Extracorporeal treatment for intoxications

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Extracorporeal treatment for intoxications

1) **Intoxications: History, frequency**
2) **Conservative management of intoxications**
3) **Extracoroporeal treatment strategies**
   - **case based approach**
1) **Summary**

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4) **Summary**

The application of hemodialysis to the treatment of barbiturate poisoning

KYLE *J Clin Invest* 32:364-371, 1953

THE APPLICATION OF HEMODIALYSIS TO THE TREATMENT OF BARBITURATE POISONING[1]

By LAURENCE H. KYLE, HAROLD JEGHERS, WILLIAM P. WALSH, PAUL D. DOOLAN, HENRY WISHINSKY, AND ARTHUR PALLOTTA

(*From the Department of Medicine, Georgetown University Medical Center, Washington, D. C.*)

(Submitted for publication August 20, 1952; accepted January 7, 1953)

Current methods of treatment of barbiturate poisoning, which consist of supportive measures aimed towards maintenance of life until the drug can be excreted or metabolized, have occasioned considerable dissatisfaction because of their lack of specificity. Ideal therapy must be directed toward either more rapid removal or accelerated detoxification of the barbiturate preparation. The closest approach to this goal has been the use of massive intravenous infusions to initiate diuresis with consequently more rapid urinary excretion of the drug.

Morbidity and mortality in a significant number of patients with barbiturate toxicity are not directly related to the primary depressant effect of the drug. Many patients, especially in the older age group, die because of respiratory difficulties. Morbidity at all ages is often increased by such complications. The number and severity of these could be reduced if the drug were removed from the body more rapidly, thus shortening the period of coma.

The application of massive hydration (1) or cross-circulation of a poisoned dog with a large

bound and there is a possibility that the binding is loose, a form of equilibrium existing between the bound and the unbound portions. On this premise it appeared worthwhile to ascertain the possibility of removing barbiturate from the body by means of hemodialysis.

METHODS

The instrument used for hemodialysis in this investigation was the Kolff type of artificial kidney, modified and utilized extensively by Merrill and his associates (4, 5) and studied further by Wolf, Remp, Kiley, and Currie (6).

Determination of the barbiturate content of the blood, urine and bath fluid was carried out in early experiments by a method (Method A) which combined the salient features of several previously described procedures (7–9). In later experiments, the procedure (Method B) of Goldbaum was employed (10). Both methods employed, as well as other methods of barbiturate analysis, suffer from a lack of specificity since they do not differentiate between the barbiturate, a breakdown product or a metabolic coupling product.

Method A

Blood: Five ml. of oxalated blood, buffered to pH 5.5 with 1 M KH_2PO_4, was extracted with 50 ml. of chloro-

2004 Annual Report of the American Association of Poison Control Centers Toxic Exposure Surveillance System

WATSON et al *Am J Emerg Med* 23: 589-666, 2005

Therapy	No.
Decontamination	
Dilution/irrigation	1127564
Activated charcoal, single dose	130938
Cathartic	44664
Gastric lavage	16179
Other emetic	8420
Ipecac syrup	4701
Whole bowel irrigation	2961
Measures to enhance elimination	
Activated charcoal, multidose	5031
Hemodialysis	1726
Other extracorporeal procedure	33
Hemoperfusion	29

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Gastric lavage

- **Gastric lavage should not be employed routinely!**
- **In experimental studies, the amount of marker removed by gastric lavage was highly variable and diminished with time.**
- **There is no certain evidence that its use improves clinical outcome and it may cause significant morbidity.**
- **Gastric lavage should not be considered unless a patient:**
  - **has ingested a potentially life-threatening amount of a poison**
  - **the procedure can be undertaken within 60 minutes of ingestion**
- **Even then, clinical benefit has not been confirmed.**
- **Unless a patient is intubated, gastric lavage is contraindicated if airway protective reflexes are lost.**

Single-dose activated charcoal

- **Based on volunteer studies, activated charcoal is more likely to produce benefit if administered within 1 h of poison ingestion. The administration of activated charcoal may be considered if a patient has ingested a potentially toxic amount of a poison up to 1 hour following ingestion. Activated charcoal may be considered more than 1 h after ingestion, but there are insufficient data to support or exclude its use.**
- **The optimal dose of activated charcoal for poisoned patients is unknown, though available data imply a dose-response relationship that favors larger doses. The United States Pharmacopeia (USP DI, 1997) recommends:**
  - **Children up to one year of age:1 g/kg**
  - **Children 1 to 12 years of age:25 to 50 g**
  - **Adults:25 to 100 g**
- **Contraindications: An unprotected airway.**

