Hemoperfusion

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Haemoperfusion is defined as "the extracorporeal procedure in which the anticoagulated patient's blood passes through a volume of adsorbent material"

Introduced in the 1940s

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The adsoprtion medium needs to have several favourable properies:

- High selectivity/ affinity for noxious solutes
- Rapid adsorption
- High capacity for adsorption (i.e. large surface area(
  - Modern sorbents have a surface area of around 1000m2 per gram of sorbent
- Chemical and thermal stability, including low water solubility
- Good structural integrity (i.e. non-crumbly(
- Good biocompatibility (to prevent inflammatory response or anaphylaxis(

Practical administration of haemoperfusion

Relevant features to make note of:

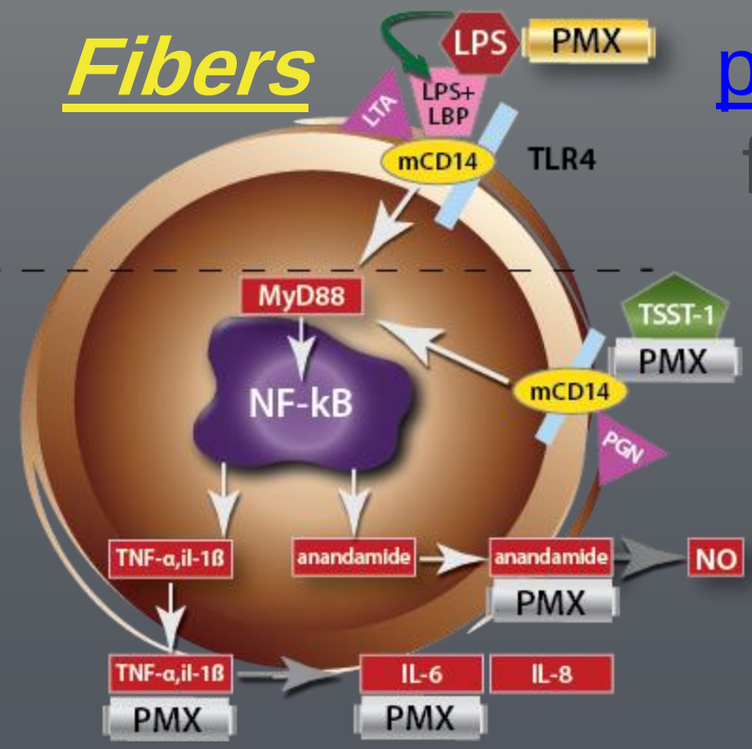
- A normal CRRT machine can be used
- Blood flow rate is about 250-300ml/min
- Anticoagulation requirements are similar to normal CRRT
- A session usually lasts about 4 hours
- At the end of the 4 hours the cartidge is depleted and must be discarded

The type of adsorbent particle

Charcoal poisoning and hepatic failure.
Water soluble substance

Resins (polystyrene, XAD series (
are most effective for the removal of
lipid-soluble drugs, with drug clearance
rates from the blood frequently exceeding
those achieved by charcoal hemoperfusion .

Fibers polymyxin B
for the removal of endotoxin and cytokines.



Antibody or antigen-coated charcoal hemoperfusion is also available for specific autoimmune states: SLE, RA ,

and to remove pathogenic *anti-human leukocyte antigen (HLA) antibodies* in some renal transplant candidates

Water- and lipid-soluble substances with molecular weights ranging from 100 to 40,000 daltons are well adsorbed with hemoperfusion

Complications of Haemoperfusion Therapy

Generic complications, common to all RRT	*Access complications* All RRT requires access of some sort. Be it fistula or vas cath, there are risks: • Bleeding • Vessel damage • Bloodstream or localised infection • Air embolism *Haemolytic complications*

Complications of Haemoperfusion Therapy

Haemolytic complications

Thrombocytopenia (most frequent (

Inflammatory reponse

The haemoperfusion membrane is a *proinflammatory surface* .
)particularly complement activation) is to be expected.
In addition to the proinflammatory effect of broken red blood cells, there is a risk of *widespread inflammation due to cartridge embolism.*

Blood loss due to circuit loss

Hypothermia

The drop in the core body temperature due to heat exchange via the circuit occurs via similar mechani

Just as in CVVHDF, one can be cooled by the haemoperfusion circuit.

