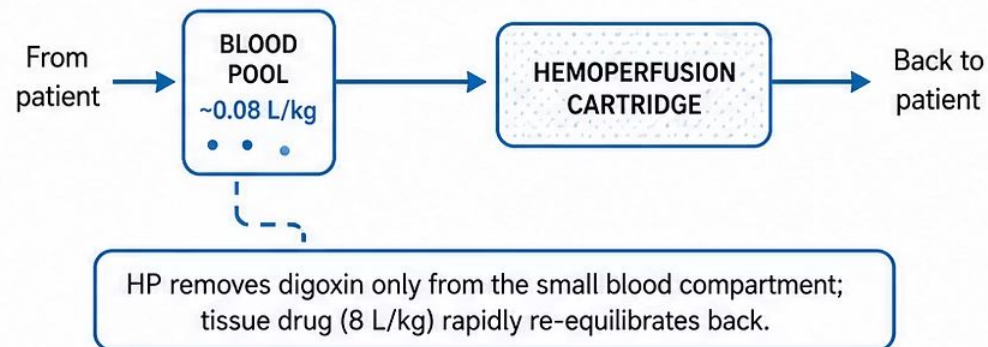
D. Digoxin (MW 781 Da) — Why ECTR Has Limited Role

- Arrhythmia probability: 50% at 2.5 ng/mL; 90% at 3.3 ng/mL.
- Correct hypokalemia, hypomagnesemia, alkalosis; give MDAC.
- $V_d = 8 \text{ L/kg}$ (normal); 4.2 L/kg in dialysis patients; only 5% body load removed by 4-hour HD.
- HP more effective than HD but total body clearance still limited by massive V_d .
- First-line: Digoxin-specific antibody fragments (Fab/Digifab) for severe toxicity.
- In dialysis patients: Fab still preferred over HP or plasmapheresis.
- Post-Fab rebound: digoxin released from Fab-digoxin complex → possible second treatment.
- Plasmapheresis after Fab promotes removal of Fab-digoxin complexes.
- High-cutoff membranes (e.g., Theralite) can also remove Fab-digoxin complexes.

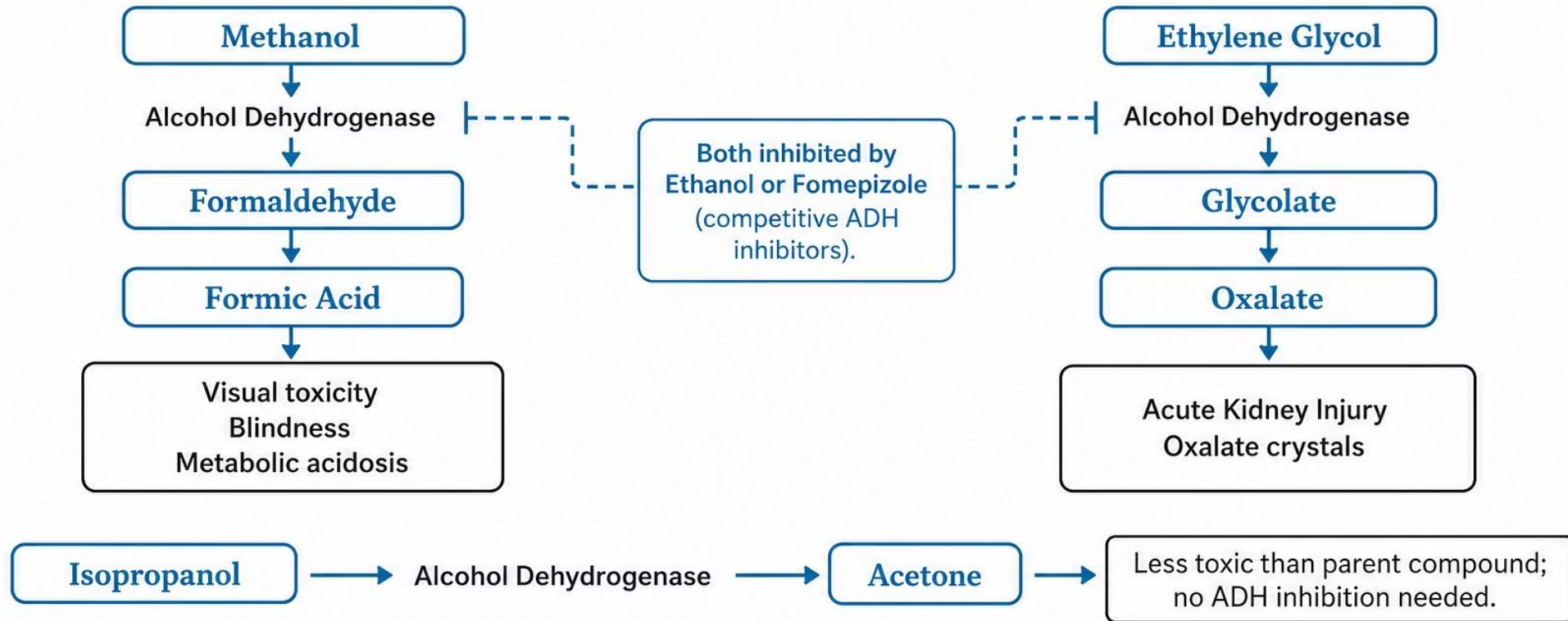
V_d CONCEPT: DIGOXIN IS EXTENSIVELY DISTRIBUTED