Gastric lavage

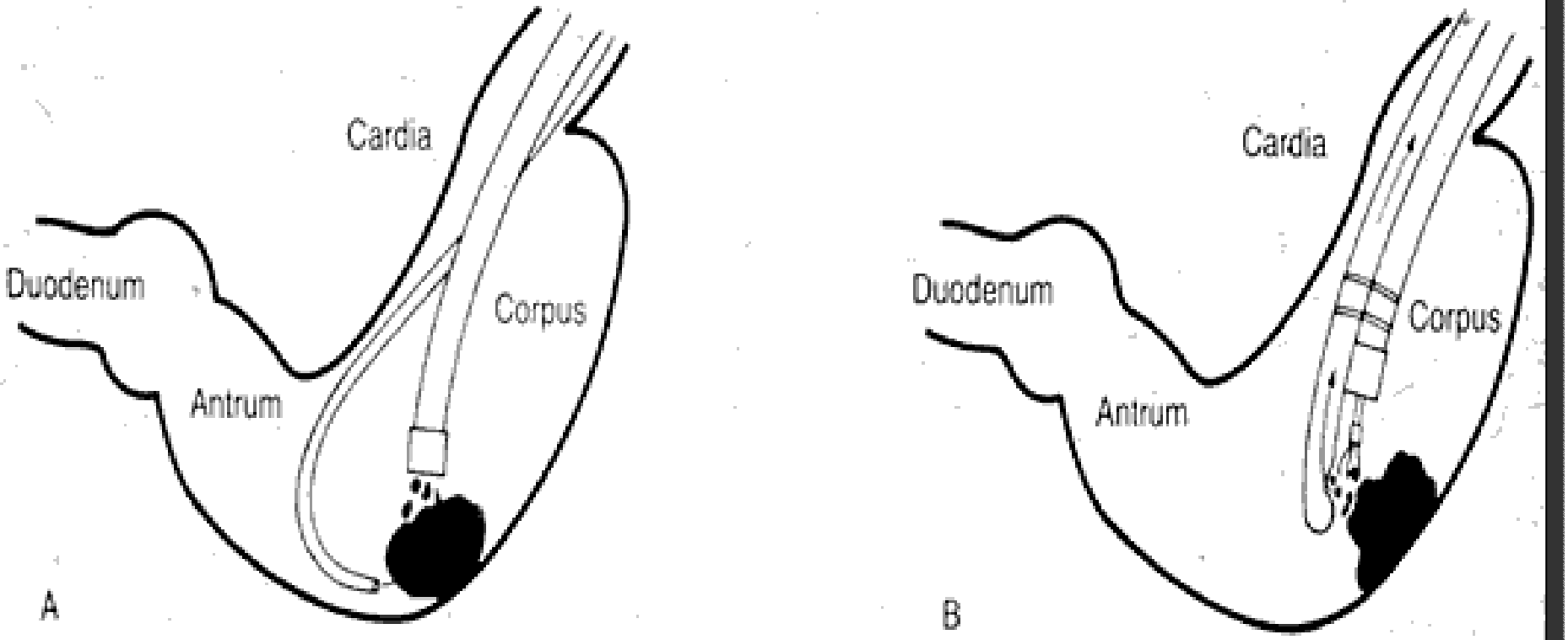

Figure 44–1 Drug conglomerate removal from the stomach by endoscopic gastric lavage. *A*, Removal of conglomerate with gastric tube and suction through the endoscope. *B*, Destroying the conglomerate with the endoscope and removal of fragments with the gastric tube.

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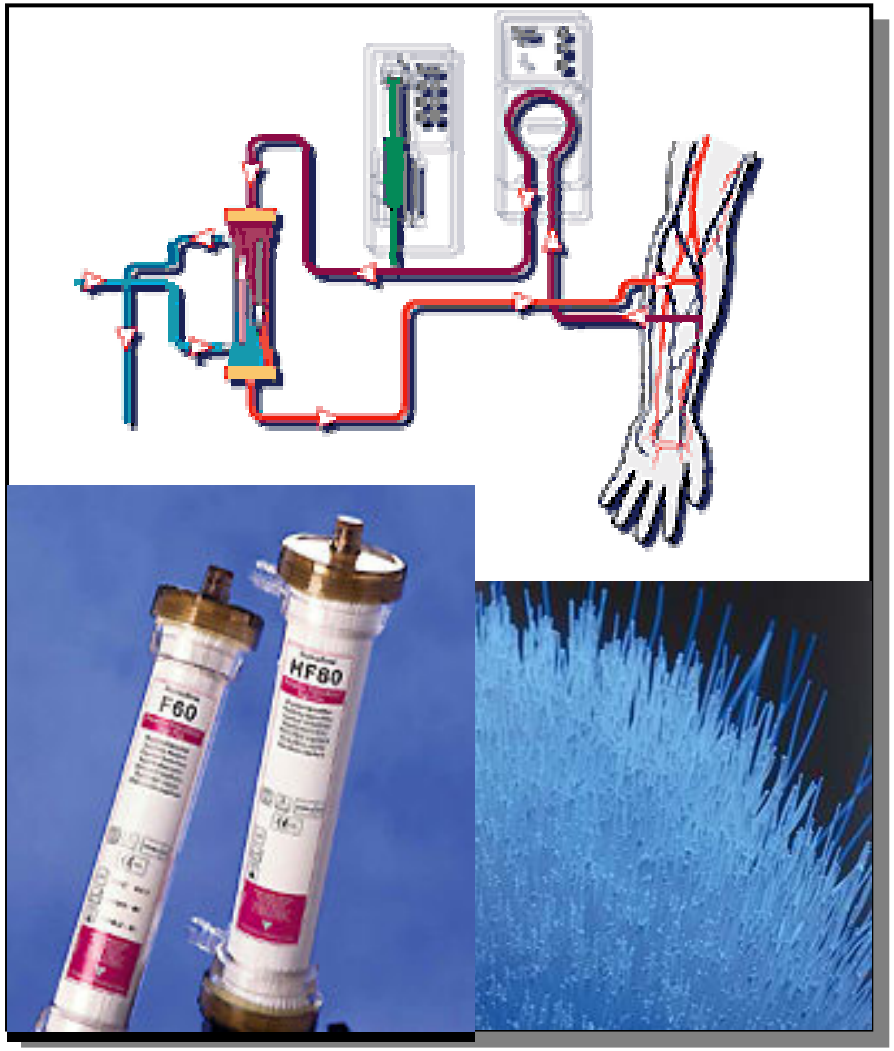
Haemodialysis

- **For substances with**
  - **High wter solubility**
  - **Low molecular weight**
  - **Low volume of distribution< 1 l/kg**
- **Disadvantage:**
  - **Not for substances with high protein binding**
- **Advantage:**
  - **Cheap**
  - **Simple**
  - **High availability**
  - **Treatment of AKI**

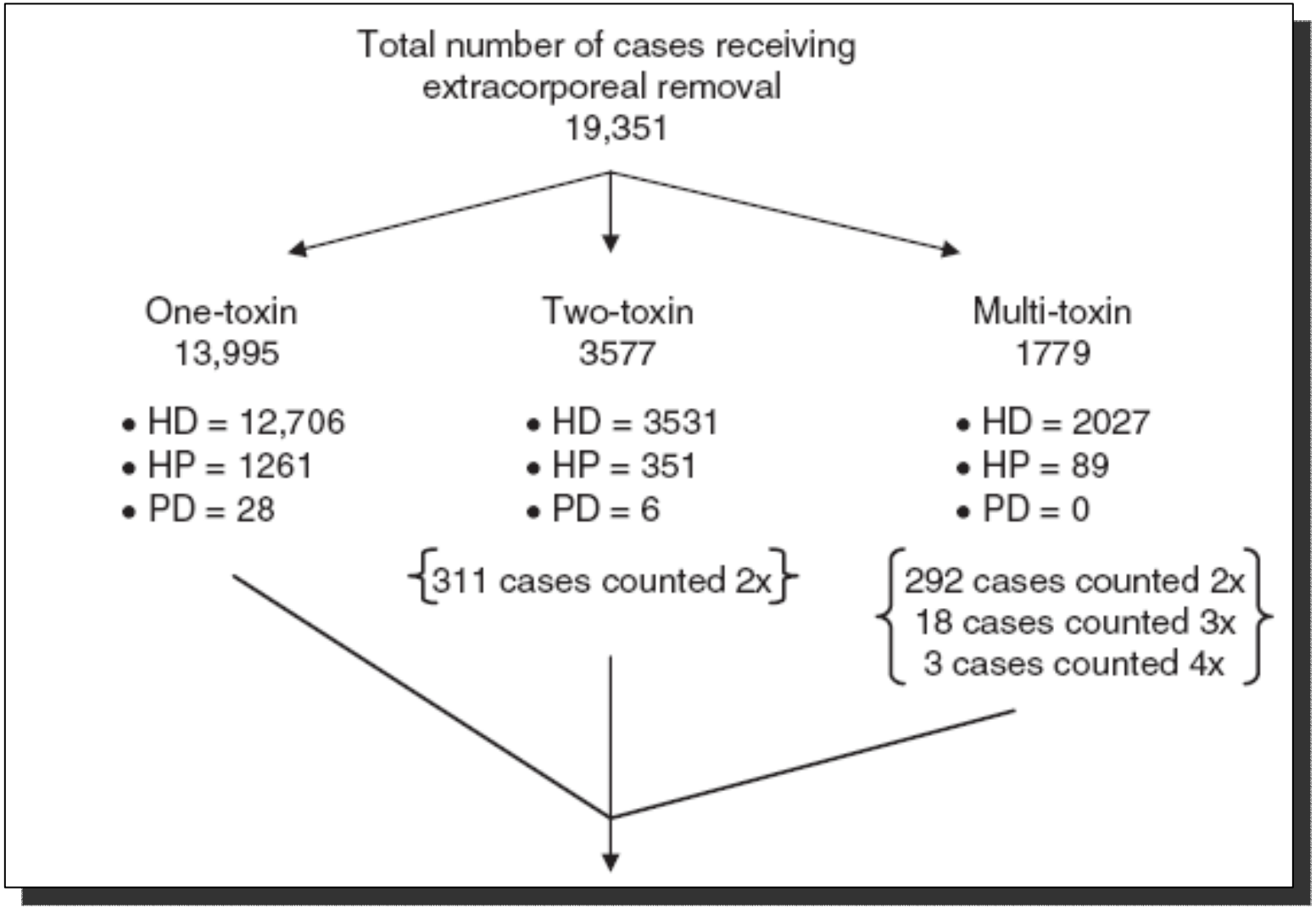


Haemoperfusion

- **For substances with**
  - **High protein biding**
  - **high volume of distribution**
- **Advantages:**
  - **Direct contact of blood with charcoal**
- **Disadvantages:**
  - **Thrombocytopenia**
  - **Hypothermia**
  - **Hypocalcemia**
  - **Logistics / Availability**
  - **Expensive**

Use of hemodialysis and hemoperfusion in poisoned patients (1985 – 2005)

HOLUBEK et al. *Kidney Int* 74, 1327–1334, 2008



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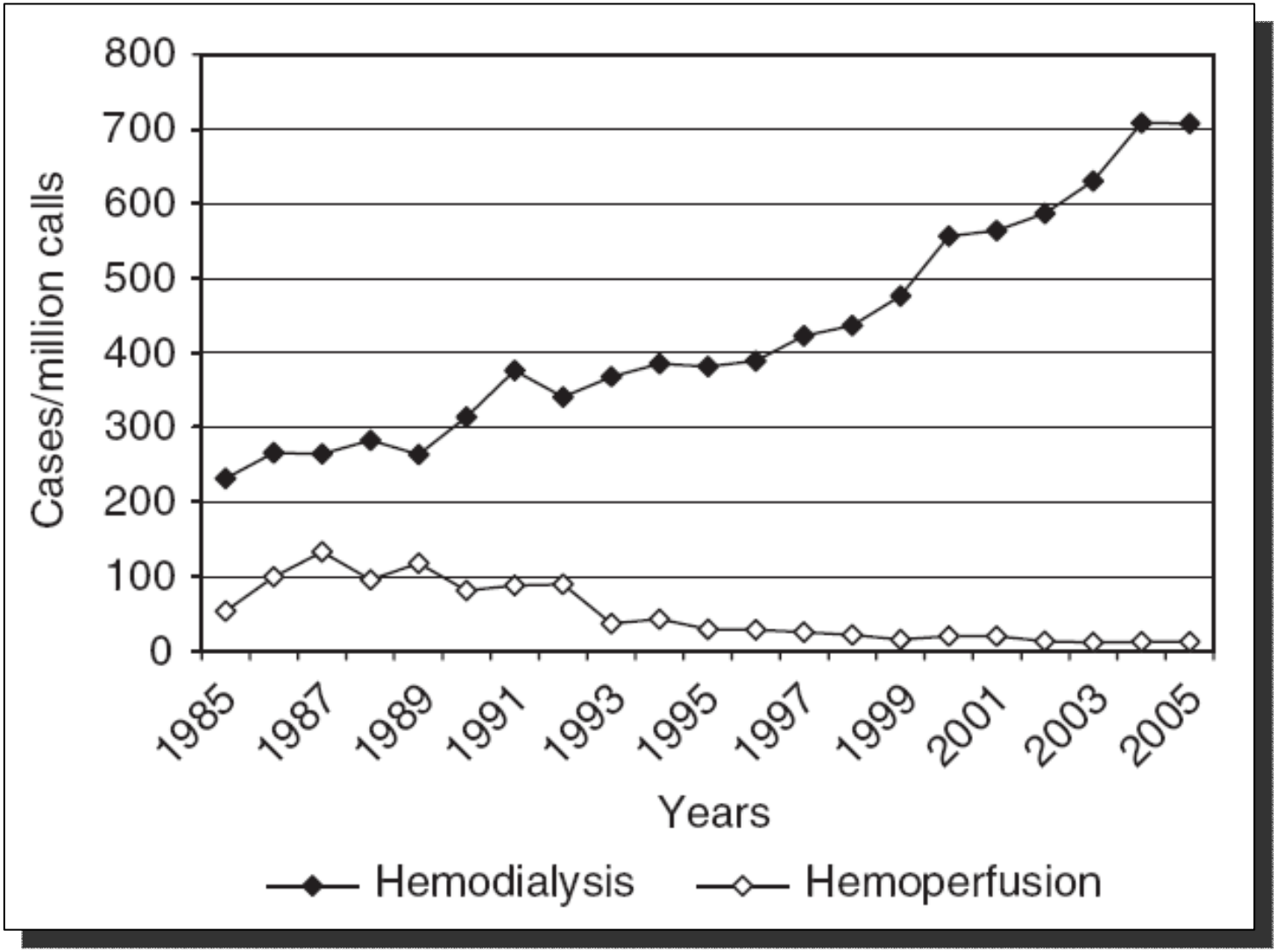

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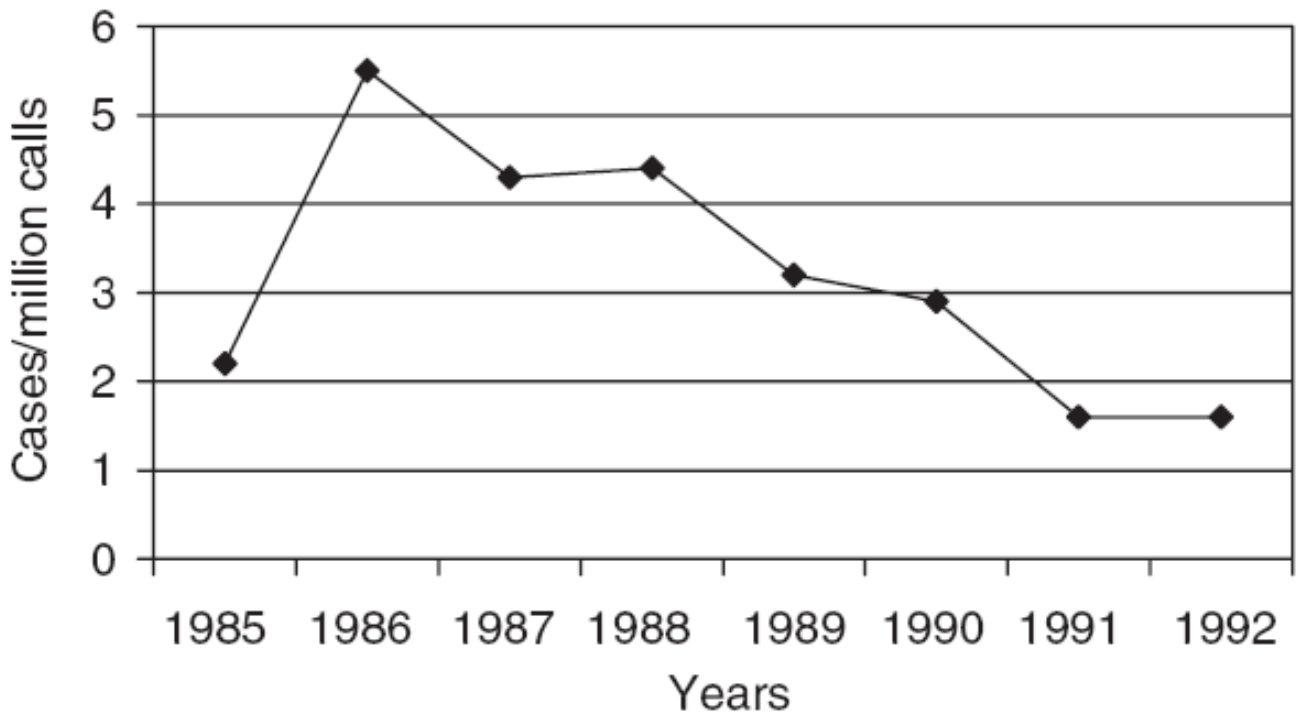


Figure 3 | Normalized number of cases receiving peritoneal dialysis. Peritoneal dialysis was no longer recorded in TESS after 1992.

Use of hemodialysis and hemoperfusion in poisoned patients (1985 – 2005)

HOLUBEK et al. *Kidney Int* 74, 1327–1334, 2008

Table 2 | The most common toxins responsible for cases receiving hemodialysis (total number)

1985–1990	1991–1995	1996–2000	2001–2005
Lithium (397)	Lithium (714)	Lithium (1178)	Lithium (2583)
Ethylene glycol (290)	Ethylene glycol (649)	Ethylene glycol (1138)	Ethylene glycol (2077)
Methanol (236)	Salicylates (358)	Salicylates (580)	Salicylates (1490)
Salicylates (233)	Aminophylline (284)	Methanol (289)	Valproic acid (516)
Aminophylline (229)	Methanol (240)	Aminophylline (240)	Acetaminophen (474)
Phenothiazine (73)	Acetaminophen (135)	Acetaminophen (192)	Methanol (463)
Ethanol (73)	Ethanol (84)	Valproic acid (170)	Ethanol (297)
Acetaminophen (71)	Phenothiazine (65)	Ethanol (111)	Benzodiazepine (281)
Isopropanol (49)	Isopropanol (59)	Other (90)	Other (274)

Table 3 | The most common toxins responsible for cases receiving hemoperfusion (total number)

1985–1990	1991–1995	1996–2000	2001–2005
Aminophylline (167)	Aminophylline (162)	Aminophylline (58)	Carbamazepine (38)
Acetaminophen (25)	Barbiturate (24)	Carbamazepine (16)	Lithium (30)
Barbiturate[a] (23)	Acetaminophen (12)	Benzodiazepine (14)	Ethylene glycol (22)
Carbamazepine (15)	Carbamazepine (11)	Valproic acid (13)	Acetaminophen (19)
Without opioid[b] (11)	Salicylates (8)	Other (12)	Valproic acid (17)
Mushroom (11)	Mushroom (6)	Ethylene glycol (9)	SSRI (17)
Salicylates (10)	Unknown[c] (5)	SSRI (9)	Phenothiazine (15)
Unknown[c] (9)	Amitriptyline (5)	Barbiturate[a] (8)	Ethanol (12)
Food poisoning[d] (8)	Valproic acid (4)	Lithium (7)	Biguanide (11)

Use of hemodialysis and hemoperfusion in poisoned patients (1985 – 2005)

HOLUBEK et al. Kidney Int 74, 1327–1334, 2008

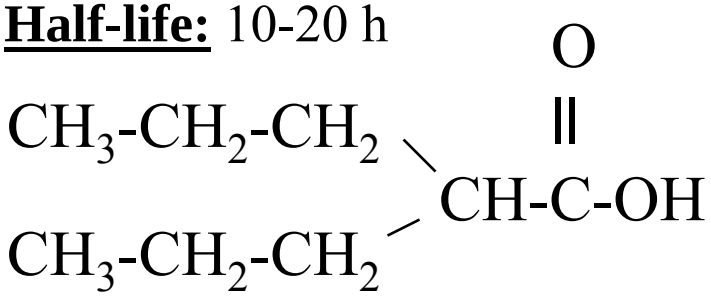
- **Lithium (2583)**
- Ethylene Glycol (2077)
- Salicylates (1490)
- **Valproic Acid (516)**
- Acetaminophen (474)
- Methanol (463)
- Ethanol (297)
- **Benzodiazepine (281)**
- **Other (274)**

Valproic Acid

- **Indication:**

- Anti seizure medication
- Bipolar disorder
- Anxiety disorder
- Migraine headache

- **Plasmalevel:** 50-100 mg/l
- **BIOV:** 100 %
- **Protein binding:** 93%
- **VOD:** 0.13 L/kg
- **Half-life:** 10-20 h



- **Letal dose:** ?, 700-1000 mg/l
- **Symptoms:**

-coma, seizures, cerebral edema
-bradycardia
-pancreatitis
-elevated transaminases
-thrombocytopenia

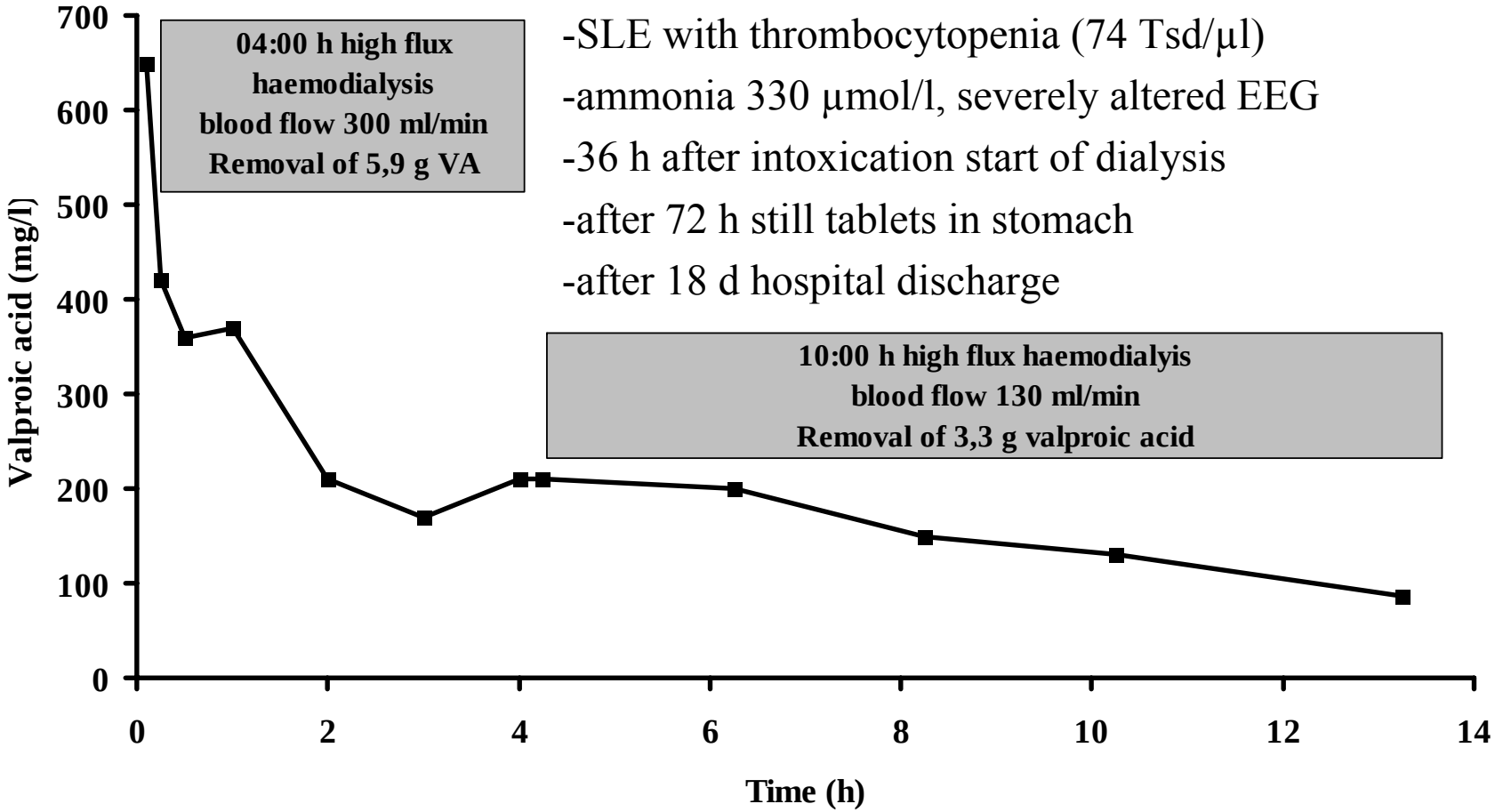
- **Detoxification:**

-active charcoal
-degree of plasma protein binding changes with plasma level
(at 450 mg/l only 70 protein bound)

Efficiency of high-flux hemodialysis in the treatment of valproic acid intoxication

KIELSTEIN et al. *J Toxicol Clin Toxicol* 41(6):873-6, 2003

-♂ 24 ca. 30 g VA in suicidal attempt, found 8 h post
-no gastric lavage
-SLE with thrombocytopenia (74 Tsd/µl)
-ammonia 330 µmol/l, severely altered EEG
-36 h after intoxication start of dialysis
-after 72 h still tablets in stomach
-after 18 d hospital discharge



Use of hemodialysis and hemoperfusion in poisoned patients (1985 – 2005)

HOLUBEK et al. *Kidney Int* 74, 1327–1334, 2008

Table 4 | Number of cases receiving hemodialysis and/or hemoperfusion normalized per million calls reported to TESS

Exposure	Therapy	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005
Valproic acid	Total	2.9	5.2	5.4	9.7	14.1	16.1	22.7	23.5	25.1	24.4	21.7	21.3	20.6
	HD	1.1	5.2	4.4	8.8	12.8	14.7	20.9	22.6	24.7	24.4	20.9	21.3	20.6
	HP	1.7	0.5	1.0	0.9	1.8	2.2	2.3	0.9	0.4	0.0	1.3	0.4	0.4

Carbamazepine

- **Indication:**

-anti seizure medication

-alcohol withdrawl

-treatment of chronic pain

-bipolar disorder

- **Plasmalevel:** 6-12 mg/l
- **BIOV:** 70 %
- **Proteinbinding:** 52-90%
- **VOD:** 0.8-1.8 l/kg

- **Half-life:** 18-65 h

- **Lethal dose:** ?, >40 mg/l
- **Symptoms:**

-anticholinergic symptomes

-stupor/coma

-arrhythimas (AV-block)

-dyspena

-neusea, pancreatitis

-huponatremia, thrombcytopenia

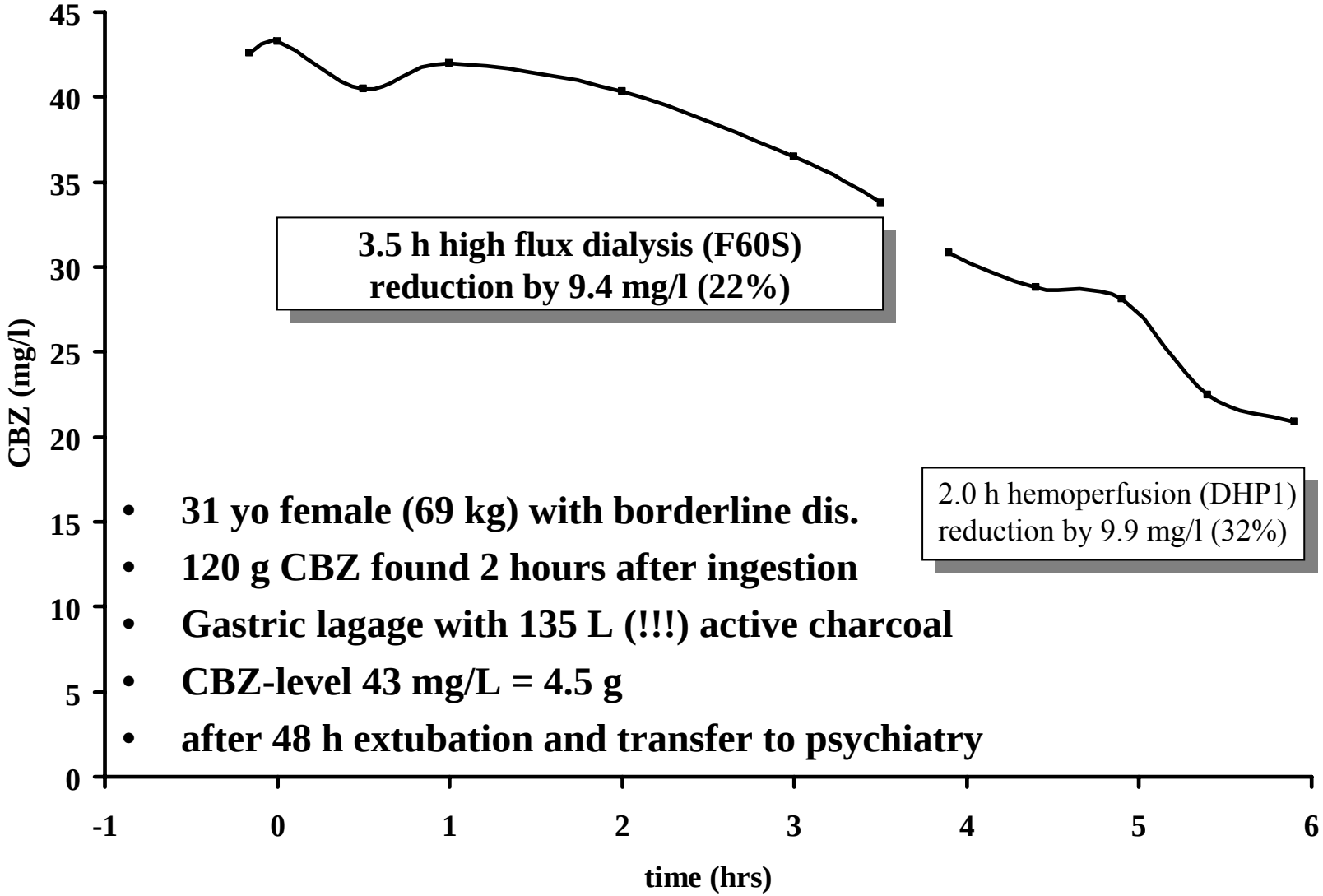
- **Detoxification:**

-gastric lavage up to 12 (24) h

-hemoperfusion

High-flux hemodialysis: an effective alternative to hemoperfusion in the treatment of carbamazepine intoxication.

KIELSTEIN et al. *Clinical Nephrology* 57: 484-486, 2002



- 31 yo female (69 kg) with borderline dis.
- 120 g CBZ found 2 hours after ingestion
- Gastric lagage with 135 L (!!!) active charcoal
- CBZ-level 43 mg/L = 4.5 g
- after 48 h extubation and transfer to psychiatry

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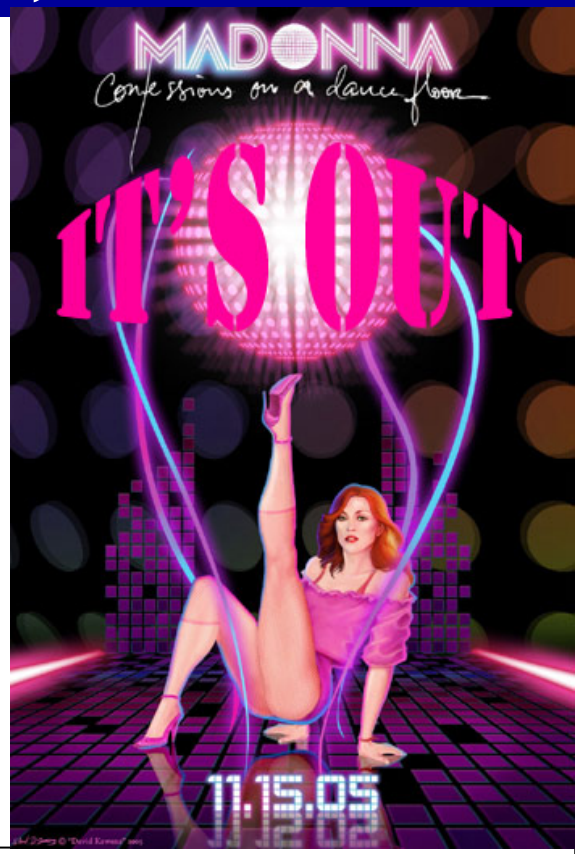

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Carbamazepine	Total	5.1	3.1	1.5	7.4	4.1	4.5	5.9	6.5	4.0	6.3	4.2	6.2	5.0
	HD	3.4	0.5	0.5	5.1	0.9	2.7	4.1	4.2	2.6	5.9	2.9	4.5	4.5
	HP	1.7	2.6	1.0	2.8	3.2	1.8	1.8	2.8	1.3	1.3	1.7	1.6	0.8

Lithium

- **Indication:**

-bipolar disorder

- **Plasmalevel:** 4.1-8.3 mg/l
- **BIOV:** 100 %
- **Proteinebndg:** 1%
- **VOD:** 0.79 l/kg
- **Half-life:** 22 h

- **Elimination:**

-renal

-reabsorption in the pxomal tubule

-Competes with sodium

- **Elevated levels:**

-Suicide

-sodium depletion

-dehydration

-diuretics (thiazides)

- **Lethal dose:** ?

