



CLINICAL TOXICOLOGY LAB.

5TH STAGE / 1ST SEMESTER

(2021 - 2022)

PRINCIPLES IN MANAGEMENT OF TOXICITY CASES (PART 2)

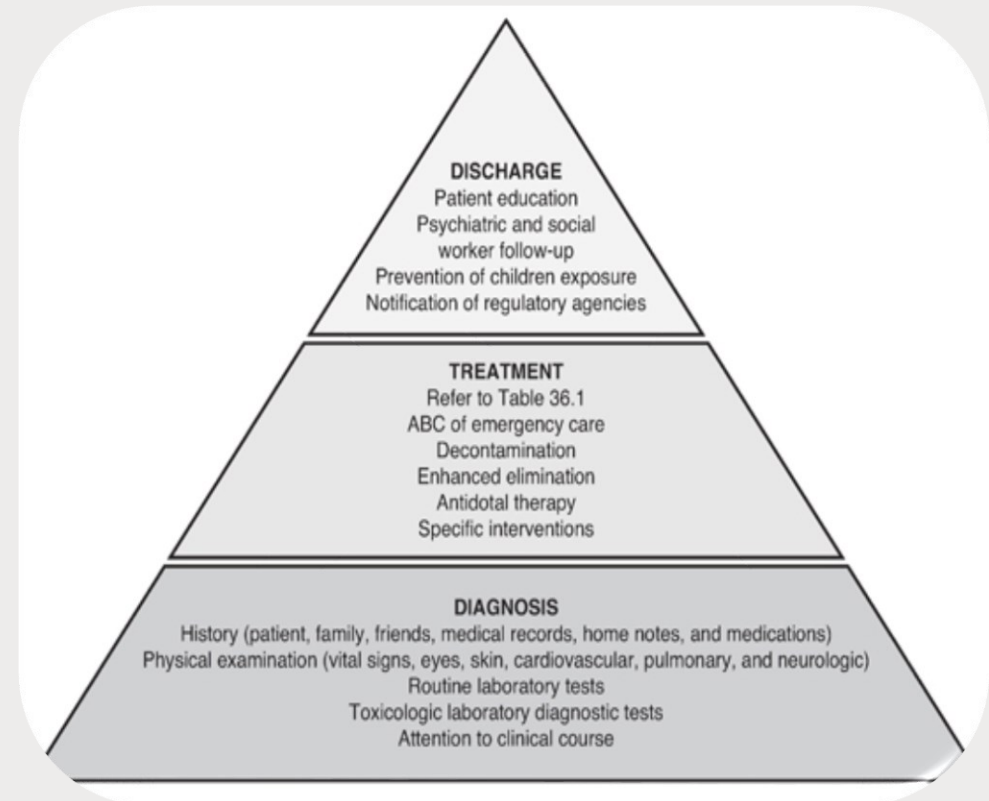
Assis. Lecturer

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3/ Enhancement of Poison Elimination:

- Accidental and intentional poisonings or drug overdoses constitute a significant source of aggregate morbidity, mortality, and health care expenditures
- Methods of enhancing the elimination:
 - *Forced diuresis*
 - *Ion trapping*
 - *Extracorporeal methods:*
 - Hemodialysis
 - Hemoperfusion
 - Hemofiltration
 - Plasmapheresis
 - Exchange transfusion
 - *Other methods:*
 - Hyperbaric oxygenation (HBO)
 - Multidose charcoal
 - Chelation



■ Indications:

1. *Toxins with small volume of distribution (remain in blood compartment).*
2. *Toxins with Low renal clearance (alcohol, beta blockers, lithium, phenytoin, theophylline, salicylates).*
3. *Toxins with low protein-binding*

Enhance Elimination

Forced Diuresis

Ion Trapping

Extracorporeal Methods

Other Methods

- The excretion of some drugs can be enhanced by increasing the urine output
- A saline solution is often used (normal saline)
- This method is not recommended
- Disadvantages:
 - *Not recommended with impaired renal function & cardiovascular disorders*
 - *Elderly patients*
 - *The agent has cardiotoxic or nephrotoxic properties*
 - *Results in electrolyte and acid-base disturbances*