Hypoxia

Activation of complement and the inflammatory mechanisms leads to an increase in the activity of nitric oxide synthase, which countracts the normal mechanisms of hypoxic pulmonary vasoconstriction. Increased shunt develops; therefore hypoxia ensues.

Electrolyte disturbance

Charcoal *does not tend to cause any sort of electrolyte changes, but the macroporous* ***resins*** *can remove calcium phosphate and potassium from the blood stream.*

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Malnutrition due to adsoprtion of useful molecules

Adsorption of all lipophilic molecules occurs, and thus one ends up missing out on the fatty acids from TPN, fat-soluble vitamins A, D, E and K, or dietary cholesterol. Over the initial hour or so, glucose and calcium levels can drop (even with charcoal hemoperfusion.(

Haemodynamic instability

The hemodynamic instability due to haemoperfusion is wholely due to the generation of an inflammatory response due to an incompatible blood/adsorbent interface. The chances of this have been greatly reduced by the use of modern immunoneutral coatings. In comparison, much of the early interest in this technique was lost due to major haemodynamic complications.

Particle embolisation

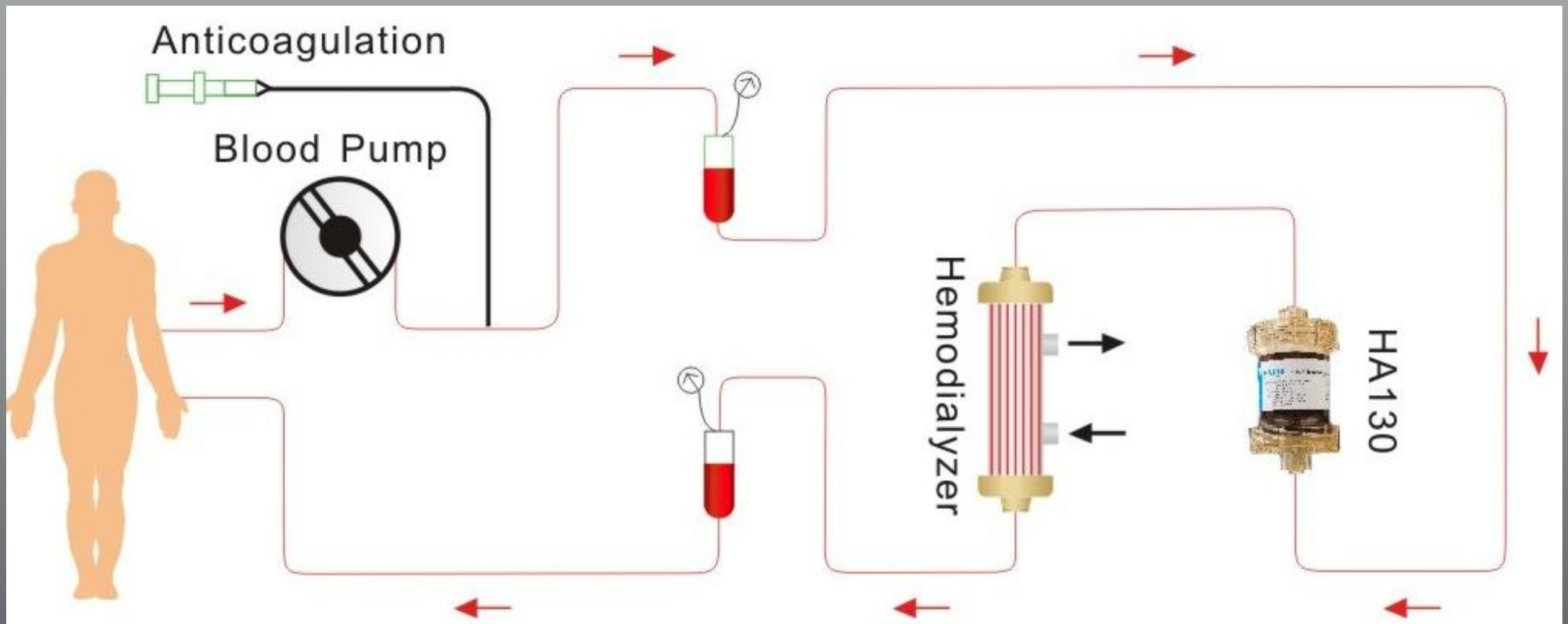
Again, this is mainly a complication of older, less "evolved" cartridges, where bits of the adsorbent would break off and embolise downstream. In modern cartridges this is almost unheard of.