-hyperreflexia, ataxia, coma

-thrombocytopenia, nephrotoxicity

- **Detoxification:**

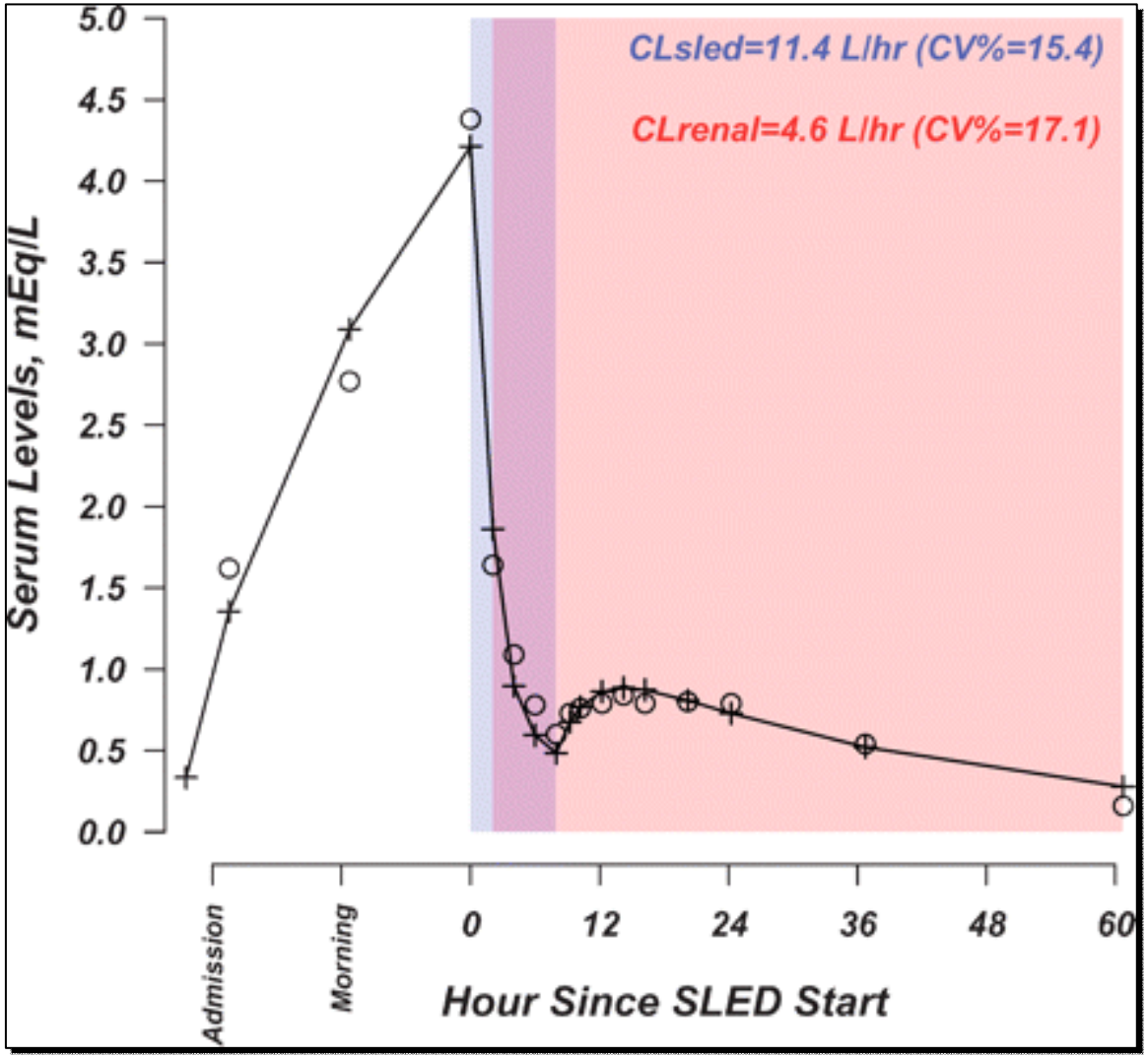
-gastric lavage, no charcoal

-NaCl

-hemoperfusion

Sustained low-efficiency dialysis (SLED) for acute lithium intoxication

FIACCADORI et al. *NDT Plus* 5: 329–332, 2008



Efficiency of the Genius batch hemodialysis system with low serum solute concentrations: the case of lithium intoxication therapy.

DHONDT et al. *Am J Kidney Dis.* 46(5):e95-9, 2005

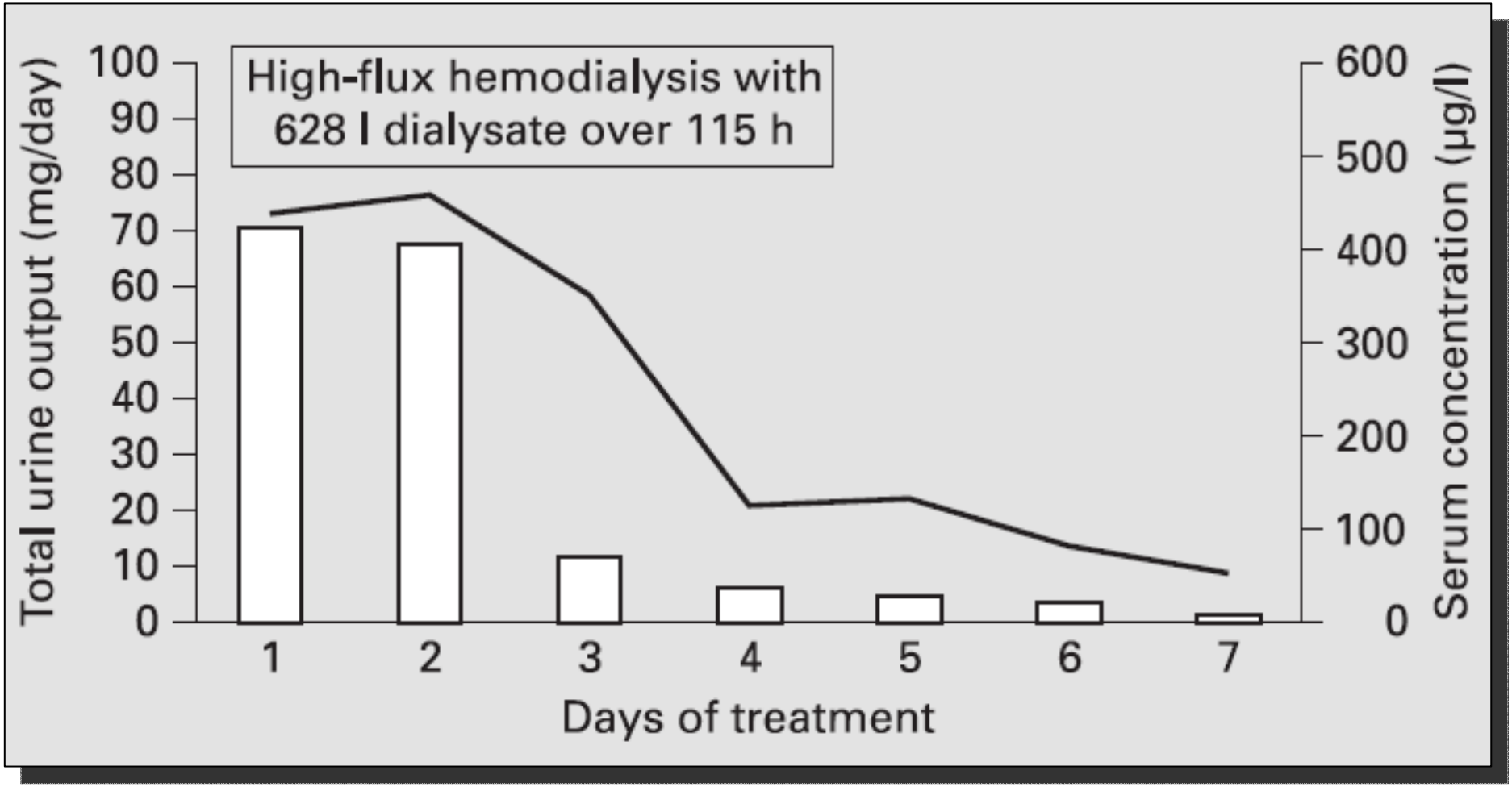
Table 1. Serum Lithium and Urea Concentrations

	Lithium-Intoxicated Patient			Control Patient With Renal Failure	
	Lithium (mmol/L)	Urea (mg/dL)	BUN (mg/dL)	Urea (mg/dL)	BUN (mg/dL)
Predialysis	2.92	23.8	11.1	135	63
After start of dialysis					
1 h	1.45	12.5	5.8	99	46
2 h	1.32	12.3	5.7	76	36
3 h	1.03	9.5	4.4	64	30
4 h	1.08	9.0	4.2	54	25
5 h	1.12	8.9	4.2	45	21

NOTE. To convert urea in mg/dL to mmol/L, multiply by 0.166; BUN in mg/dL to mmol/L, multiply by 0.357.

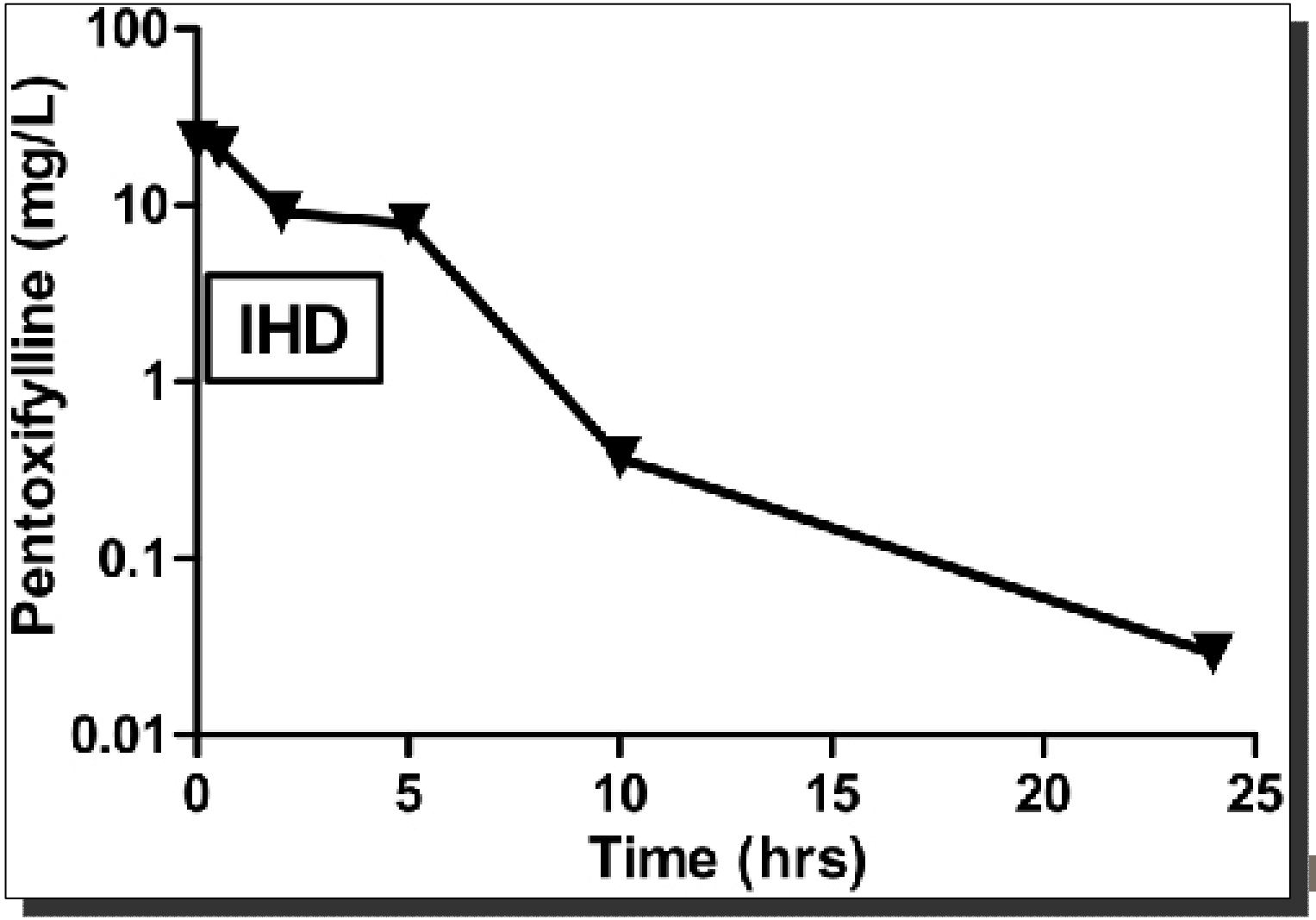
One for all--a multi-use dialysis system for effective treatment of severe thallium intoxication.

KIELSTEIN et al. *Kidney Blood Press Res* 27(3):197-9, 2004



Successful treatment of life-threatening pentoxifylline intoxication by high-flux hemodialysis

EDEN et al *Clinical Nephrology* , 2010



Medizinische Hochschule Hannover

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Summary

Pharmacokinetics ≠ Toxicokinetics !!!!

Extrakorporeal therapy is rarely necessary 0.05 % of all intoxications

Hemodialysis (with high flux filtres) is efficient in the treatment of most intoxications

Dont buy charcoal cartridges!

The availability and use of charcoal hemoperfusion in the treatment of poisoned patients.

SHALKHAM et al. *Am J Kidney Dis.* 48(2):239-41, 2006

NYC PCC Survey of **40 dialysis** units at hospitals taking 911 calls

34 units responded

10 have charcoal hemoperfusion cartridges

-most have cartridges that expire in the next 2 years

-**1** had expired cartridges

-**1**site performed charcoal HP in the last 5 years(theophylline)

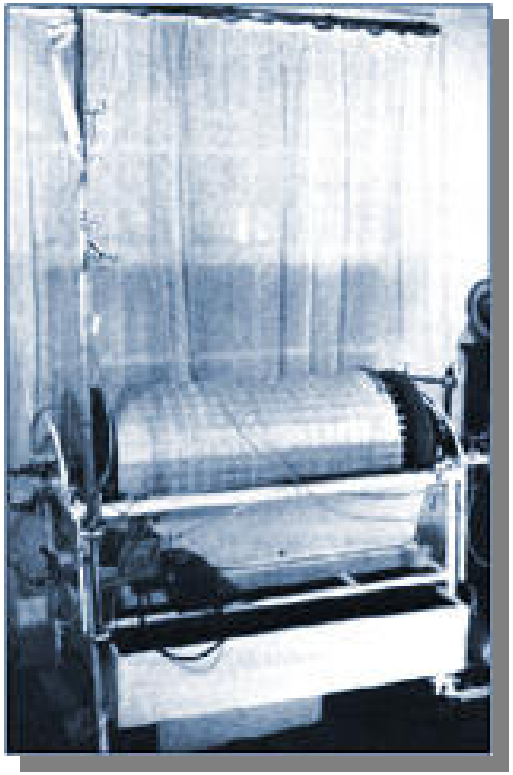
-**4** sites performed HP in the last 10 years (could remember why)

All **24** sites without cartridges said that they don't stock them because:

1. they rarely require their use
2. most toxins can be cleared with HD

„Dosis sola facit venenum“

„Dosis dialysis sola facit salutem“



2010

ADQI International Consensus Conference on Blood Purification in Toxicology

The Dialysis and Other Extracorporeal TReatments in Drug Overdose (DEXTRO) Workgroup