HOW HP CIRCUIT EXTRACTS ONLY FROM TINY BLOOD POOL



E. Toxic Alcohols – Pathophysiology Overview



Early: elevated osmolal gap
(parent alcohols).



Late: elevated anion gap metabolic acidosis
(toxic metabolites).



MDAC: No role for MDAC or GI decontamination in alcohol poisonings.

E1. Ethylene Glycol (MW 62 Da) — Three Phases and ECTR

Phase 1 (0–12h)

CNS depression mimicking ethanol intoxication; coma and seizures in severe cases.

Phase 2 (12–24h)

Glycolic acid toxicity → cardiac and respiratory failure; severe metabolic acidosis.

Phase 3 (24–48h)

Oxalate precipitation in kidneys → AKI, flank pain, hypocalcemia, ATN, urine oxalate crystals.

MANAGEMENT

- Early aggressive NaHCO_3 for acidosis.
- Antidote indications per Table 18.4.
- HD indications: shock, coma, seizures, AG >24 mmol/L, AKI, EG level >310 mg/dL (with antidote).
- Fomepizole alone sufficient if no AKI and no acidosis — but monitor closely.
- Half-life of EG with fomepizole: ~34 hours.
- HD target: AG <18, acidosis resolved, EG <25 mg/dL (4 mmol/L).
- Pyridoxine 50 mg IM QID + Thiamine 100 mg IM QID to enhance glyoxylate metabolism.

E2. Methanol (MW 32 Da) — Vision, Acidosis, and ECTR

- **Phase 1:** transient CNS depression (early).
- **Latent period:** 6–24 hours before metabolic acidosis and visual symptoms.
- **Formic acid accumulation** → blurred vision, decreased acuity, photophobia, visual field defects, blindness.
- **Early signs:** optic disc hyperemia, decreased pupillary light reflex.