Toxin elution

Carbon in the cartridge, though a highly purified form, is still an organic product, and therefore prone to the usual peculiarities of natural materials. Weird hydrocarbons and potentially even toxic heavy metals may elute out of the cartridge and into the patient. Repeated treatments will therefore result in accumulation toxicity. This is largely a theoretical complication; as far as I am aware, such heavy metal elution has only ever been observed in vitro.

Drug features which favour haemoperfusion rather than dialytic removal

- ***High lipid solution***
- ***Large volume of distribution***
- ***High protein binding***


Anticoagulation
Blood Pump
Hemodialyzer
HA130

Drugs which are easily extracted by haemoperfusion :

- ***Paraquat .***
- ***Parathion***
- ***Theophylline***
- ***Carbamazepine***
- ***Phenytoin***
- ***Paracetamol***
- ***Barbiturates***
- ***Digoxin (maybe(***
- ***Diltiazem***
- ***Metoprolol***
- ***Colchicine***
- ***Promethazine***
- ***Amanita phalloides mushroom toxin (phalloidin(***

Non-toxicological indications for haemoperfusion

- ***Lipopolysaccharide endotoxin*: The cell wall component of gram-negative bacteria, which is responsible for much of the nastiness you see in septic shock**
  - **The sorbent for this tends to be a polymyxin-impregnated polystyrene fiber**

- ***Superantigen*: The secreted exotoxin of gram-positive bacteria, which directly activates T cells by binding to the MHC class II molecules.**

- ***Various cytokines*: Both proinflammatory and antiinflammatory ones are cleared by hemoperfusion**

- ***Hepatic failure:* accumulated toxins can be susceptible to haemoperfusion**

- ***End stage renal failure with aluminium intoxication*: where it is used along with a chelating agents.**

End-stage renal disease with aluminum intoxication; hemoperfusion has been used in conjunction with chelating agents (deferoxamine) to remove aluminum .

Hemofiltration using charcoal hemoperfusion doubles the rate of removal of the deferoxamine-aluminum chelate compared with standard hemodialysis membranes.

However, given the necessity for roughly one year of therapy, the most economical alternative is the use and reuse of a high-flux hemodialyzer rather than the very expensive charcoal hemoperfusion cartridge.

In acute aluminum poisoning, high-flux dialysis (using deferoxamine as the chelating agent) was superior to that of charcoal hemoperfusion in removing aluminum

EFFICACY

An international working group (Extracorporeal Treatments in Poisoning *[EXTRIP2012]*made up of experts in nephrology, clinical toxicology, critical care, and pharmacology *does not support the use of hemoperfusion in severe intoxication.*

With *"rebound,"* the drug redistributes from tissues into the plasma following its removal from the plasma compartment. This is consistent with the pharmacokinetic handling of drugs after their removal from the central compartment; the rebound in drug concentration in plasma may be clinically significant, including a return to severe neurologic dysfunction or coma (as with glutethimide poisoning.(

Intermittent hemoperfusion helps minimize this "rebound" effect (as with paraquat and glutethimide(

Extraction ratios for some drugs and chemicals with hemodialysis, charcoal hemoperfusion and resin hemoperfusion*

	Cuprophane hemodialysis	Coated OR uncoated charcoal hemoperfusion	XAD-2 or XAD-4 resin hemoperfusion
Acetylsalicyclic acid	0.5	0.5	-
Digoxin	0.2	0.3 to 0.6	0.4
Glutethimide	0.16	0.65	0.8
Paraquat	0.5	0.6	0.9¶
PhenobarbitalΔ	0.27	0.5	0.85
Theophylline	0.5	0.7	0.75
Tricyclic antidepressants◊	0.35	0.35	0.8

* Calculated for blood flow rate of 200 mL/min.

¶ Specially prepared ion-exchange resin.

Δ 0.36 to 0.47 with high-flux membranes.

◊ Large volume of distribution mitigates against removal of appreciable quantities of drug.