Enhance Elimination

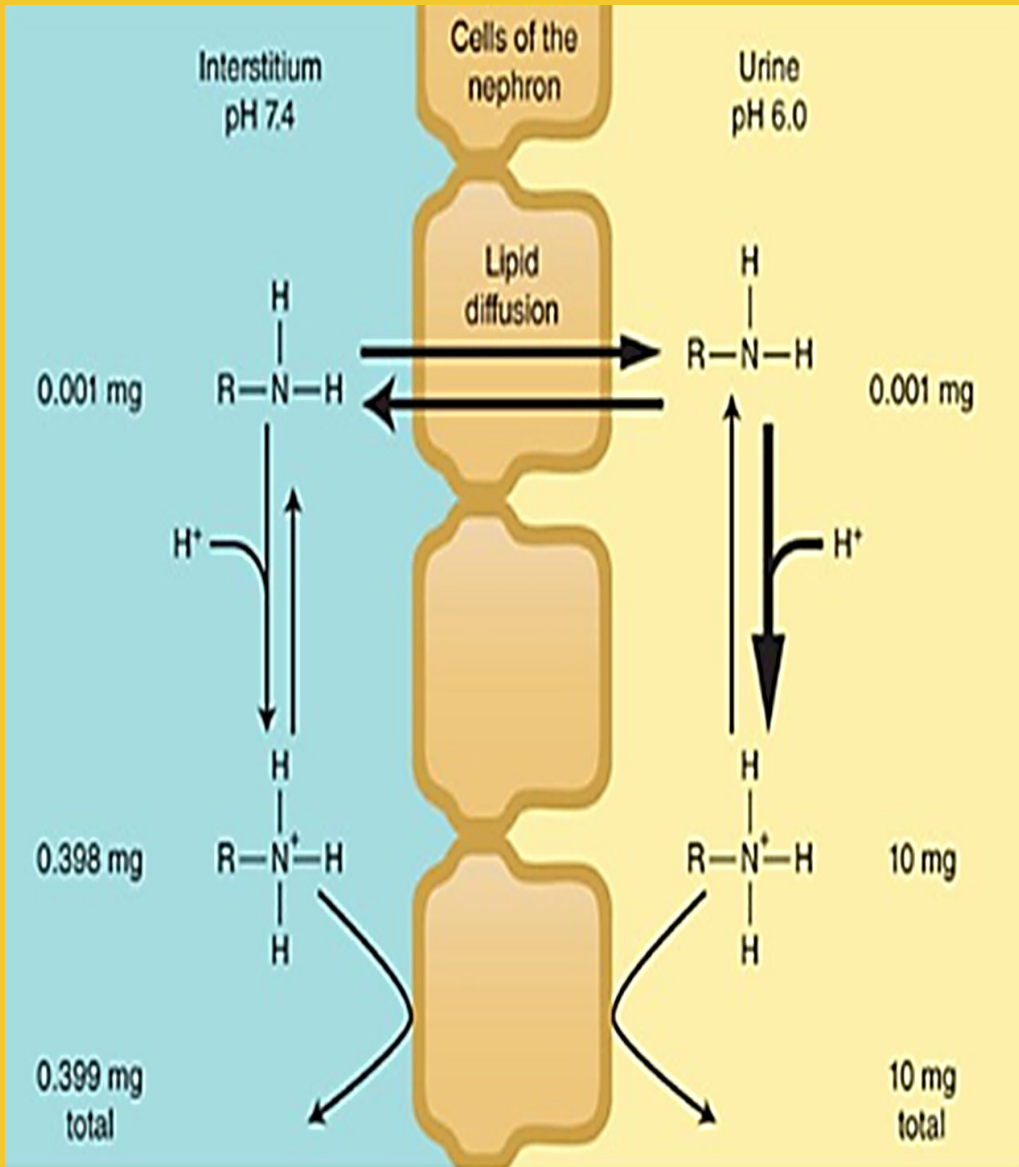
Forced Diuresis

Ion Trapping

Extracorporeal Methods

Other Methods

- Is a method of enhancing elimination of certain agents by altering the PH of the urine
- Elimination can be enhanced depending on the pKa of the of the drug, and PH of the medium
- Urine alkalinization:
 - *Urine PH (7.5 - 8) >>> Sod. Bicarbonate*
 - *considered for all weak acids such as salicylate , phenobarbital*
- Urine acidification:
 - *Urine PH (4.5 - 6) >>> ammonium chloride, ascorbic acid*
 - *Considered for weak bases like quinine, amphetamine poisoning*
 - *Rarely done in practice because of risk of metabolic acidosis*



Protonated weak base (charged, More water-soluble)
 unprotonated weak base (uncharged, more lipid-soluble)



Protonated weak acid (uncharged, more lipid soluble)
 Unprotonated weak acid (charged, more water-soluble)

Enhance Elimination

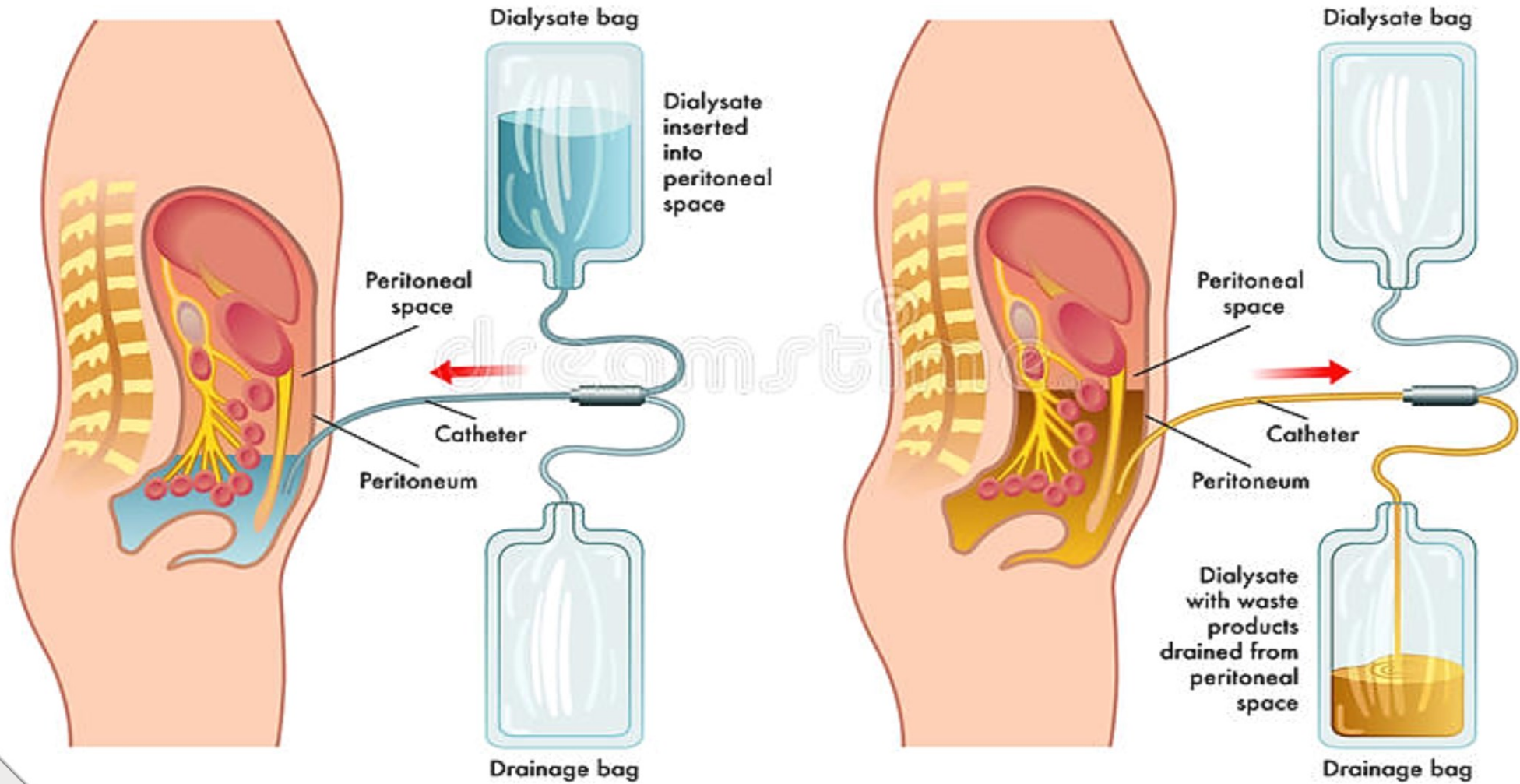
- Forced Diuresis
- Ion Trapping
- Extracorporeal Methods
- Other Methods

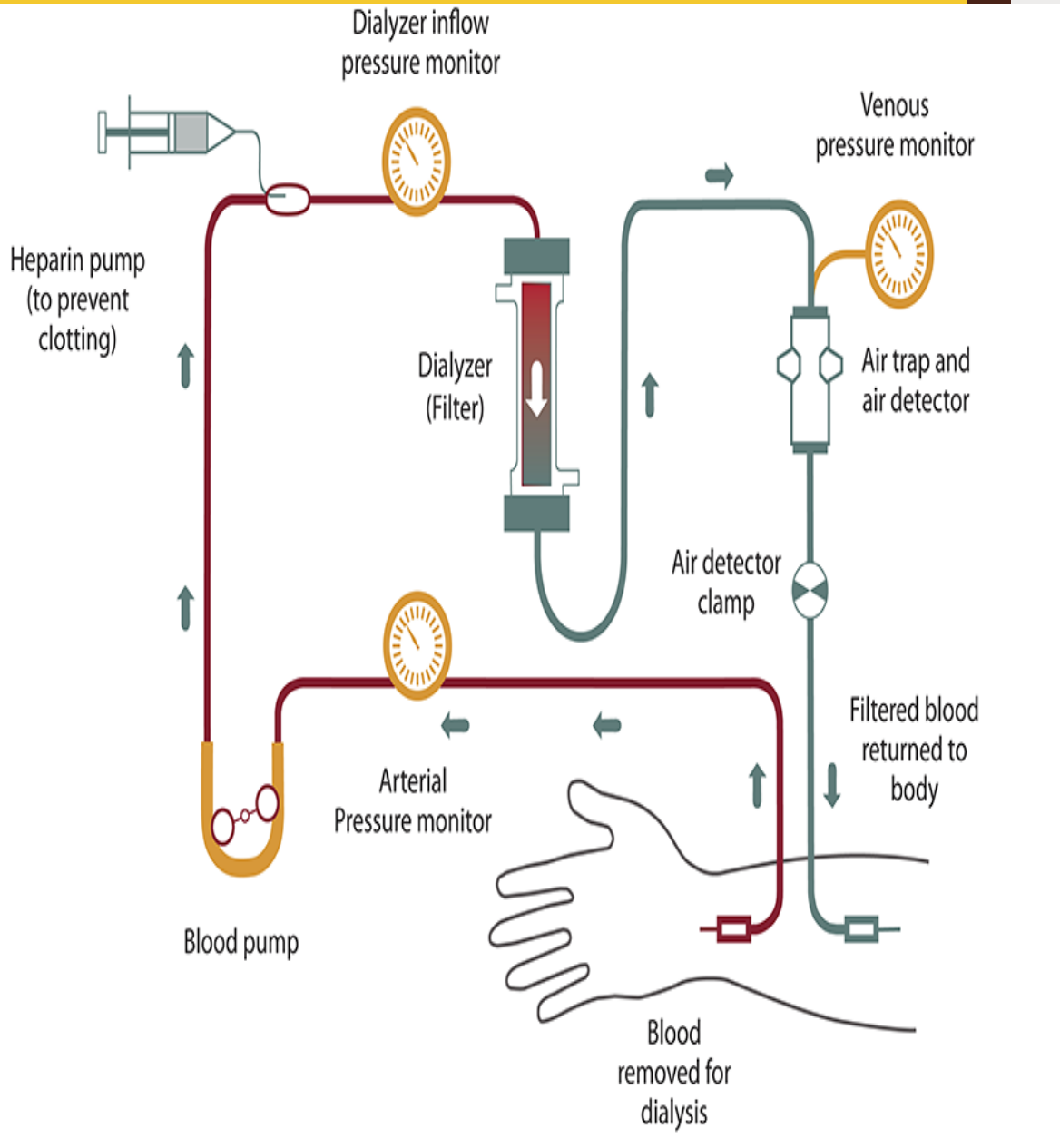
■ Dialysis:

- *Removal of water soluble toxins and waste products from the blood*
- *Patient not responding or deteriorating in spite of good medical care*
- *There are two types of dialysis procedures:*
 - Peritoneal dialysis
 - Hemodialysis

- a) *Peritoneal dialysis/*
 - Require a dialysate solution
 - Targets only the peritoneal cavity
 - Enhance the elimination of water soluble, and low M.Wt. agents
 - Time-consuming
 - Provides about 20% of efficiency
 - Not recommended

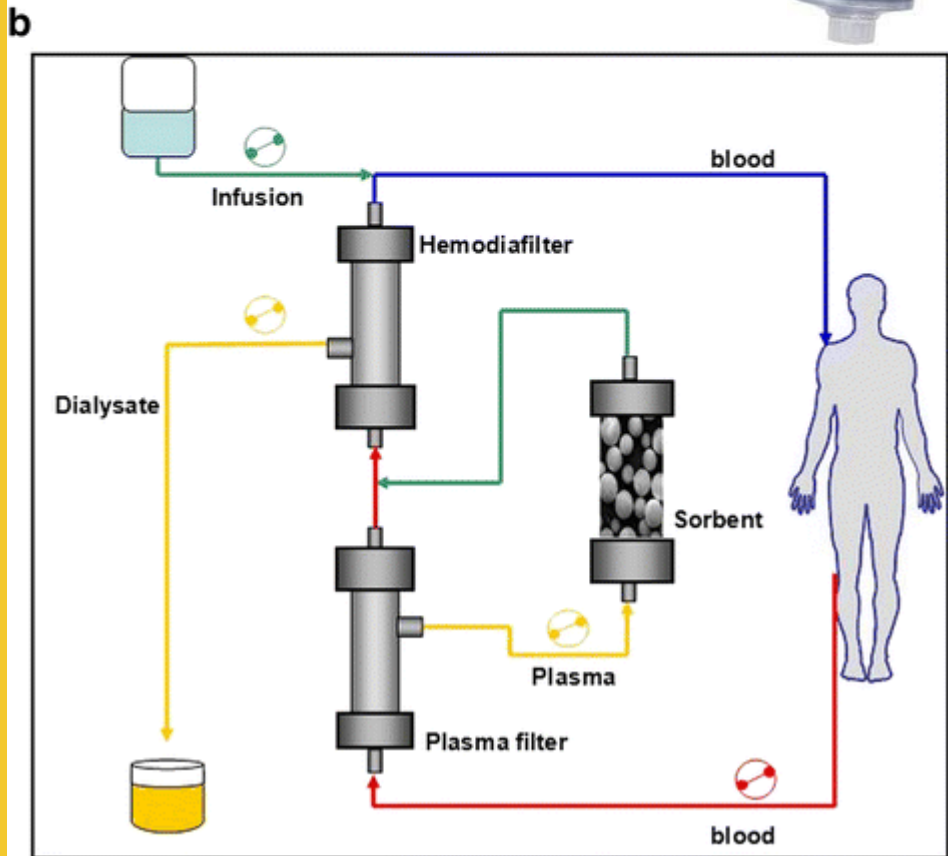
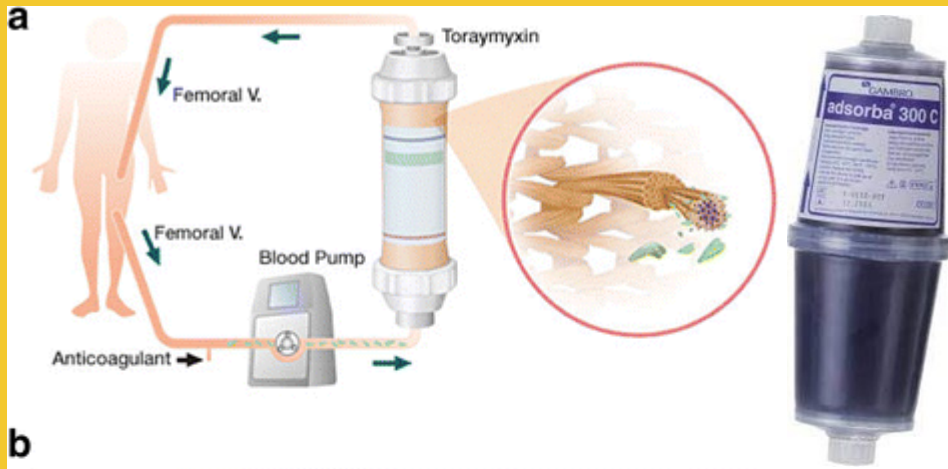
Peritoneal Dialysis





b) Hemodialysis/

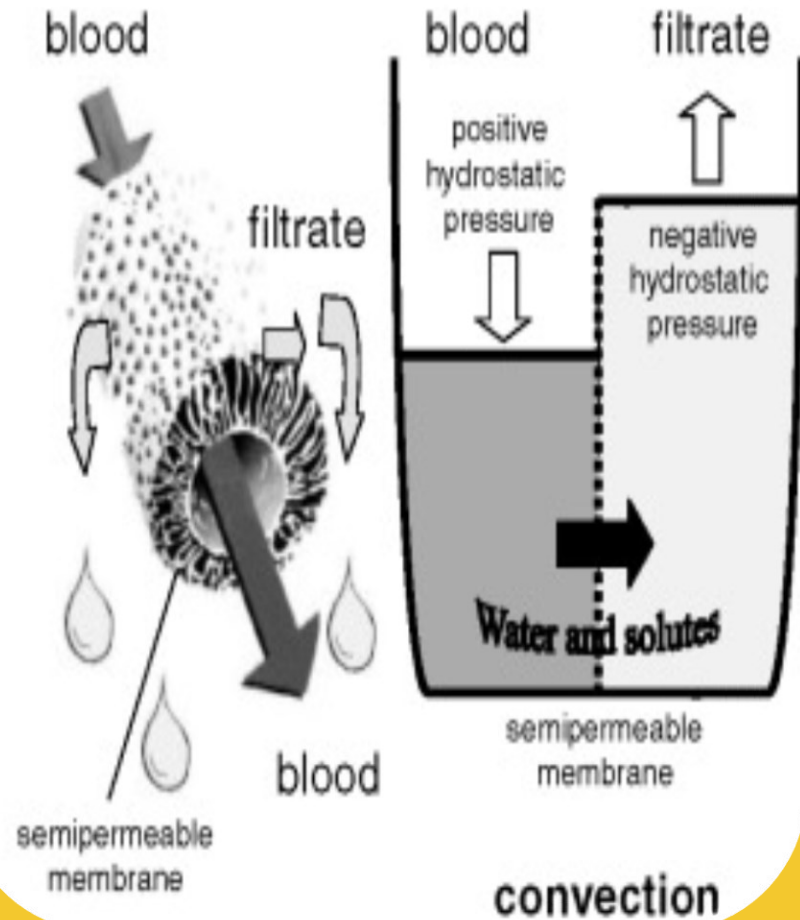
- Blood is circulated past a semipermeable membrane
- A method used to enhance the elimination of toxins and waste products in case of renal impairment or hepatic impairment
- Criteria required:
 - *Water soluble agents*
 - *Low M.Wt. (less than 500 Dalton)*
 - *Minimum protein-binding*
 - *Low volume of distribution (1L/kg or less)*
 - *Slow metabolic rate, and low renal clearance*
 - *Require the administration of anti-coagulants (heparin)*
 - *Require a dialysate solution*
- Effective for (barbiturates, salicylates, lithium, alcohols, some anti-depressants, theophylline)
- Complications/ bleeding, air embolism, nosocomial infection



■ Hemoperfusion:

- The blood is passed through a column containing adsorbent agent (activated charcoal or ion-exchange resin)
- **Criteria required:**
 - Lipid soluble agents
 - High protein binding
 - Low volume of distribution
 - Agents with long half-life
 - Require anti-coagulants (heparin)
- Effective for (phenytoin, carbamazepine, some anti-depressants, MTX)
- Complications/ same as hemodialysis

Hemofiltration

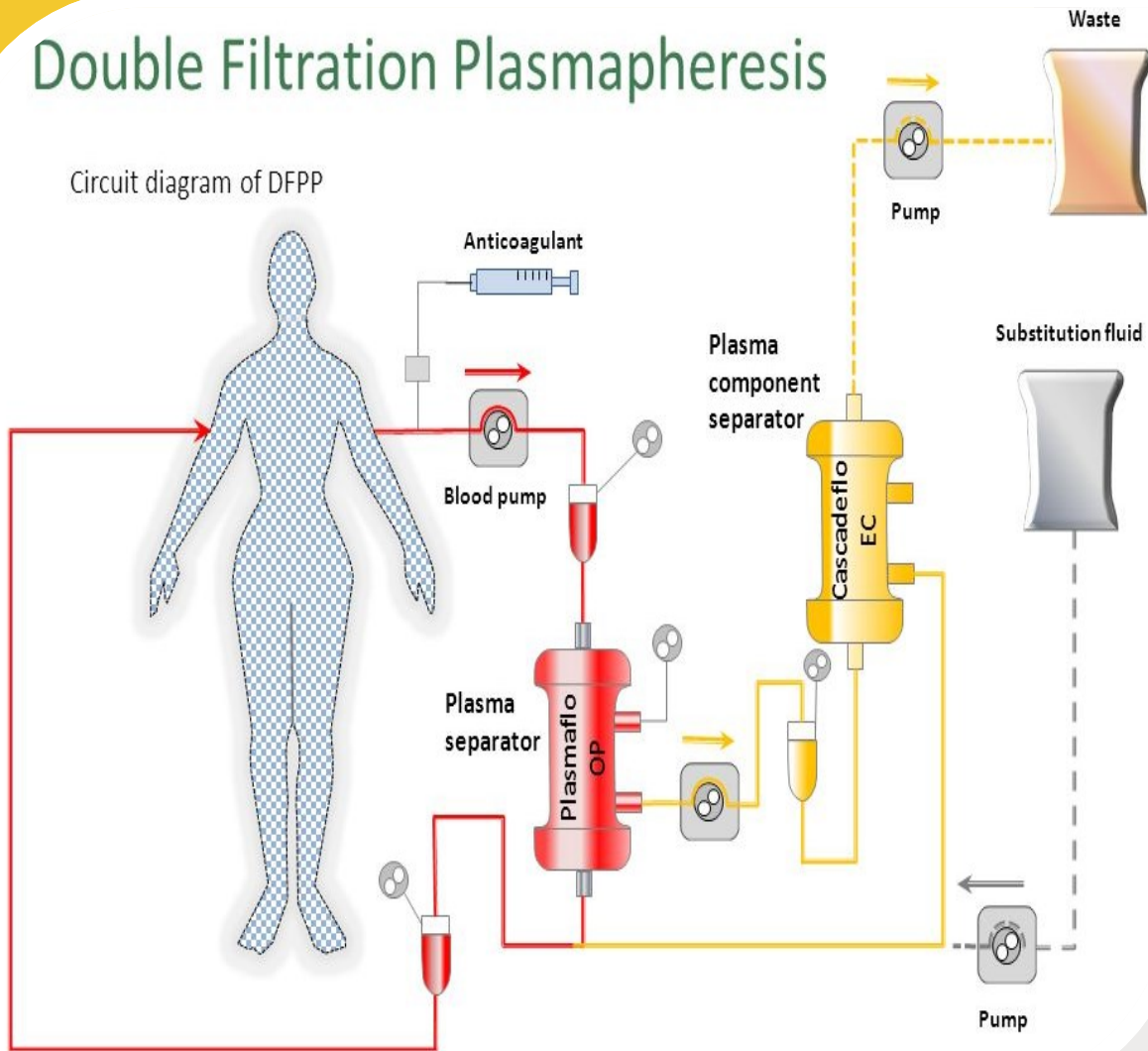


■ Hemofiltration:

- Blood passes through filters with large pores, and an ultrafiltrate forms that drags solutes with M.Wt. up to 50000 Dalton
- Plasma moves across a semipermeable membrane under hydrostatic pressure
- **Criteria required:**
 - Solutes with high M.Wt. (up to 50000 Dalton)
 - Water soluble solutes
 - Low volume of distribution
 - Minimum protein binding
 - Require anti-coagulant
 - No dialysate solution
- Effective for (aminoglycosides, vancomycin, metal-chelate complex)
- Complications/ same as hemodialysis with electrolyte disturbance and removal of essential nutrients

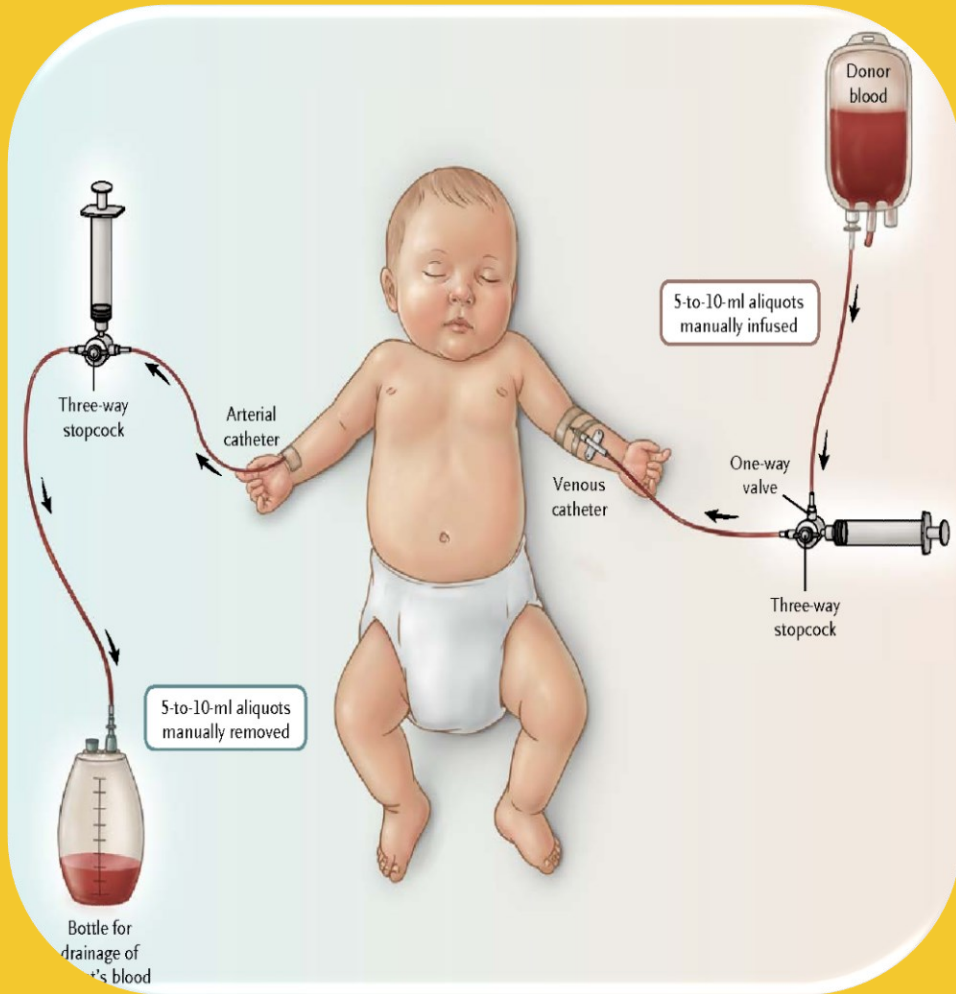
Double Filtration Plasmapheresis

Circuit diagram of DFPP



■ Plasmapheresis:

- *The process of filtration of blood plasma for removal of toxins and waste products, then returned back to the blood*
- **Criteria required:**
 - Large M.Wt. compounds (more than 15000 Dalton)
 - Highly protein-bound
 - Require anti-coagulant
 - Require a supplement of fresh frozen plasma (FFP) and albumin
- *Effective for (removing antibodies and Ag/Ab complex like digoxin-Fab complex)*
- *This process can be used for therapeutic purposes (autoimmune disorders, high cholesterol, synthesis of Ab for certain toxins)*
- *Complications/ mostly transfusion related allergic reactions*



■ Exchange Transfusion:

- *The process that involves the removal of quantity of blood from a poisoned person and replace it with identical quantity of whole blood*
- *The process is usually repeated two or three times*
- *Effective for:*
 - Hemolytic disease of newborn
 - Hemoglobinopathies (thalassemia or sickle cell anemia)
- *Complications/ transfusion related allergic reaction or anaphylaxis*

Enhance Elimination

- Forced Diuresis
- Ion Trapping
- Extracorporeal Methods
- Other Methods

- Hyperbaric Oxygenation (HBO):
 - Primarily used for patients poisoned by gases that interferes with oxygen transport
 - Oxygen is administered in to a patient in an enclosed chamber at a pressure greater than the pressure at sea level
 - Effective for:
 - Carbone monoxide
 - Cyanide
 - Hydrogen sulfide
 - Complications/ pressure – related pain (ear, sinus, and teeth)

Enhance Elimination

- ❑ Forced Diuresis
- ❑ Ion Trapping
- ❑ Extracorporeal Methods
- ❑ Other Methods

- Multidose Activated Charcoal (MDAC):
 - *Multidose of activated charcoal is administered to the patient orally through nasogastric tube*
 - *MDAC is believed to enhance elimination by interrupting enterohepatic and entero-enteric circulation, by promoting passive diffusion of drugs from the intestine*
 - *Example (dapson, valproate, salicylate, MTX, diazepam)*
- Chelation:
 - *The process of administering organic compounds with 2 or more electronegative groups that form stable bond with cationic metals, used in heavy metal poisoning which make the metal more water soluble and readily excreted out of the body*

4/ Administer Antidotes:

- An antidote is a substance which can counteract a form of poisoning
- The antidotes for some particular toxins are manufactured by injecting the toxin into an animal in small dose and extracting the resulting antibodies from the host animals blood.
- This results in anti-venom that can be used to counteract poison produced by certain species of (snakes , spiders, and others)
- Types of mechanism of antidotes:
 - *Neutralization by antibodies (anti-venom, digoxin immuneFab)*
 - *Neutralization by chemical binding (chelating agents)*
 - *Metabolic antagonist (interferes with certain important metabolic enzymatic activity like dihydrofolate reductase <<< inhibited by MTX <<< effects reversed by folinic acid)*
 - *Pharmacological antagonist (naloxone for opioid overdose, atropine for organophosphate poisoning, and flumazenil for benzodiazepines overdose)*

Most important types of toxicities and their antidotes

Toxin	Antidote/ Treatment
Paracetamol	N- acetylcysteine; Methionine
Opiates	Naloxone
Benzodiazepines	Flumazenil*
B Blockers	Glucagon**
Tricyclic antidepressants	Sodium Bicarbonate (for ECG changes)
Iron	Desferrioxamine
Calcium Channel Blockers	Calcium Gluconate/ Calcium Chloride†
Carbon Monoxide	Oxygen (High flow/ Hyperbaric)
Digoxin	Digoxin specific antibodies (Digibind)
Ethylene Glycol, Methanol	Ethanol; Fomepizole
Organophosphates	Atropine; Pralidoxime
Cyanide	Dicobalt Edetate; Hydroxocobalamin; Methylene Blue; Sodium nitrite/ thiosulphate
Sulphonylurea	Octreotide, Glucose
Warfarin	Vitamin K; FFP; Prothrombin Complex Concentrate (Beriplex)
Salicylates	Sodium Bicarbonate
Antipsychotics	Procyclidine
Cocaine	Benzodiazepines; GTN; Calcium Channel Blockers
Malignant Hyperthermia	Dantolene
Arsenic/ Heavy Metals	Dimercaprol; Succimer
Methotrexate	Folic acid (High dose 'rescue regime')
Lead	Succimer; Sodium Calcium Edentate



Thank You
For Your
Attention