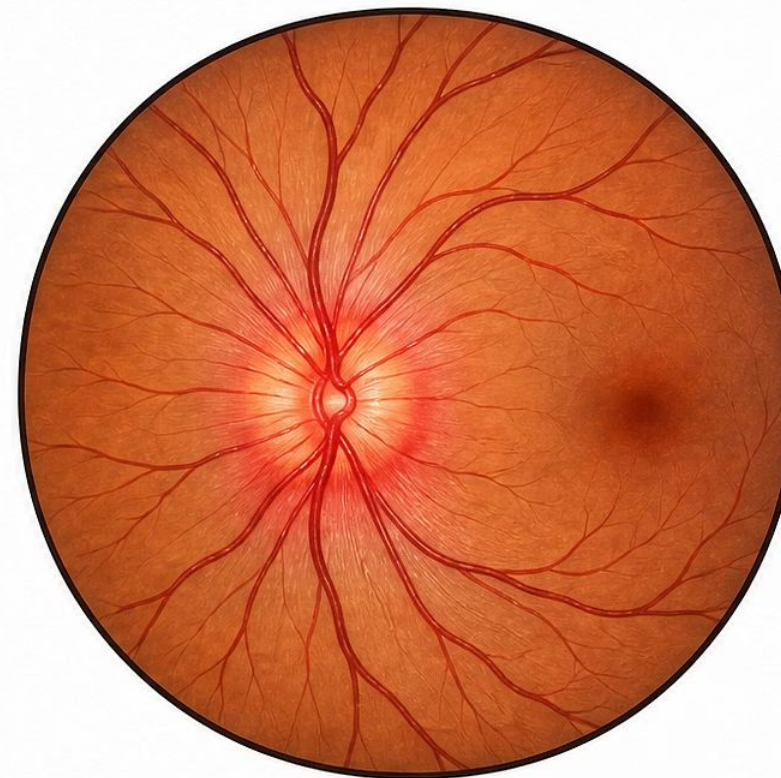
MANAGEMENT

- Correct acidosis: NaHCO_3 to pH 7.35–7.40.
- Fomepizole preferred ADH inhibitor; give as soon as possible.
- Half-life of methanol with fomepizole alone: up to 87 hours (Maskell, 2016).
- Folinic acid IV 1 mg/kg (max 50 mg) q4h to enhance formate metabolism; substitute folic acid if unavailable.

HD INDICATIONS: coma, seizures, new vision deficits, pH <7.15, AG >24 mmol/L, methanol >50–70 mg/dL depending on antidote used.

HD TARGET: acidosis corrected, methanol <20 mg/dL (6.2 mmol/L).

Fundoscopy Illustration



Optic Disc Hyperemia

E3 & E4. Isopropanol and Other Toxic Alcohols

Isopropanol (MW 60 Da):

- Found in rubbing alcohol, antifreeze, frost remover. Oxidized by ADH → Acetone (less toxic than parent compound).
- High osmolal gap WITHOUT acidosis + elevated acetone = classic presentation.
- Supportive care is usually sufficient. ADH inhibition not warranted.
- HD consideration: isopropanol >400 mg/dL (67 mmol/L) + CNS depression, renal failure, or hypotension.

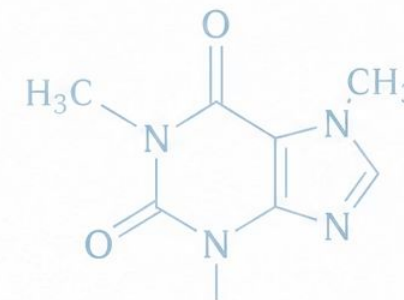
Other Toxic Alcohols

Propylene Glycol (MW 76)	lactic acidosis + elevated osmolal gap	pharmaceutical excipient (lorazepam, nitroglycerin)
2-Butoxyethanol (MW 118)	resins, varnishes, glass cleaners	metabolic acidosis, hepatic injury, respiratory distress
Diethylene Glycol (MW 106)	metabolic acidosis, AKI, hypertension, arrhythmias	fomepizole recommended
All	Hemodialysis effective and indicated in severe intoxications.	

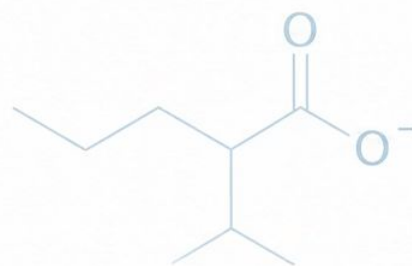
PART VII:

Drug-Specific Management — F to O

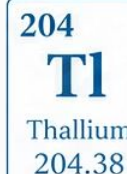
Lithium • Mushroom Toxins • Paraquat •
 Phenothiazines/TCAs • Anticonvulsants • Theophylline •
 Dabigatran • Metformin • Thallium.



Theophylline



Valproate





F. Lithium (MW 7 Da) — The Ideal HD Candidate

TOXICITY GRADING

Grade	Clinical Features
Mild (Li 1.5–2.5 mmol/L)	neuromuscular irritability, nausea, diarrhea.
Moderate (2.5–3.5 mmol/L)	tremor, ataxia, confusion.
Severe (>3.5 mmol/L)	seizures, stupor, permanent neurologic deficit.

COMMON CAUSES

chronic accumulation, renal failure,
diuretics, dehydration, ACE inhibitors, NSAIDs.

MANAGEMENT

- Stop diuretics immediately. Prompt IV rehydration.
- Sodium polystyrene sulfonate may facilitate Li elimination.
- Lithium: 0% protein bound, $V_d = 0.8 \text{ L/kg}$ → excellently removed by HD.
- HD indications: decreased LOC, seizures, dysrhythmias, AKI, or Li >5.0 mEq/L.
- Cessation: Li <1.0 mEq/L sustained for 6–8 hours post-dialysis.
- Rebound from intracellular compartment common → additional HD or CKRT often required.
- Prolonged continuous hemodiafiltration may reduce rebound extent.



G & H. Mushroom Poisoning and Paraquat

Mushroom (Amanita):

- α -amanitin and phalloidin (MW ~900 Da): severe GI symptoms $\rightarrow$ hepatic insufficiency $\rightarrow$ cardiovascular collapse.
- Both removed in vitro by HD and HP — but clinical efficacy unproven.
- Activated charcoal adsorption of amanitin; silibinin (milk thistle flavonolignan) prevents hepatocyte amanitin uptake.
- Early referral to poison center and liver transplantation unit is imperative.

Paraquat (MW 257 Da):

- Delayed toxicity: pulmonary fibrosis, renal failure, multiorgan failure after >10 mL concentrate.
- Plasma level >3 mg/L regardless of timing: usually fatal.
- Initial: gastric lavage + activated charcoal or Fuller earth + cathartic + immunosuppressants + antioxidants.
- HP or HD within first 4 hours; consider when plasma paraquat ≥ 0.1 mg/L (0.4 μ mol/L).
- Repeated/continuous ECTR may be needed for days — slow intercompartmental transfer.
- Mortality >50% even after 10 mL ingestion. If presentation delayed with respiratory failure: offer palliation.





I & J. TCAs, Phenothiazines, and Anticonvulsants



Phenothiazines and Tricyclic Antidepressants

- Protein binding: >90%; Vd: 14–21 L/kg — prohibitive for ECTR.
- Treatment is largely supportive: bicarbonate therapy for widened QRS complex.
- Neither HD nor HP recommended.

Anticonvulsants

Phenytoin (MW 252 Da)

- 90% protein bound (70% in uremia); Vd 0.64 L/kg.
- Despite high PB, moderately well removed by HD or HP.
- Consider HD for prolonged coma or ataxia.

Valproic Acid (MW 144 Da)

- Small Vd; hepatic metabolism; high PB saturates in OD.
- HD: cerebral edema, coma, shock, AH, pH ≤ 7.10 , respiratory depression, or level >1,300 mg/L (9,000 $\mu\text{mol/L}$).

Carbamazepine (MW 236 Da)

- HP for severe intoxications. High-flux HD also effective.
 - HD indications: refractory seizures, dysrhythmias, prolonged coma, respiratory depression despite MDAC.
 - Cessation: clinical improvement or level <10 mg/L.
- 

K. Theophylline (MW 180 Da) – ECTR and MDAC Strategy

TOXICITY THRESHOLDS

Therapeutic:	Toxic:	Seizures:	Cardiovascular collapse:
10–20 mg/L (56–112 mcmol/L)	>25 mg/L (139 mcmol/L)	typically >40 mg/L (222 mcmol/L)	>50 mg/L (278 mcmol/L)

Chronic intoxication: more severe symptoms at equivalent levels.

PHARMACOKINETICS

Vd = 0.5 L/kg; 56% protein bound; poor intrinsic metabolism; well adsorbed by charcoal.

MANAGEMENT

- MDAC first-line even for IV overdose (protracted vomiting limits use).
- Propranolol 1–3 mg IV for tachyarrhythmia; correct hypokalemia.
- HD preferred over HP for ECTR; CKRT second line.
- ECTR indications: vomiting prevents MDAC; seizures, shock, arrhythmia.
- HD if: acute OD >100 mg/L (555 mcmol/L); chronic OD >60 mg/L (333 mcmol/L); elderly or infants <6 months >40 mg/L.
- Cessation: level <15 mg/L (83 mcmol/L).
- Coadminister MDAC during ECTR.



L & M. Dabigatran and Metformin — ECTR Considerations

Dabigatran (Pradaxa):

- Oral direct thrombin inhibitor for nonvalvular AF thromboembolism prophylaxis; approved US 2010.
 - Hemorrhagic complications reported; vitamin K / FFP / cryoprecipitate ineffective for reversal.
 - 4-hour HD removes 49–59% of total dabigatran (Khadzhynov, 2013); first-order kinetics during HD.
 - CVVHDF useful in severe cases.
 - Idarucizumab (specific monoclonal antibody): now preferred where available — may obviate HD.
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Metformin (MW 129 Da):

- Biguanide antihyperglycemic; lactic acidosis in OD or AKI-related accumulation.
 - Mortality ~30% in severe cases (Peters, 2008).
 - 90% renally eliminated; serum $t_{1/2}$ = 1.5–5h; V_d = 3 L/kg limits removal.
 - Dialyzer extraction ratio = 60% (Nguyen, 2011) but V_d reduces net benefit.
 - HD indications: shock, decreased LOC, lactate >20 mmol/L, pH <7.0, failure of supportive measures.
 - HD also rapidly corrects associated metabolic acidosis — key benefit.
 - Cessation: lactate <3 mmol/L and pH >7.35. Repeat HD/CKRT sessions often needed.
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N & O. Thallium and Other Agents

Thallium (MW 204 Da):

- Highly toxic metal; industrial exposure, herbal product contamination, drugs of abuse, homicide.
- Fatal dose as low as 6 mg/kg.
- Presentation: alopecia, painful ascending peripheral neuropathy, abdominal pain, vomiting, constipation, autonomic instability, cranial nerve involvement; severe: coma, respiratory paralysis, cardiac arrest.
- Screening: urine thallium (normal <5 mcg/L).
- Treatment: MDAC + Prussian blue (GI elimination).
- Hourly HD + charcoal HP clearance superior to normal renal function; comparable to Prussian blue.
- HD beneficial if instituted early, before full tissue distribution.

Other Notable Agents:

- **Baclofen:** HD if coma + MV + renal impairment; watch for withdrawal seizures.
 - **Gabapentin/Pregabalin:** HD if coma + renal impairment.
 - **Isoniazid:** HD if pyridoxine cannot be given + refractory seizures.
 - **Methotrexate:** HD if soon after IV exposure; leucovorin antidote preferred.
 - **Boric acid, Bromide, Fluoride:** HD effective.
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Table 18.6 (Part 1) — Extracorporeal Removal of Common Poisons: A–G

Drug	MW (Da)	Vd (L/kg)	Protein Binding	ECTR Recommendation
Acetaminophen	151	0.9	25%	Effective antidote; HD if mitochondrial toxicity.
Acyclovir	225	0.6	15%	HD if renal impairment.
Amanita	990	0.3	2%	HD if soon after ingestion.
Amiodarone	645	66	99%	None — Vd too large.
Baclofen	214	0.9	30%	HD if renal impairment.
Boric acid	62	0.4	20%	HD.
Carbamazepine	236	1.1	75%	HD.
Chloral hydrate	165	0.8	75%	HD.
Chloroquine	320	130	60%	None — Vd too large.
Digoxin	781	6	25%	None — Vd too large; effective antidote.
Ethylene glycol	62	0.6	0%	HD.

CL = endogenous clearance; HD = hemodialysis; HP = hemoperfusion; KI = kidney impairment; TPE = therapeutic plasma exchange.

Table 18.6 (Part 2) — Extracorporeal Removal of Common Poisons: L–V

Drug	MW (Da)	Vd (L/kg)	Protein Binding	ECTR Recommendation
Lithium	7	0.8	0%	HD (ideal candidate)
Methanol	32	0.7	0%	HD
Metformin	165	4	<5%	HD if renal impairment and severe toxicity
Paraquat	186	1.5	5%	HD + HP only if early after exposure
Phenobarbital	232	0.7	40%	HD
Phenytoin	252	0.7	90%	HD, HP
Pregabalin	159	0.5	0%	HD
Salicylate	138	0.2	90%	HD (protein binding saturates in OD)
Theophylline	180	0.5	50%	HD, HP
Thallium	204	5	0%	HD only if soon after exposure
Valproic acid	144	0.3	90%	HD (protein binding saturates in OD)
Vancomycin	1449	0.7	55%	HD if renal impairment

Vd >2 L/kg generally predicts poor ECTR yield. PB >80% limits removal unless saturated in OD.



Table 18.6 (Part 3) — Drug Class ECTR Summary



Drug/Poison Class

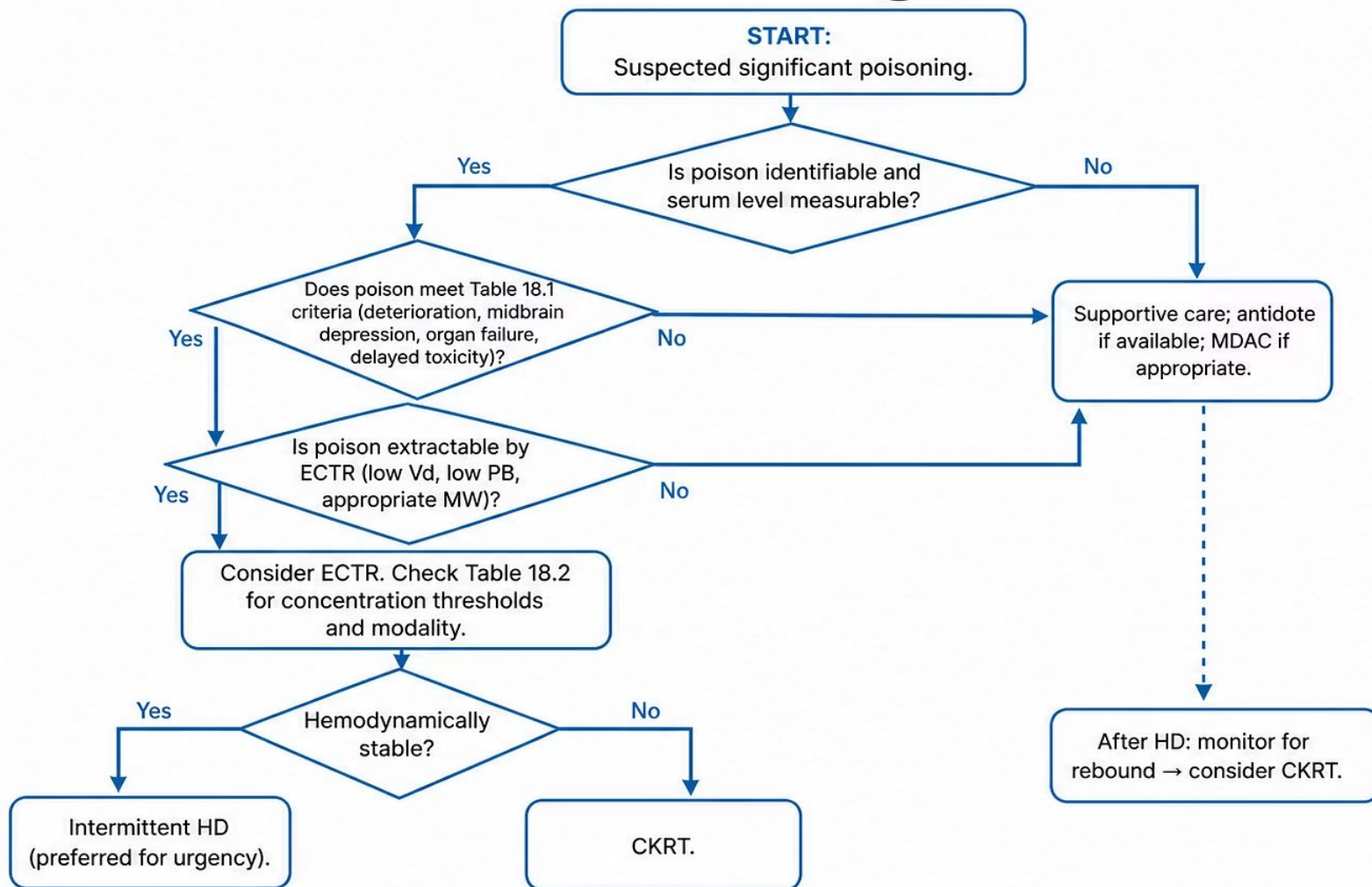
ECTR Recommendation

1 Aminoglycosides	HD.
2 Benzodiazepines	None — effective antidote (flumazenil).
3 Beta-adrenergic antagonists	HD for atenolol, bisoprolol, nadolol, sotalol only (others: Vd too large).
4 Calcium channel blockers	None — Vd too large.
5 Endogenous metals (Mg, K, Ca, PO ₄)	HD.
6 Monoclonal antibodies	TPE (MW >100,000 Da; rarely indicated).
7 NSAIDs	TPE (rarely indicated; protein binding limits standard HD).
8 Opioids	None — effective antidote (naloxone).
9 Organophosphates	None — Vd too large, slow intercompartmental transfer.
10 Other metals (Al, Hg)	HD with chelation.
11 Tricyclic antidepressants	None — Vd too large (14–21 L/kg).

Drug class behaviors are generalizable but individual agents may differ; consult EXTRIP guidelines.



Algorithmic Approach to ECTR Decision-Making in Poisoning



★
Always continue
antidote administration
during ECTR with
dose adjustment.

Clinical Pearls: What Every Clinician Must Remember



1.

Hemodialysis is the default ECTR modality — superior clearance, corrects acid-base/electrolytes.



2.

Hemoperfusion largely supplanted by high-flux HD in the US; limited availability.



3.

High Vd (>2 L/kg) and high protein binding ($>80\%$) are the two biggest barriers to ECTR.



4.

In overdose, protein binding saturates — increasing free drug available for dialysis (salicylate, valproate, phenytoin).



5.

CKRT: for hemodynamically unstable patients — lower but sustained clearance, reduces rebound.



6.

Fomepizole: preferred ADH inhibitor for toxic alcohol poisoning; dose must be increased during HD.



7.

NAC must exceed 12.5 mg/kg/h IV during HD for acetaminophen poisoning — NAC is dialyzed.



8.

Lithium rebounds from intracellular stores — monitor 6–8h post-dialysis; CKRT reduces rebound.



9.

Phosphate supplementation in dialysate prevents dangerous hypophosphatemia during intensive HD.



10.

Baclofen removal may precipitate withdrawal — reintroduce baclofen + GABA-A agonist.

EXTRIP Workgroup: Evidence-Based Framework



Primary reference: Lavergne V, et al. Clin Toxicol (Phila). 2012;50:403–413.



Key Takeaways

- ECTR is adjunctive — supportive care and antidotes remain the foundation of poisoning management.
- Hemodialysis is preferred for most ECTR-amenable toxins; CKRT for hemodynamic instability.
- Pharmacokinetic properties (V_d , protein binding, MW) determine ECTR feasibility.
- Use EXTRIP evidence-based tables for concentration thresholds, modality choice, and cessation criteria.
- Always adjust antidote doses (NAC, fomepizole, ethanol) during extracorporeal treatments.



Prepared by
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Based on: Harbord NB, Ghannoum M, Charen E. Use of Dialysis and Hemoperfusion in the Treatment of Poisoning.