Graphic 62301 Version 4.0

Drugs and chemicals removed with hemoperfusion

Barbiturates
Amobarbital
Butabarbital
Hexabarbital
Pentobarbital
Phenobarbital
Quinalbital
Secobarbital
Thiopental
Vinalbital
Antidepressants
(Amitryptiline)
(Imipramine)
(Tricyclics)
Metals
Aluminum*
Cisplatin*
Iron*
Thallium
Miscellaneous
Aminophylline
Cimetidine
(Fluoroacetamide)
(Phencyclidine)
Phenols
(Podophyllin)
Theophylline
Solvents, gases
Carbon tetrachloride
Ethylene oxide
Trichloroethane

Antimicrobials/anticancer
(Adriamycin)
Ampicillin
Carmustine
Chloramphenicol
Chloroquine
Clindamycin
Dapsone
Doxorubicin
Gentamicin
Isoniazid
(Methotrexate)
Thiabendazole
Vancomycin
Pentamidine
Analgesics, antirheumatic
Acetaminophen
Acetylsalicylic acid
Colchicine
D-propoxyphyene
Methylsalicylate
Phenylbutazone
Salicylic acid
Tramadol
Cardiovascular
Digoxin
Diltazem
(Disopyramide)
Metoprolol
N-acetylprocainamide
Procainamide
Quinidine
Cibenzoline

Plant and animal toxins, herbicides, insecticides
Amanitin
Chlordane
Demeton sulfoxide
Dimethoate
Diquat
Methylparathion
Nitrostigmine
Organophosphates ¶
Phalloidin
Polychlorinated biphenyls
Paraquat
Parathion
Star fruit
Tetramine
Nonbarbiturate hypnotics, sedatives and tranquilizers
Carbromal
Chloral hydrate
Chlorpromazine
(Diazepam)
Diphenhydramine
Ethchlorvynol
Glutethimide
Meprobamate
Methaqualone
Methsuximide
Methyprylon
Promazine
Promethazine
Valproic acid

( ): not well removed.
* Removed with chelating agent.
¶ With lipid emulsion.

Graphic 52887 Version 2.0

In general *hemoperfusion* is preferred to hemodialysis for the removal of chemicals that are lipid soluble or are highly protein bound . *Hemodialysis* is preferred for water-soluble, low-molecular-weight compounds .

However, the advantage of hemoperfusion over cuprophane dialyzers has lessened with the advent of high-flux dialysis membranes .

***If a poison is eliminated equally well with hemodialysis and hemoperfusion, hemodialysis is preferred* since it will also correct a concurrent acid-base disturbance. Additionally, there is generally greater expertise and availability with respect to hemodialysis than hemoperfusion**

In general, hemoperfusion should only be employed in the setting of intoxication with a drug or poison that can be removed at a rate that exceeds endogenous elimination by the liver or kidney.

Among patients who are poisoned, hemoperfusion should be considered in
patients who demonstrate progressive deterioration despite intensive supportive therapy ;

those with severe intoxication with depression of midbrain function, leading to hypoventilation, hypothermia, and hypotension ;

and in the setting of development of complications of coma, such as pneumonia or septicemia, or underlying conditions that predispose to such complications (eg, obstructive airway disease.(

Hemoperfusion may also be considered when there is impairment of normal drug excretory function due to hepatic, cardiac, or renal insufficiency ;

when there is intoxication with agents with metabolic and/or delayed effects, such as mushrooms and paraquat ;

and in patients with end-stage renal disease with aluminum intoxication.

Hemoperfusion may be used in the setting of hepatic failure to prevent or delay hepatic coma and serve as a bridge to hepatic transplantation.

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HA130 (ESRD)

Remove β_2-MG, PTH, Leptin IL-6, AGEs, Hcy, AOPP.....
Treat for dialysis complications ie. Refractory Hypertension, Pruritus, Renal Osteopathy, Micro-inflammation

HA230 (Poisoning)

Organophosphorous pesticide,
Paraquat,Tetramine,Atropine,Snake/Bee venom etc.

HA280 (Immune Disease)

HSP, Pemphigus, vasculitis, Rheumatoid,
Arthritis, Dermatitis, Psoriasis etc.

HA330 (ICU)

Sepsis, SIRS, CARS, MODS, SAP, ARDS, MOF,
Severe burns, Severe infection, Inflammatory factor imbalance etc.

HA330-II (Hepatic Failure)

Severe Hepatitis, High bilirubine, Ammonia,
TNF-α, Hepatic encephalopathy, Obstinate Cholestasis etc.

BS330 (Bilirubin Adsorption)

Hyperbilirubinemia and Hyperbileacidemia, Severe hepatopathy etc.

DNA230 (SLE)

Systemic Lupus Erythematosus and the related complications.

Note: