Joint ASM of HKSCCM & HKACCN 2009

Recent Advances in Extracorporeal Blood Purifications to manage Poisoning in ICU

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Main principles of treatment

- Emesis / gastric lavage
- Activated charcoal
- Antidote
- Supportive care
  - Airway
  - Breathing
  - Circulation
  - Organs support
- Elimination
  - Gut irrigation
  - Forced diuresis
  - Extracorporeal elimination

Toxic Exposure Surveillance System

American Association of Poison Centers

- In the year of 2004
- 3% require ICU
- 0.05% extracorporeal treatment
  - (1 out of 60 poisoned ICU patients)
  - (1 out of 2,000 total poisoned patients)
- Many many different kinds of toxins / drugs (toxic dose)

- Evidence on the extracorporeal management of individual poison
  - Single case report / case series

Recent advances

- Not in provision of good evidence in treatment of individual poison

- In advances of different blood purification techniques originally designed for organ support (clearance of metabolic waste products)
  - Potentially effective
    - Many recent studies
  - Enhance toxin removal
  - Sustain life to buy time for natural /artificial removal of toxins

Indications of extracorporeal elimination

Orlowski JM et-al, Clinical Toxicology 2001 p43-50

- Ingested quantity associated with severe toxicity
- Ingestion of a toxin with serious delayed effects
- Natural removal mechanism impaired
  - Renal / Liver failure / Circulatory failure
- Clinical condition deteriorating
- Clinical evidence of severe toxicity: hypotension, coma, metabolic acidosis, respiratory depression, dysrhythmias or cardiac decompensation

Traditional extracorporeal elimination methods

- >30 years
- Haemodialysis (low flux)
  - For patients with end-stage renal disease
- Haemoperfusion
  - Charcoal

Haemodialysis (low flux)

- Diffusion across a semipermeable membrane down a concentration gradient from blood to dialysate
- Water soluble
- Low molecular weight (<0.5 kD)
- Low protein binding
- Low volume of distribution
- Clearance depends on membrane surface area, Qb and Qd
- A form of renal replacement therapy
- High clearance but problem of rebound
  - >250ml/min

US Toxic Exposure Surveillance System (TESS)

renamed as National Poison Data System since 2007

The most common toxins responsible for cases receiving HD

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

Haemoperfusion

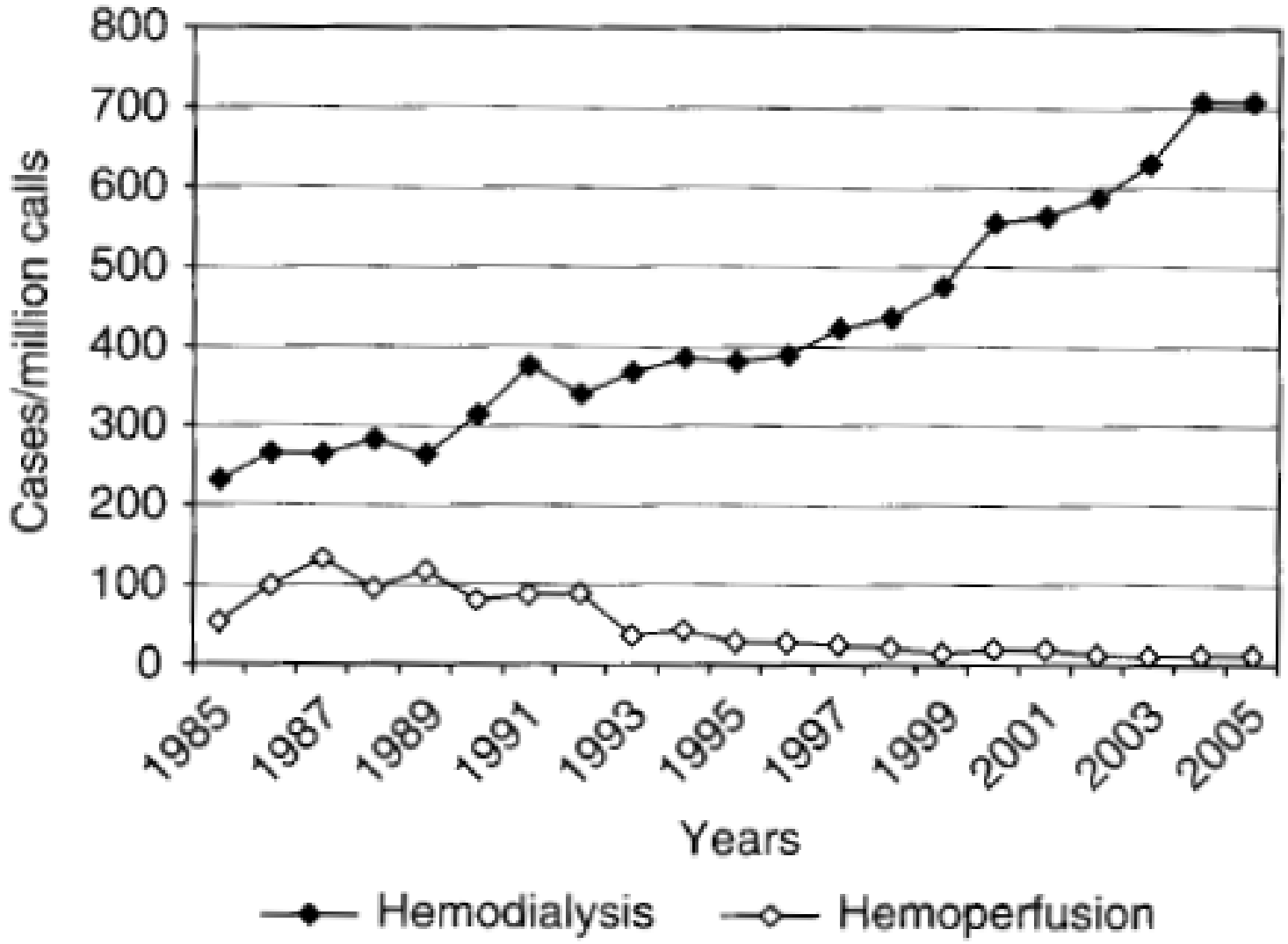
- Cartridge containing sorbent material capable of toxin adsorption
- Charcoal, synthetic resins, anion exchange resins
- Binding affinity with sorbent
- Low volume of distribution
- Charcoal for 1 to 1.5 kD, less effective for protein bound molecules
- Resins effective in protein bound & lipid soluble molecules
- No renal replacement therapy
- Side effects
  - Thrombocytopenia, leucopenia, coagulopathy
  - Embolisation of sorbent particles
  - Febrile reaction, hypotension
  - Hypoglycaemia, hypocalcaemia

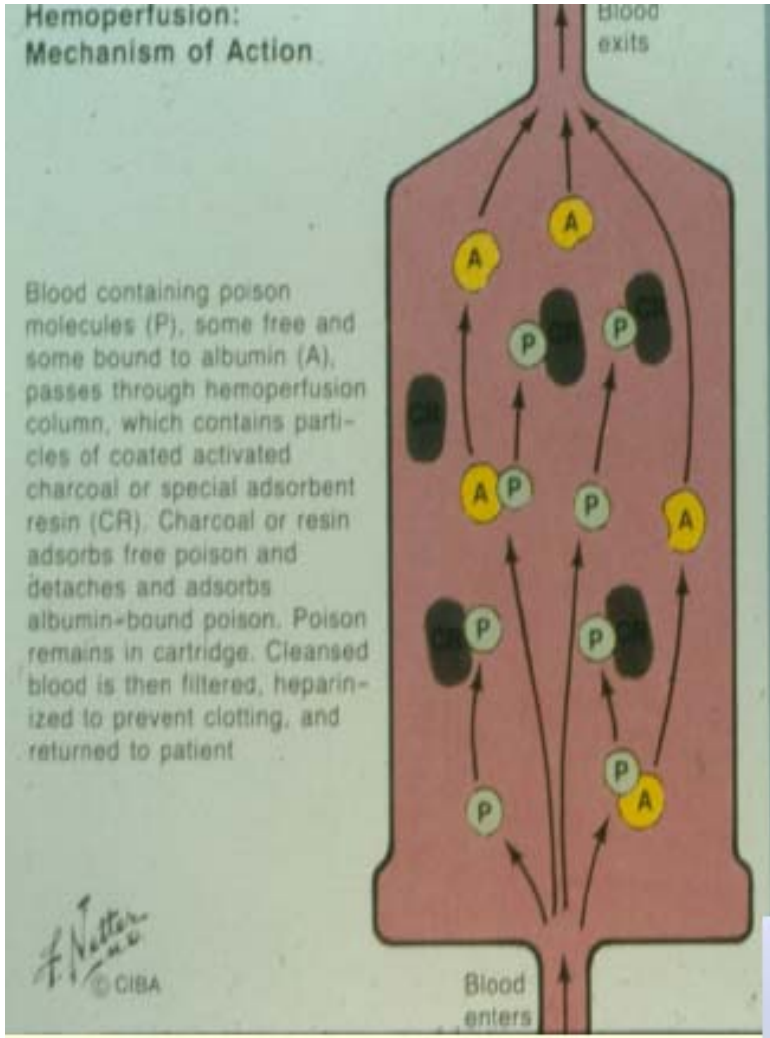
US Toxic Exposure Surveillance System (TESS)

The most common toxins responsible for cases receiving HP

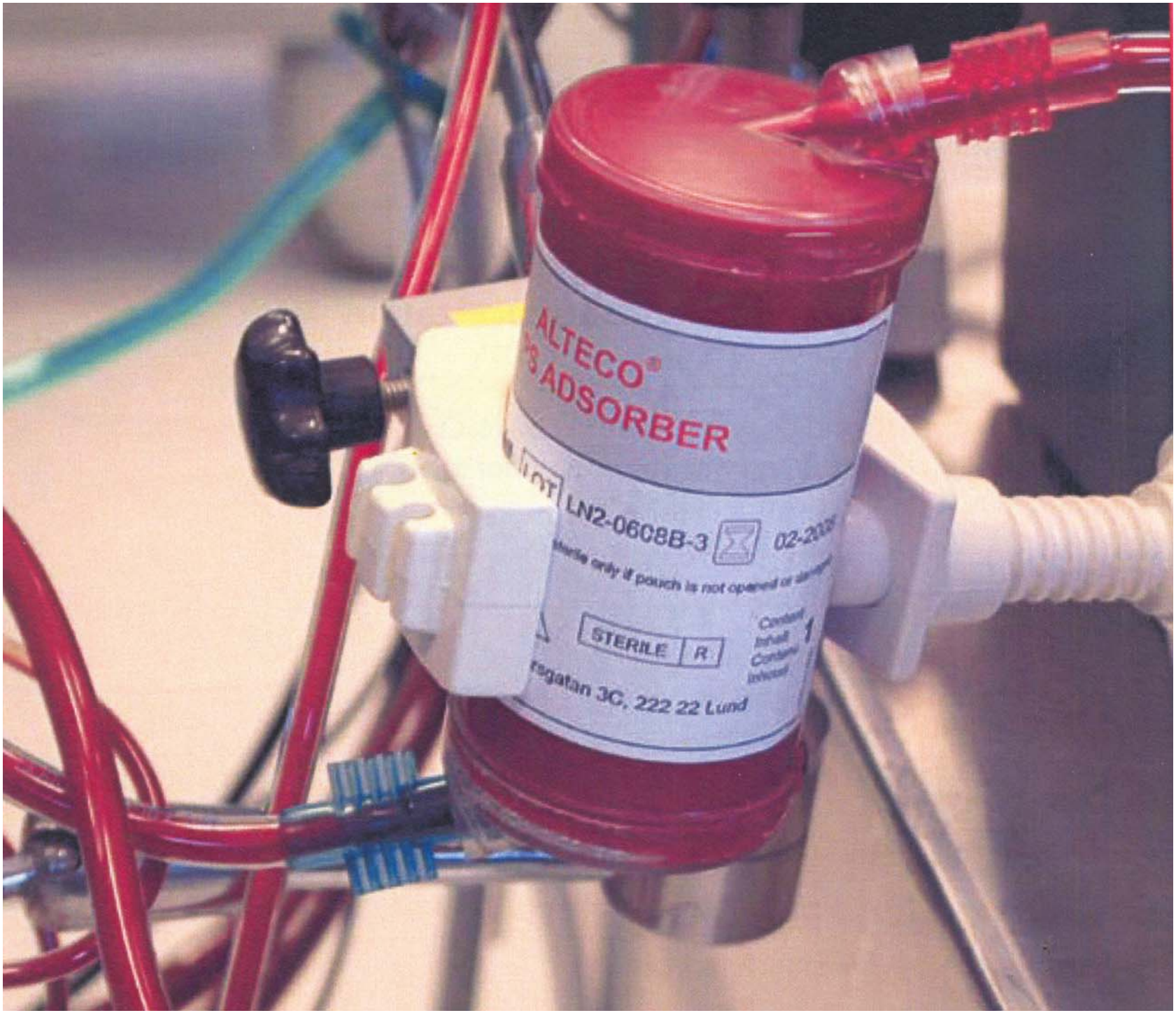
1991 – 1995	1996 – 2000	2001 – 2005
Aminophylline (162)	Aminophylline (58)	Carbamazepine (38)
Barbiturate (24)	Carbamazepine (16)	Lithium (30)
Acetaminophen (12)	Benzodiazepine (14)	Ethylene glycol (22)
Carbamazepine (11)	Valproic acid (13)	Acetaminophen (19)
Salicylates (8)	Other (12)	Valproic acid (17)
Mushroom (6)	Ethylene glycol (9)	SSRI (17)
Unknown (5)	SSRI (9)	Phenothiazine (15)
Amitriptyline (5)	Barbiturate (8)	Ethanol (12)
Valproic acid (4)	Lithium (7)	Biguanide (11)
Doxepin (4)	Methanol (7)	Other (10)
Barbiturate (4)		Salicylate (10)
Antiarrhythmic (4)		Carisoprolol (10)
Bee/wasp/hornet (4)		
Gastrointestinal irritant (4)		

HD vs. HP (from 1985 to 2005)




Hemoperfusion:
Mechanism of Action
Blood exits
Blood containing poison molecules (P), some free and some bound to albumin (A), passes through hemoperfusion column, which contains particles of coated activated charcoal or special adsorbent resin (CR). Charcoal or resin adsorbs free poison and detaches and adsorbs albumin-bound poison. Poison remains in cartridge. Cleansed blood is then filtered, heparinized to prevent clotting, and returned to patient
A
P
CR
© CIBA
Blood enters


仕様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The Bulletin Journal of the HKMA, 1984;65:65-70

MANAGEMENT OF SEVERE POISONING CASES BY HAEMODIALYSIS AND HAEMOPERFUSION

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The Bulletin Journal of the HKMA, 1984;65:65-70

Table I: No. of Cases of Accidental Poisoning by Drugs, Medicaments and Biologicals Each Year

	Government Hospitals	All Hospitals	Deaths	Mortality Rate %
1979	1,656	1,831	22	1.2
1980	1,727	1,844	23	1.2
1981	1,663	1,757	37	2.1
1982	2,073	2,196	47	2.1

The Bulletin Journal of the HKMA, 1984;65:65-70

NATURE OF THE POISON AND INDICATIONS FOR HD AND HP

The nature of the drugs or chemicals and the mortality are tabulated below:-

	No. of Patients	No. of Deaths
Salicylate	2	0
Barbiturate	2	1
Amitriptyline	3	2
Lithium Carbonate	1	1
Paraquat	2	1
Dettol	1	0
Total:	11	5

Necessary properties for extracorporeal removal

	Haemodialysis	Haemoperfusion
Solubility	Water	Water or lipid
Molecular weight	< 0.5 kD	< 40 kD
Protein binding	Low(<80%)	Low or high
Volume of distribution	<1l/kg	<1l/kg
Endogenous clearance	<4ml/min/kg	<4ml/min/kg
Distribution time	Short	Short

Commonly Dialyzed Intoxications

Substance	Methanol	Eth. Glycol	Salicylate	Lithium	Theophylline	Acetamino phen(??)
Weight (Daltons)	32	62	138	7	180	151
& Protein Bound	0	0	50-90	0	56	0-25
Vd (L/Kg)	0.6	0.6	0.2	0.8	0.5	1.0
Endog. CL ml/min/kg	0.7	2	0.88	0.35	0.65	5.0

Recent advances in Extracorporeal techniques

- Haemodialysis (high flux)
- Haemofiltration (CVVH / CVVHDF)
- High volume haemofiltration
- Super-high flux haemofiltration
- MARS
- Prometheus
- Single pass albumin dialysis
- Coupled plasma filtration adsorption
- Plasmapheresis
- Extracorporeal life support
  - VV-ECMO
  - VA-ECMO

Haemodialysis (High flux)

- Mechanism similar to low flux haemodialysis
- Allow removal of larger size molecules (<5kD)
  - Still much less as compared with haemofiltration (40kD)
- Ultrapure dialysate required (lower level of endotoxin)

Haemodialysis (High flux)

- Barbiturate
- Salicylate
- Ethylene glycol
- Valproic acid
- Carbamazepine
- Cephalosporin induced neurotoxicity

Haemofiltration

- In form of continuous therapy
  - Continuous veno-venous haemofiltration (CVVH)
  - Continuous veno-venous haemodiafiltration (CVVHDF)
- Blood passing through haemofilter
- Allow convective removal of molecules of up to 40kDa
- Lower Qb, stable in haemodynamics
- Prolonged duration of therapy
  - Lower rebound
  - Protein bound or second compartment
- Low clearance
  - ~ effluent rate 20-40 ml/min
  - Not good for highly toxic substance which requires rapid removal

Protein binding equilibrium

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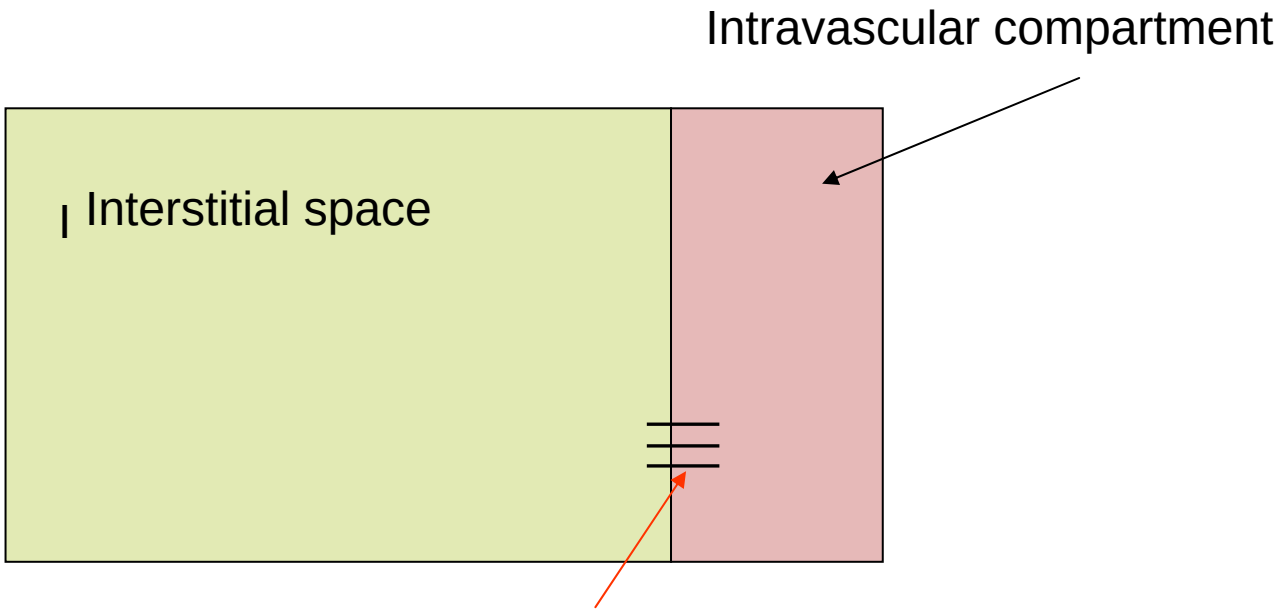


If long distribution time: HD not effective but CVVH is more favourable

Haemofiltration (cont.)

- Anticoagulation required
  - Systemic anticoagulation
  - No anticoagulation
    - Pre-dilution replacement
    - Saline flush
  - Regional anticoagulation
    - Regional citrate anticoagulation

	Haemodialysis	Haemofiltration	Haemoperfusion
Solubility	Water	Water	Water or lipid
Molecular weight	< 0.5 kD < 5 kD (high flux)	<40 kD	< 40 kD
Protein binding	Low(<80%)	Low(<90%)	Low or high (>90%)
Volume of distribution	<1l/kg	<1l/kg	<1l/kg
Endogenous clearance	<4ml/min/kg	<4ml/min/kg	<4ml/min/kg
Distribution time	Short	longer	short

CVVH / CVVHDF

- Metformin associated lactic acidosis
- Star-fruit poisoning in chronic renal failure patients (with charcoal HP)
- Barbiturate
- Theophylline
- Methanol
- Valproic acid

High Volume Haemofiltration

- Higher clearance (compared with CVVH)
  - Continuous or pulsed
  - 40-100 ml/min (still low vs. HD)
- Effective in lowering the cytokines mediated toxicity
- Immunomodulation
- Additional renal replacement therapy

High Volume Haemofiltration

- Disadvantages
  - Technically difficult, high nursing workload
  - High cost
  - High blood flow required, maybe a challenge to haemodynamic unstable patients
    - If pre-dilution, reduce efficiency
  - Loss of essential small molecules, aminoacids, glucose, vitamins, …etc.

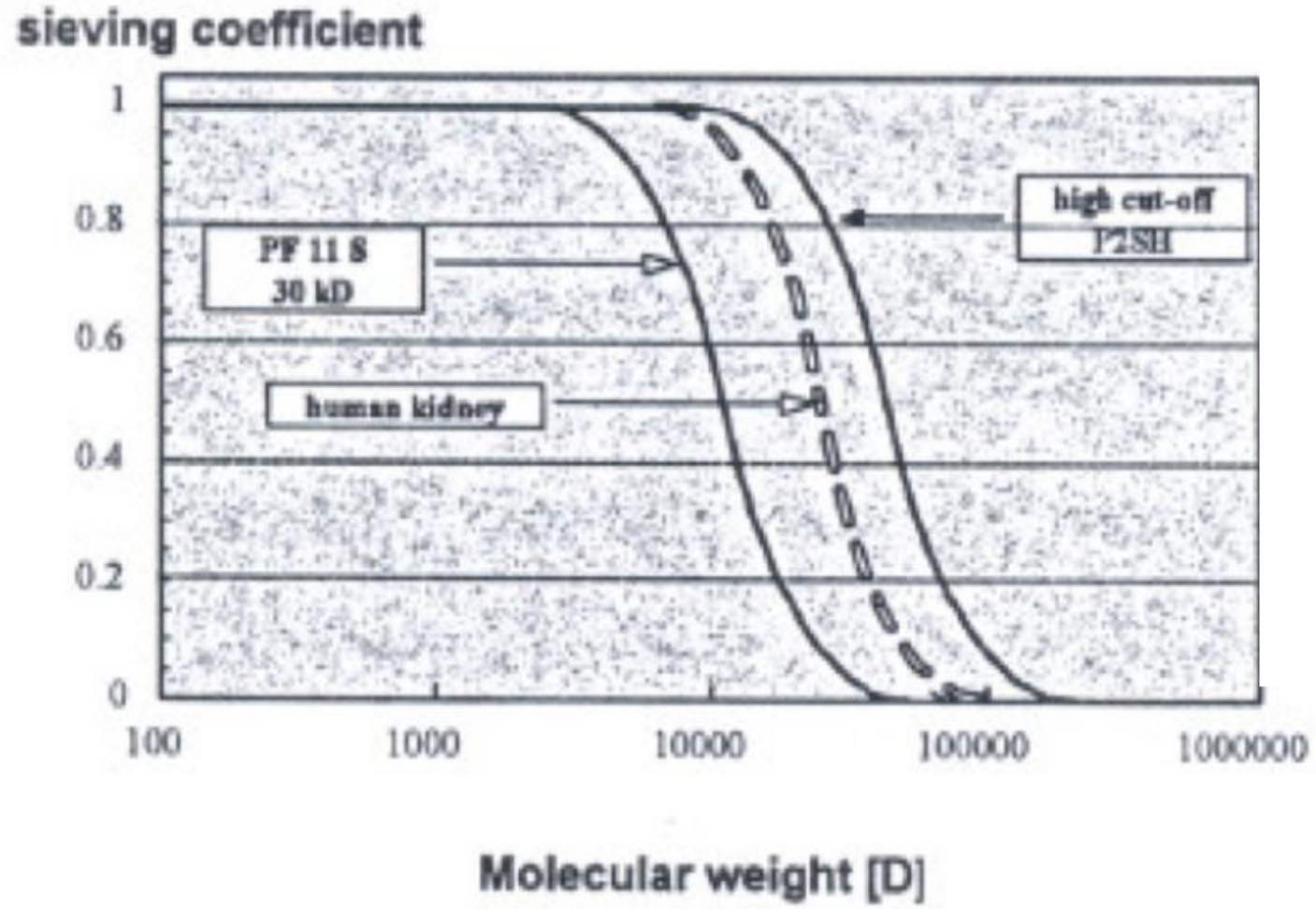
High Volume Haemofiltration

- Any poisoning with CVVH/CVVHDF
- Cephalosporin induced neurotoxicity
- Lithium toxicity
- Tetramine poisoning (charcoal haemoperfusion)
  - Chau CM et al, Hong Kong Med J, 2005;11:511-514

Super High Flux Haemodialysis /Haemofiltration

High Cut-off Protein-permeable Membrane

Super High Flux Haemofilter
High Permeability Haemofilter
High Cut-off Haemofilter



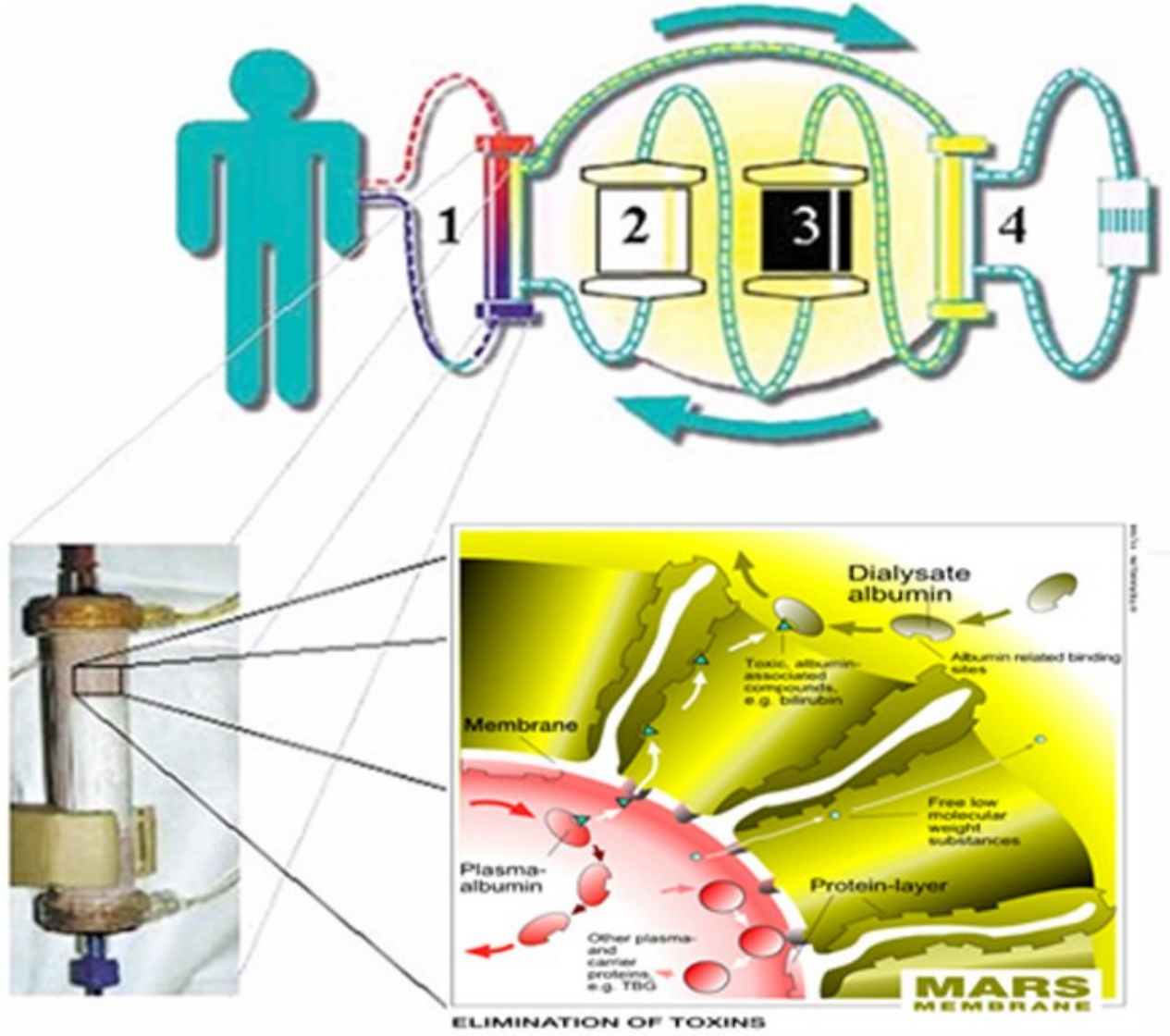
Super High Flux Haemodialysis /Haemofiltration

- High cut off > 50 kD
- Efficient removal of free light chain immunoglobulin for multiple myeloma
  - Hutchison et-al, J Am Soc Nephrol 2007;18:886-895
- Effective cytokine removals
  - Lambertmont et-al, Artificial Organs 2006;30(7):560-564
  - Morgera et-al, Nephrol Dial Transplant 2003,18(7):1361-1369
- Rhabdomyolysis (myoglobin 17kD)
  - Marked increased clearance
    - Naka et-al, Critical Care 2005;9:R90-R95
- Albumin loss requiring replacement

Molecular Adsorbent Recirculating System (MARS)

- Liver support system
- Have been shown to remove
  - Ammonia
  - Bilirubin
  - Bile salts
  - Aromatic amino acids
  - Short & medium chain fatty acids
- Have been shown to improve
  - short term survival
  - hepatic encephalopathy
  - Haemodynamics
  - intracranial pressure and
  - coagulopathy in patients with liver failure

Molecular Adsorbent Recirculating System (MARS)



MARS

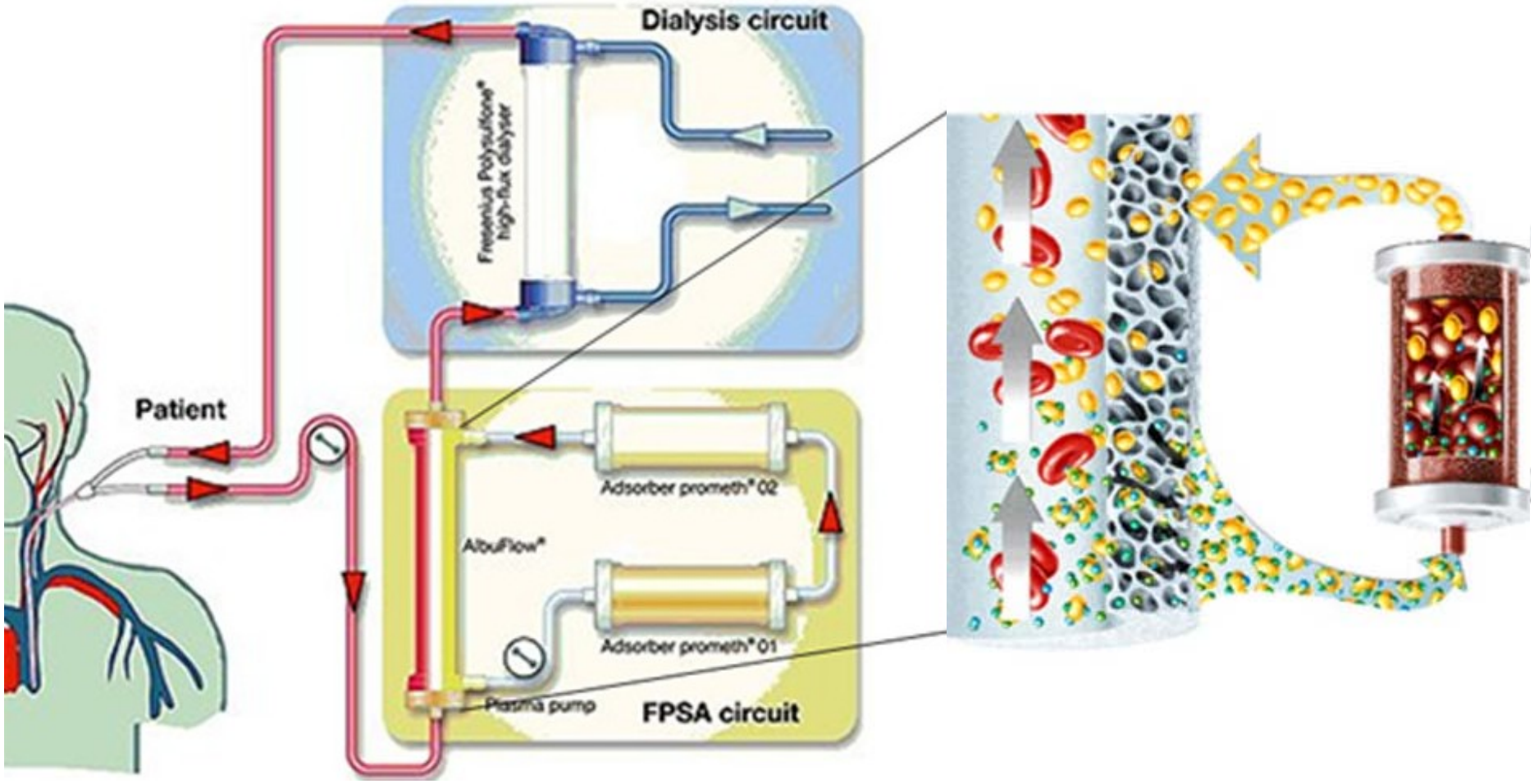
- Circuit
  - Blood circuit
  - Albumin detoxification circuit
  - Haemodialysis circuit
- Removing albumin bound toxic molecules and e.g. phenytoin, theophylline, diltiazem
- Small water molecules too
- Provide temporary liver and renal support too
- Limitations
  - High cost
  - Technically complicated
  - Availability

MARS

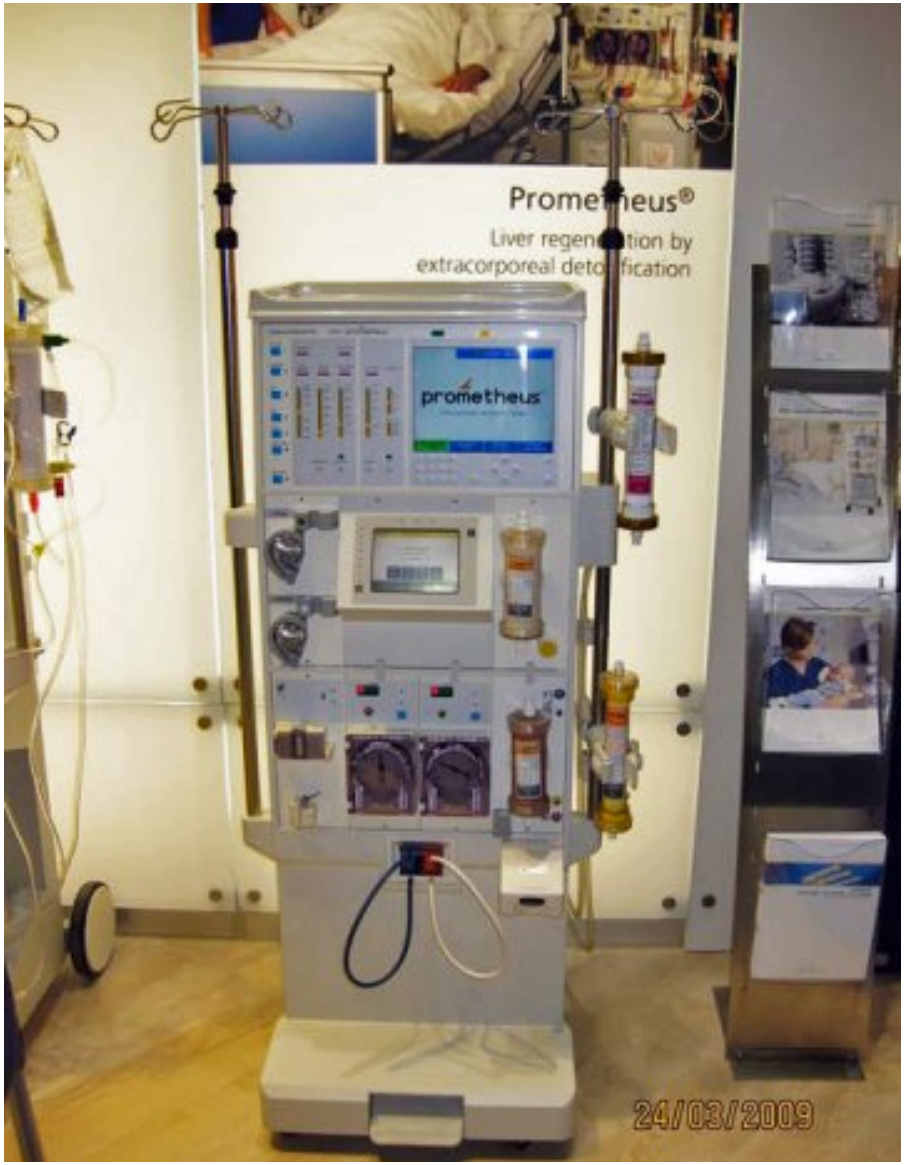
- Theophylline
- Phenytoin
- Diltiazem

Prometheus

Fractionated Plasma Separation, Adsorption (FPSA)



Prometheus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Liver regen tion by
extracorporeal deto fication
prometheus
24/03/2009

Prometheus
Fractionated Plasma Separation, Adsorption (FPSA)

- Plasma filtration with adsorption, run in series with high flux haemodialysis
- Remove
  - Albumin bound (unconjugated bilirubin, bile salts, hydrophobic amino & fatty acids)
  - Small and middle molecules
- Only small scale clinical studies
- Temporary liver and renal support

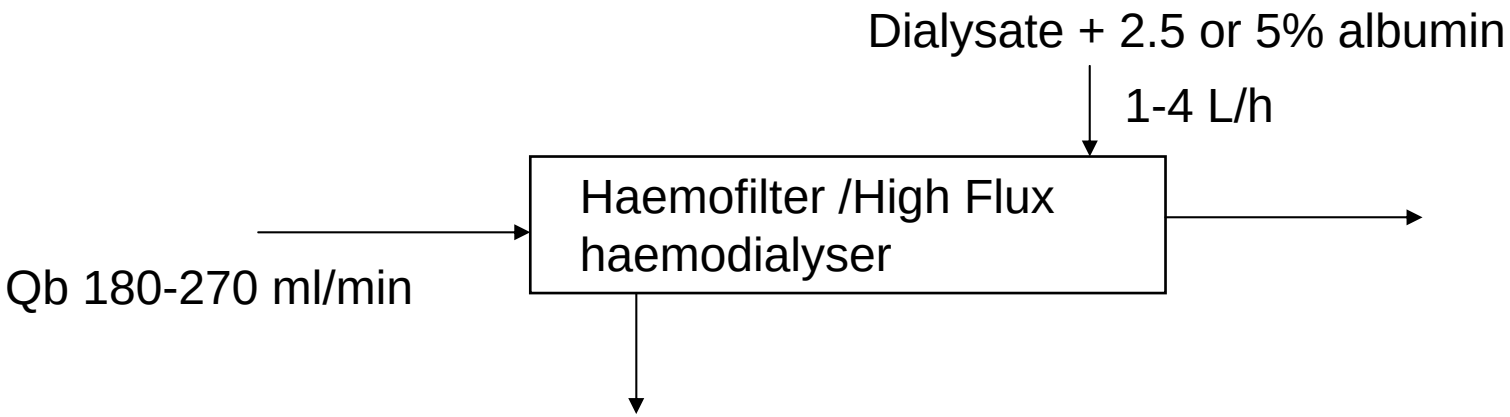
Single Pass Albumin Dialysis

Pediatrics 2004;113:406-409

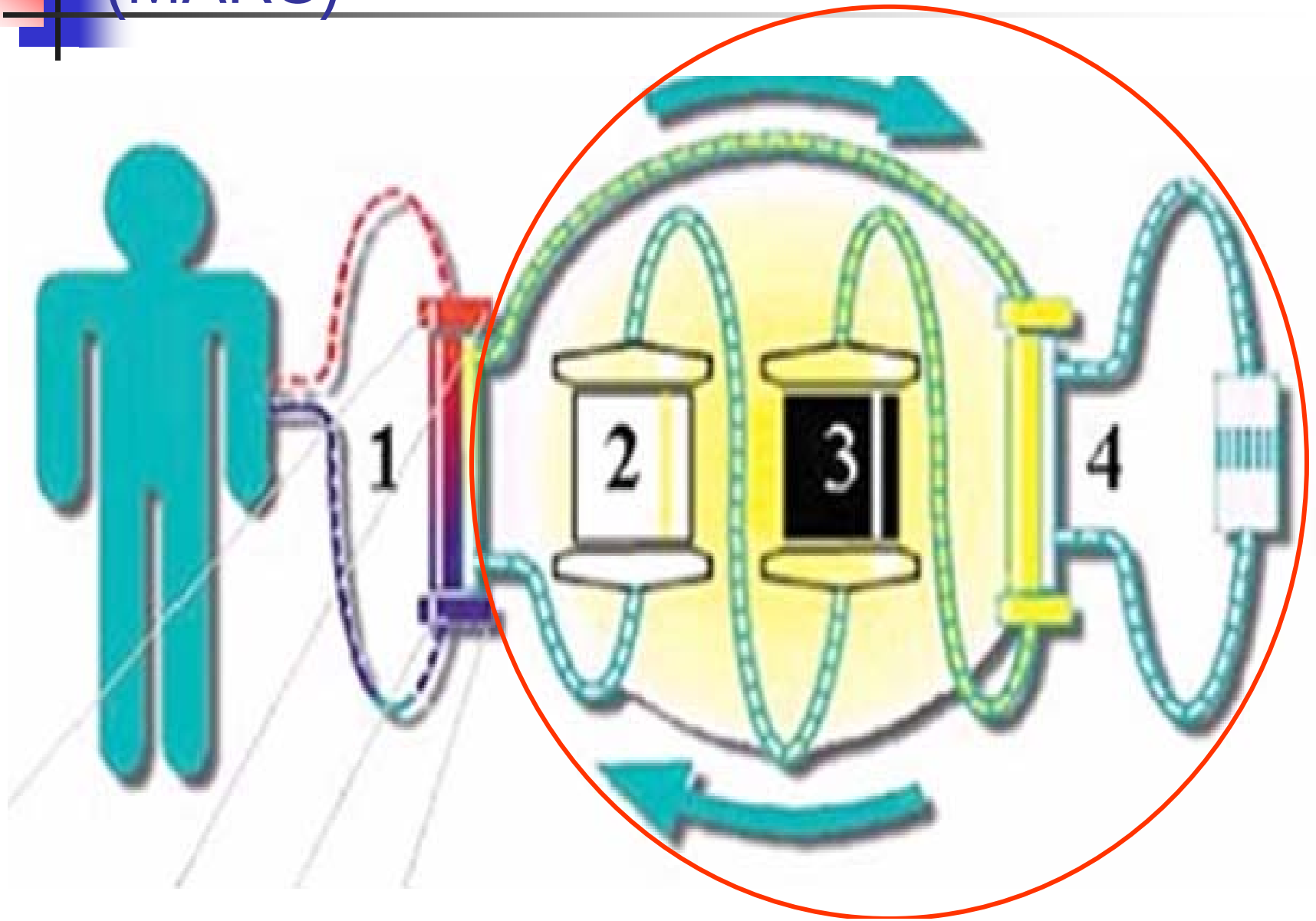
Nephrol Dial Transplant 2009;24:231-238

- Modified CVVHD with albumin dialysate
- Infrastructure similar to CVVHD
- Qb (180 - 270 ml/min)
- Qd (1 – 4 L/h)
- Haemofilter / high flux haemodialyser
- Addition of 2.5% to 5 % albumin in dialysate
- Adding albumin in dialysate compartment
  - Increase valproic acid and carbamazepine clearance
  - Not pheytoin clearance

Single Pass Albumin Dialysis



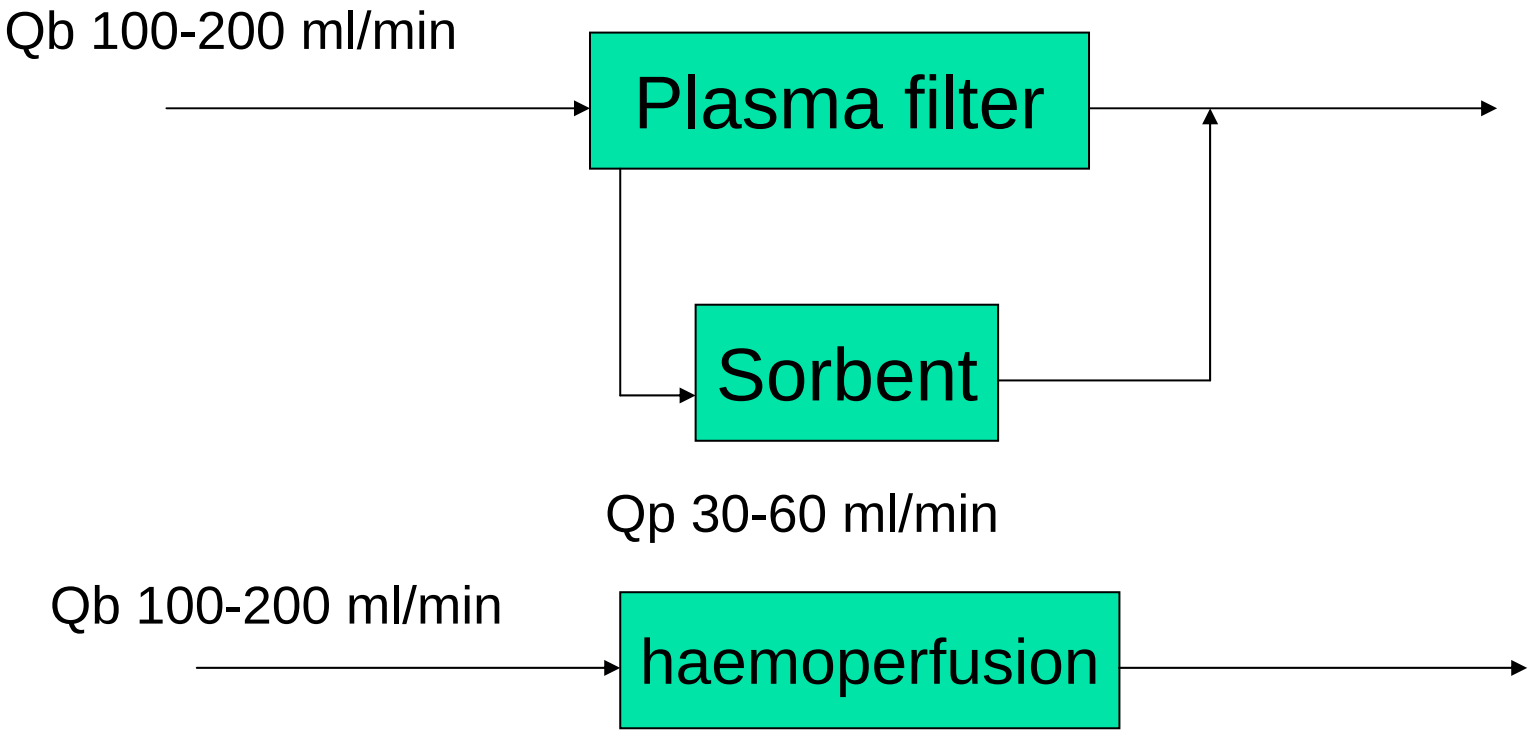
Molecular Adsorbent Recirculating System (MARS)



Coupled Plasma Filtration with Adsorption

- Effective removal of sepsis related endotoxins and inflammatory mediators
  - Improved survival in animal trials
  - Improved haemodynamic in clinical trials
    - Ronco, et al. Contrib Nephrol 2004;144:376-386
    - Ronco, et al. Crit Care Med 2002;30:1250-1255.
- Similar to haemoperfusion
- Plasma instead of whole blood passing through sorbent
  - Less complication like thrombocytopenia (should be considered in patients still requiring HP but with severe thrombocytopenia)
  - Less efficient in clearance

Coupled Plasma Filtration with Adsorption

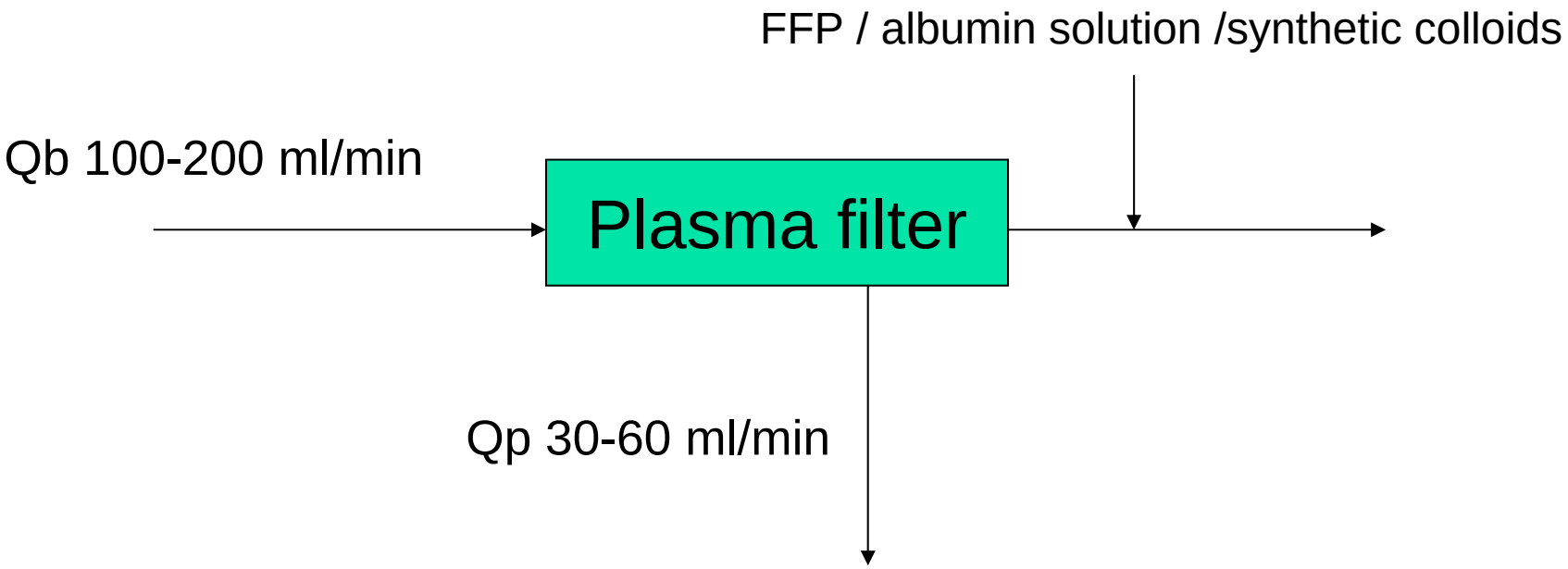


Coupled Plasma Filtration with Adsorption

Plasmapheresis or Therapeutic plasma exchange (TPE)

- High MW > 100 kD
- Water / Lipid soluble
- High plasma protein binding (>80%)
- Low volume of distribution (<0.21l/kg)

Plasmapheresis or Therapeutic plasma exchange (TPE)



Plasma Separator

- Centrifugal separation

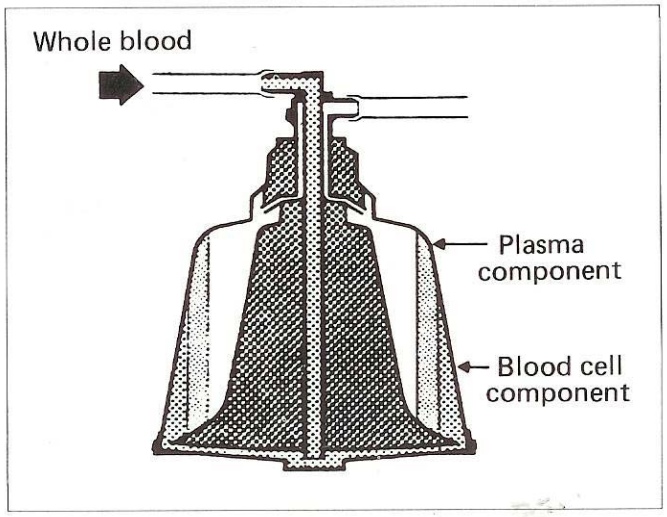


Fig. 2 Haemonetics rotating bowl

- Membrane separation

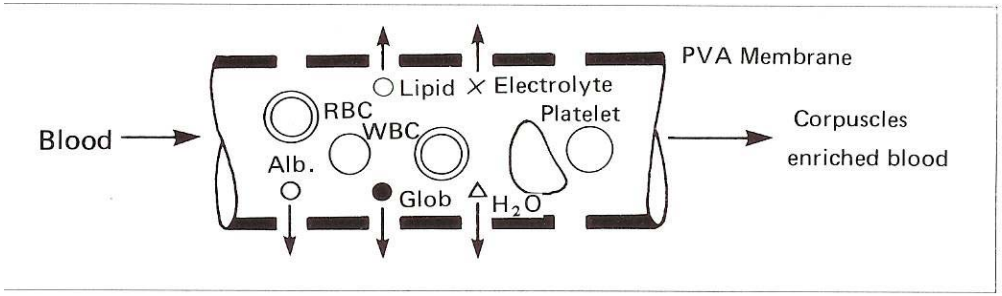
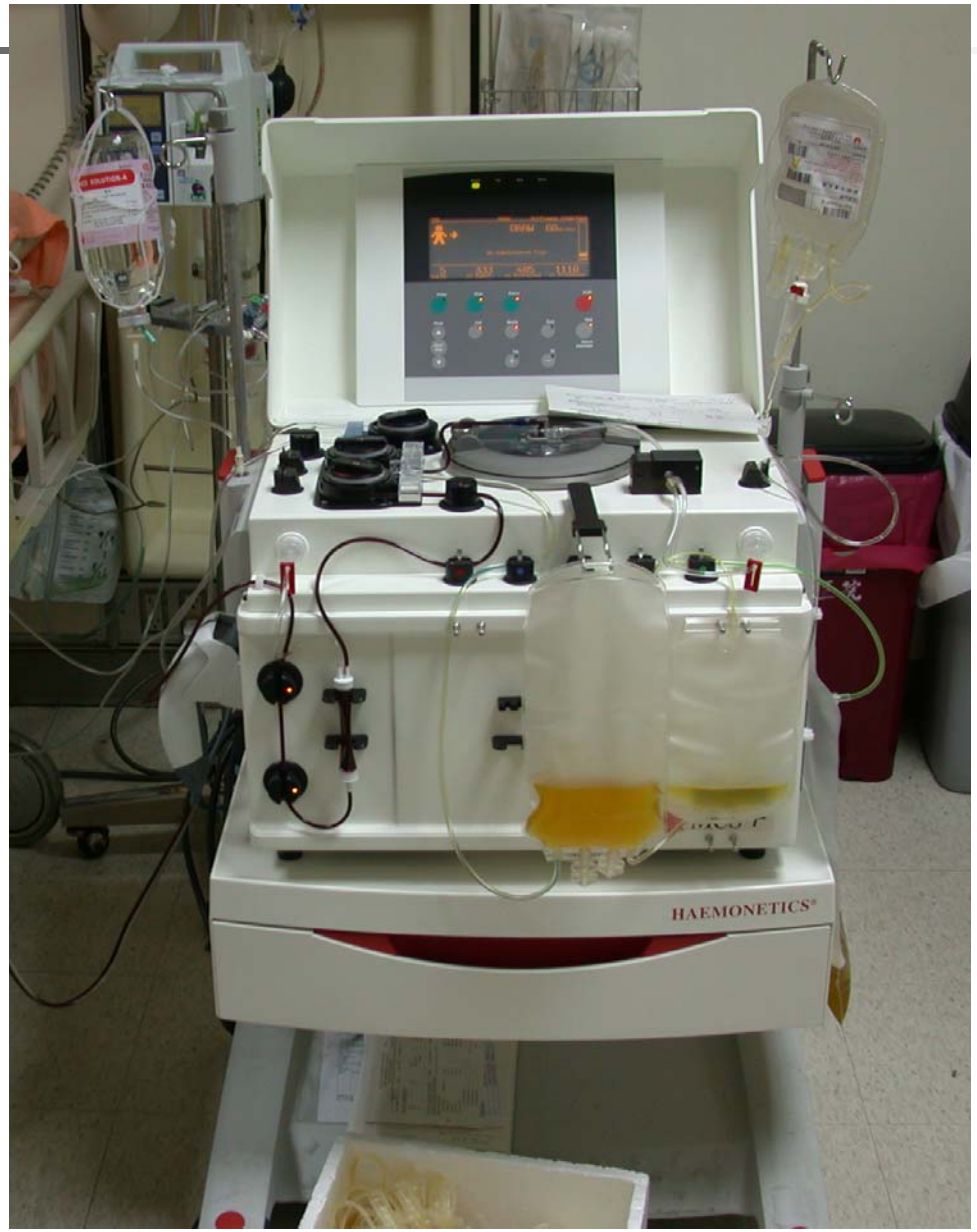


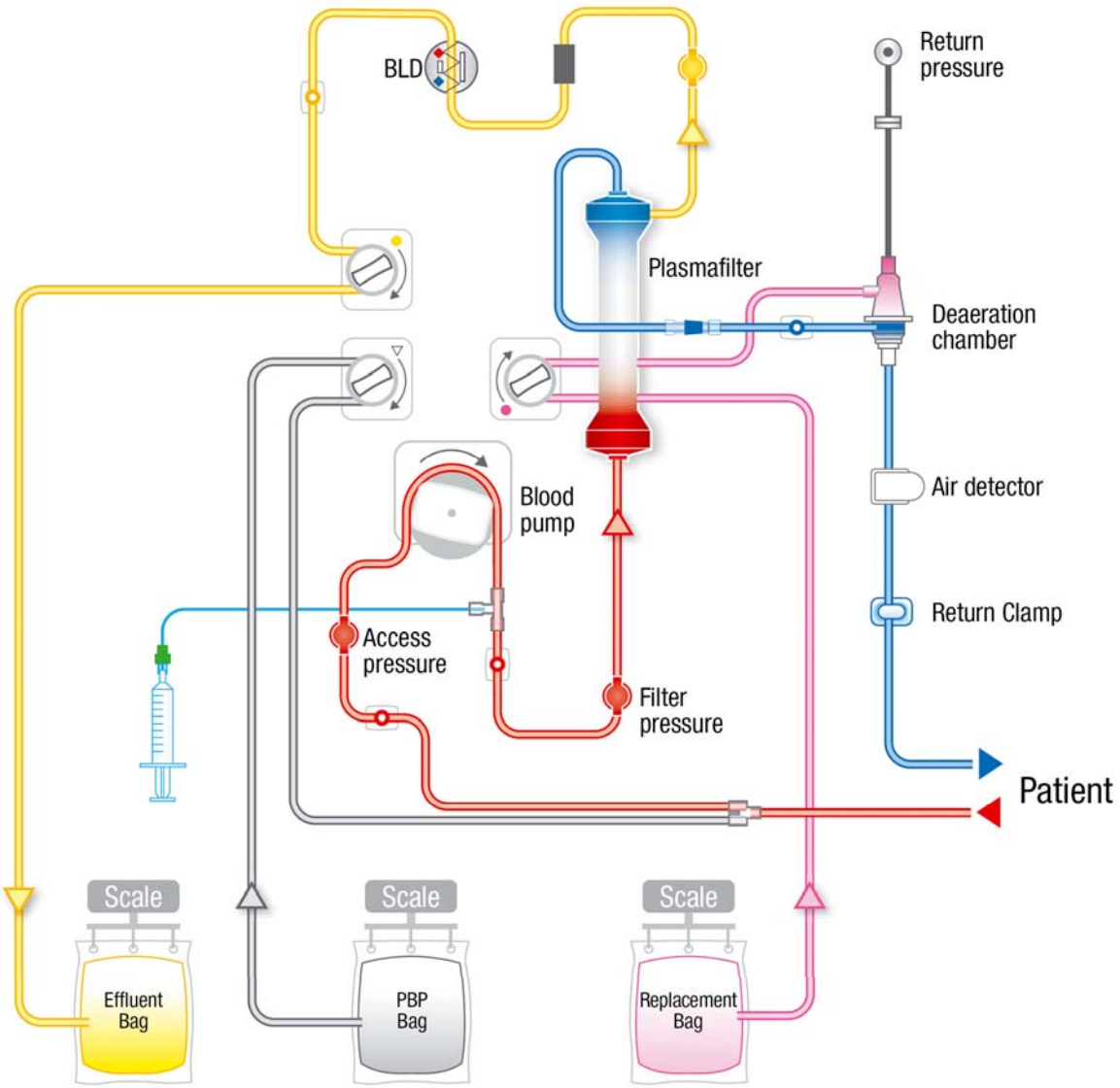
Fig. 3 Principle of membrane plasma separation

Centrifugal Separation



Prismaflex

Therapeutic Plasma Exchange with Prismaflex



Plasmapheresis

Nenov et-al, Nephrol Dial Transplant 2003;18[Suppl 5]:v56-v58

- Phalloid mushroom intoxication
  - When compared with charcoal HP
    - mortality reduced from 30-50% to <20% in general
  - From >20% to 4.8% in a series of 21 patients
    - Ther Apher 2000;4:303-307
- Tricyclic and tetracyclic antidepressant
  - In life threatening cardiac and CNS toxicity, plasmapheresis can be life saving
    - Nephrol Dial Transplant 1996;11:743
  - After a single plasmapheresis, amitriptyline level drop from 4.03 to 1.49ug/ml; 63% reduction in plasma level
- L-thyroxine
  - Intensive Care Med 1987;13:33-38

Amanita Phalloides mushroom

Plasmapheresis (2)

Nenov et-al, Nephrol Dial Transplant 2003;18[Suppl 5]:v56-v58

- Verapamil
- Diltiazem
- Carbamazepine
- Adjunctive therapy with antidigoxin antibodies for digitalis intoxication
  - In patients with renal failure
  - To prevent rebound caused by dissociation of digoxin-antidigoxin complexes
    - Am J Nephrol 1990;10:518-521
- Theophylline
    - Crit Care Med 1991;19:288-290
- Heavy metals (mercury & vandate)

Exchange transfusion

- Not new technique but it is potentially useful
- Severe malarial falciparum infection
- Neonatal jaundice
  - Unconjugated bilirubin
- Quinine intoxication in a child
  - *Archives of Disease in Childhood* 1972;47:304-305;

Extracorporeal Life Support
VA-ECMO

- Cardiovascular drug toxicity
  - 5.8% (3.5%) of total poisoning
  - 19% (16.4%) of total poison mortality
- Antidotes,
  - digoxin specific Fab fragment
  - Calcium
  - Dobutamine
  - Glucagon
  - Insulin high dose + dextrose
- VA-ECMO
  - Percutaneous cardiopulmonary support peripherally without the need of sternotomy
  - Severe drug –induced cardiotoxicity
    - Persistent hypotension
    - Cardiogenic shock
    - Pulseless ventricular tachycardia
    - Asystole
  - Temporal circulatory support to vital organs
    - Unloading the heart to encourage recovery

Drugs having “membrane stabilising activity” with potential for severe cardiotoxicity

FJ Baud et-al, Critical Care 2007,11:207

Class 1 anti-arrhythmics	Flecainide, disopyramide, propafenone, quinidine,lignocaine, procainamide
Beta-blockers	Propranolol, acebutolol, nadolol, pindolol, labetalol, oxprenolol, metoprolol
Polycyclic antidepressants	Imipramine, desipramine, amitritptyline, clomipramine, doxepine
Selective serotonin reuptake inhibitors	Venlafaxine, citalopram
Dopamine and noradrenaline uptake inhibitors	Bupropion
Anti-epileptics	Carbamazepine, phenytoin
Phenothiazines	Thioridazine
Opioids	Dextropropoxyphene
Antimalarial agents	Chloroquine, quinine
Anaesthetic-recreational agents	Cocaine

Extracorporeal life support in severe drug intoxication: a retrospective cohort study of seventeen cases

Critical Care 2009,13:R138

- A case series of 17 cases
  - 10 refractory shock & 7 prolonged cardiac arrest
  - 15 (88%) wean off ECLS
  - 13 (76%) hospital discharge without sequelae
- Consider ECLS as a last resort, efficient, and relatively safe therapeutic option

Paraquat poisoning

- A lady of 27 year-old with good past health took 100ml 24% concentrated paraquat solution after quarrel with her boy friend
- 24g (480mg/kg) paraquat

- > 40mg/kg universally fatal
  - Bismuth C, et-al, Drug Saf 1990;5(4):243-251
  - Vale JA, et-al, Hum Toxicol 1987;6(1):41-47

#	Sex/ age	Amount	Presenting time and symptoms	Urine Dithio nite	GI decon	CHP	Immunosup pression	NAC	Outcome
1	M/78	? 2100 ml	25 mins	×	Cannot tolerate AC	×	×	×	Developed gasping and cardiac arrest in AED
2	M/49	Ocular contact	3 hrs	×	×	×	×	×	Uneventful with local irrigation
3	M/46	Inhaled diluted soln Left knee contact	19 hrs vertigo	-ve	×	×	✓	✓	Survive with minimal lung fibrosis
4	M/84	Inhalation during spray	Few hours V, D	×	×	×	×	×	Uneventful
5	M/38	Ocular contact	2 hrs	×	×	×	×	×	Uneventful with local irrigation
6	M/25	One mouthful	Immediate throat discomfort. SOB 2/7 later	+ve	×	×	✓	×	Survive ARF Cr 141 Decreased DLCO
7	F/79	Empty bottle	6 hrs	HPLC	AC	✓ 15 min	✓	✓	Died 24 hrs after admission
8	F/63	60 ml oral	12 hrs. V, SOB	+ve	AC	×	✓	✓	Died on D3
9	F/27	100-150 ml oral	40 mins	+ve	AC	✓	✓	✓	Died on D15
10	F/73	Empty bottle	? 8 hrs. V,drowsy	+ve	GL, AC	×	×	✓	Died 8 hours

Courtesy Dr. SH Ng, HKPIC

Table 1. Case summary of paraquat poisoning from 1998 to 2005

Case no.	Date of attendance	Age/sex	Routes of exposure	Amount of exposure	Specific treatment	Complications	Outcome (survival/death)
1	7/3/1998	58/F	Oral	500 ml	GL & FE	ARF (Cr up to 564 µmol/L) paralytic ileus & respiratory failure	Death (12 hours after admission)
2	31/3/1999	24/M	Oral	20-40 ml	FE & ST	Renal impairment (Cr 172 µmol/L), PF (normal CXR but abnormal lung function test) & painful dysphagia	Survival, renal function recovered without dialysis, refused endoscopic examination
3	25/12/2000	23/M	Oral	– One mouthful	FE &HD	ARF (Cr up to 700 µmol/L & progressive PF	Death (15 days after admission)
4	16/5/2002	20/M	Oral	Half-spoonful	AC, FE, ST, CH & HD	ARF (Cr up to 400 µmol/L) & oropharyngeal erosions	Survival, renal function gradually improved to normal, water soluble contrast study showed no oesophageal involvement
5	21/7/2003	25/F	Oral	200 ml	FE, ST, CH, HD & AOT	Oropharyngeal excoriation, oesophagitis, haemorrhagic gastritis, ARF (Cr up to 600 µmol/L), acute interstitial pneumonitis & acute hepatic failure	Death (3 weeks after admission), no improvement of renal function
6	5/12/2004	76/M	Eyes	Few drops	Nil	Nil	Survival
7	13/2/2005	70/M	Oral	100 ml	FE & HP	ARF (Cr up to 337 µmol/L) & progressive pneumonitis	Death (3 days after admission)

AC: activated charcoal; AOT: antioxidant therapies; ARF: acute renal failure; CH: charcoal haemoperfusion; Cr: creatinine; CXR: chest X-ray; F: female; FE: Fuller's earth; GL: gastric lavage; HD: haemodialysis; HP: haemoperfusion; M: male; PF: pulmonary fibrosis; ST: steroid therapy.

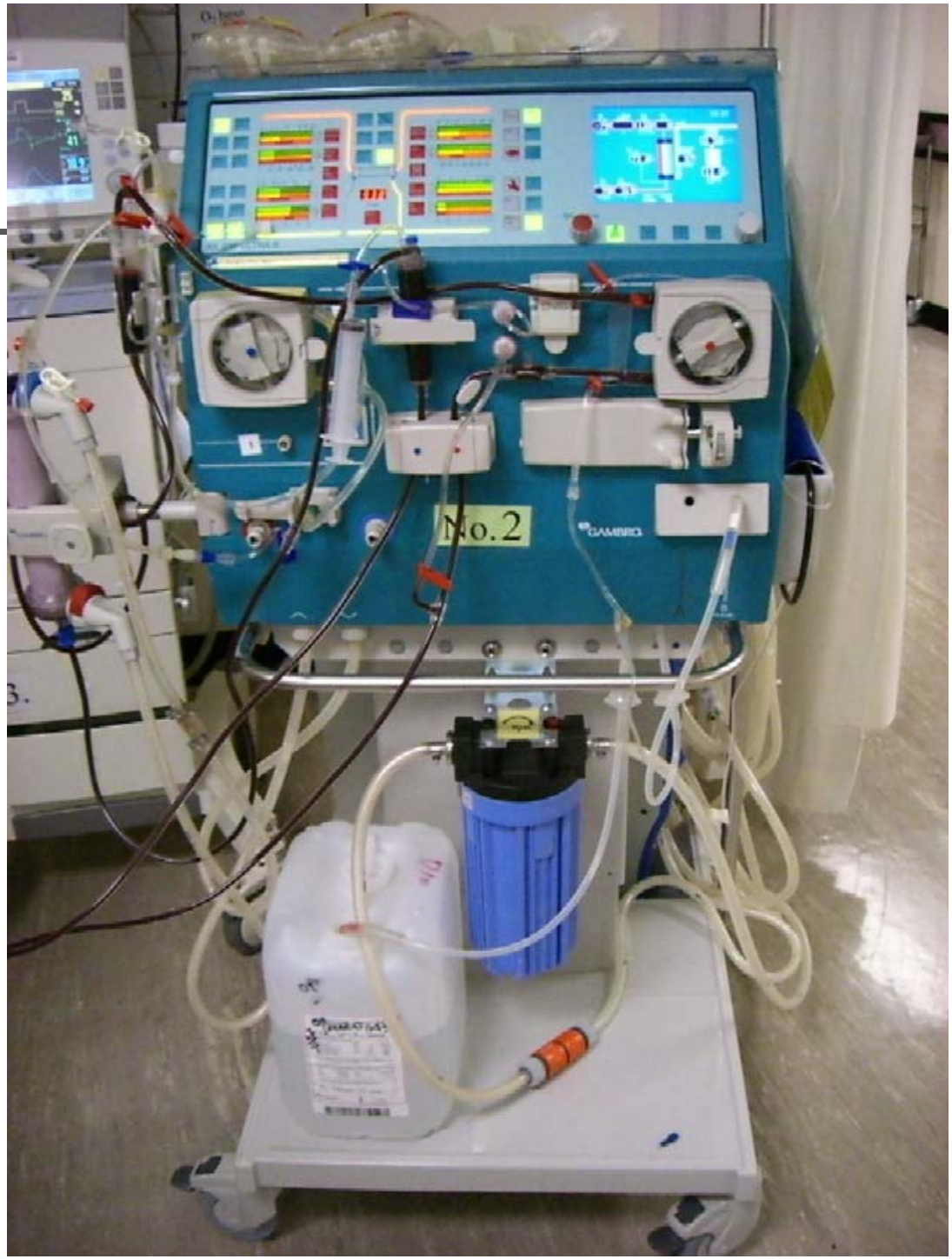
WONG et-al, Hong Kong J Emerg Med 2006;13(3):155-160

Paraquat poisoning (2)

- Gastric lavage followed by 50g activated charcoal was given at the A&ED
- To ICU for further management
- Charcoal haemoperfusion for 8 hours followed by high volume haemofiltration (64ml/kg/h) for 16 hours daily for the initial two days. Thereafter only HVHF continued
- N-acetylcysteine IV infusion
- Pulse steroid
- Cyclophosphamide

Paraquat poisoning (3)

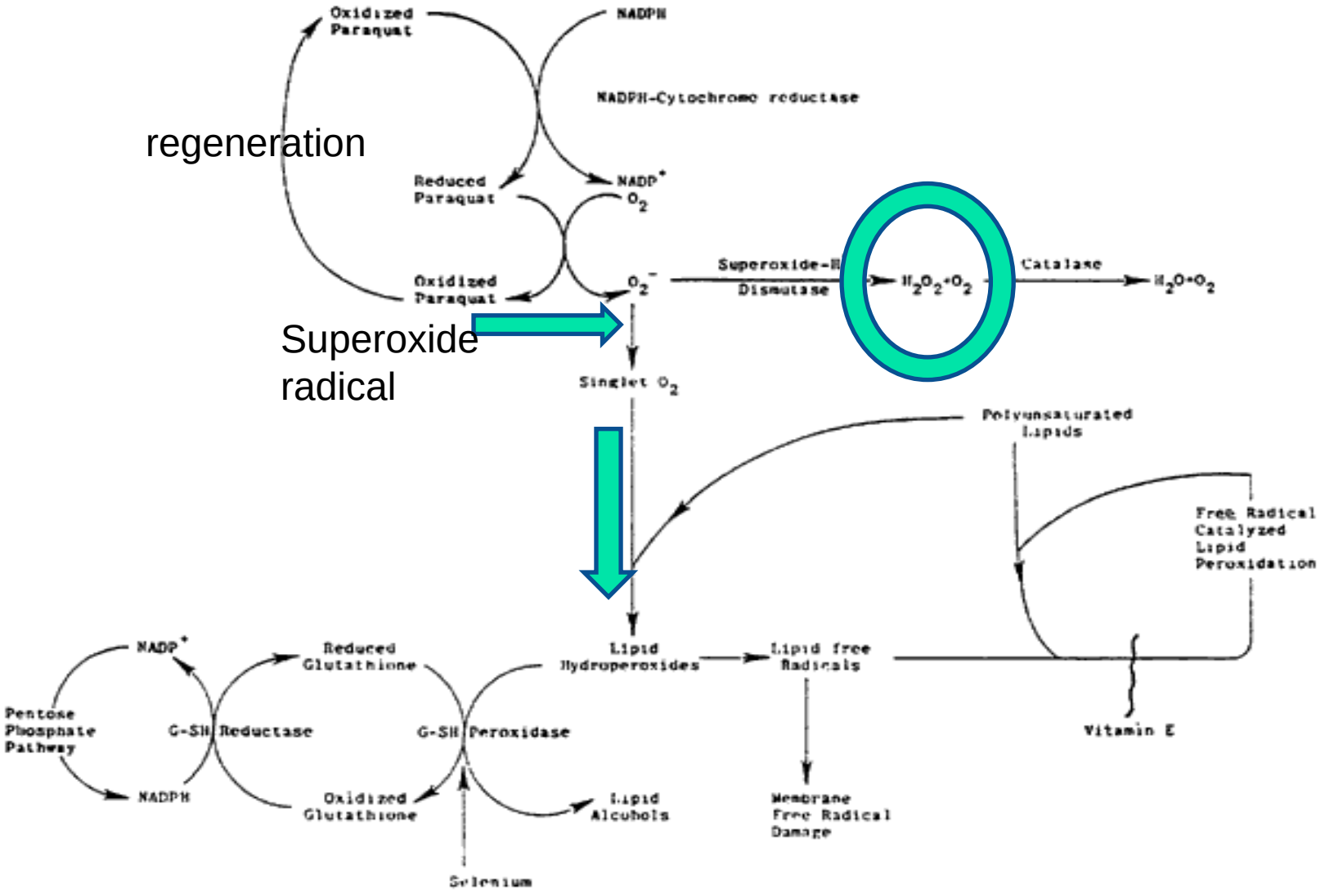
- The patient regretted for what she had done
- Expressed she want to live. However,
- Her condition gradually deteriorated
  - Impaired renal function
  - Increased pulmonary oedema, increased oxygen requirement
- Intubation & IPPV
  - Oxygenation desaturation with FiO2 100%
- Decided VV-ECMO
  - Support the failing lung
  - To buy time for removal of toxin by HVHF / natural healing process


No.2

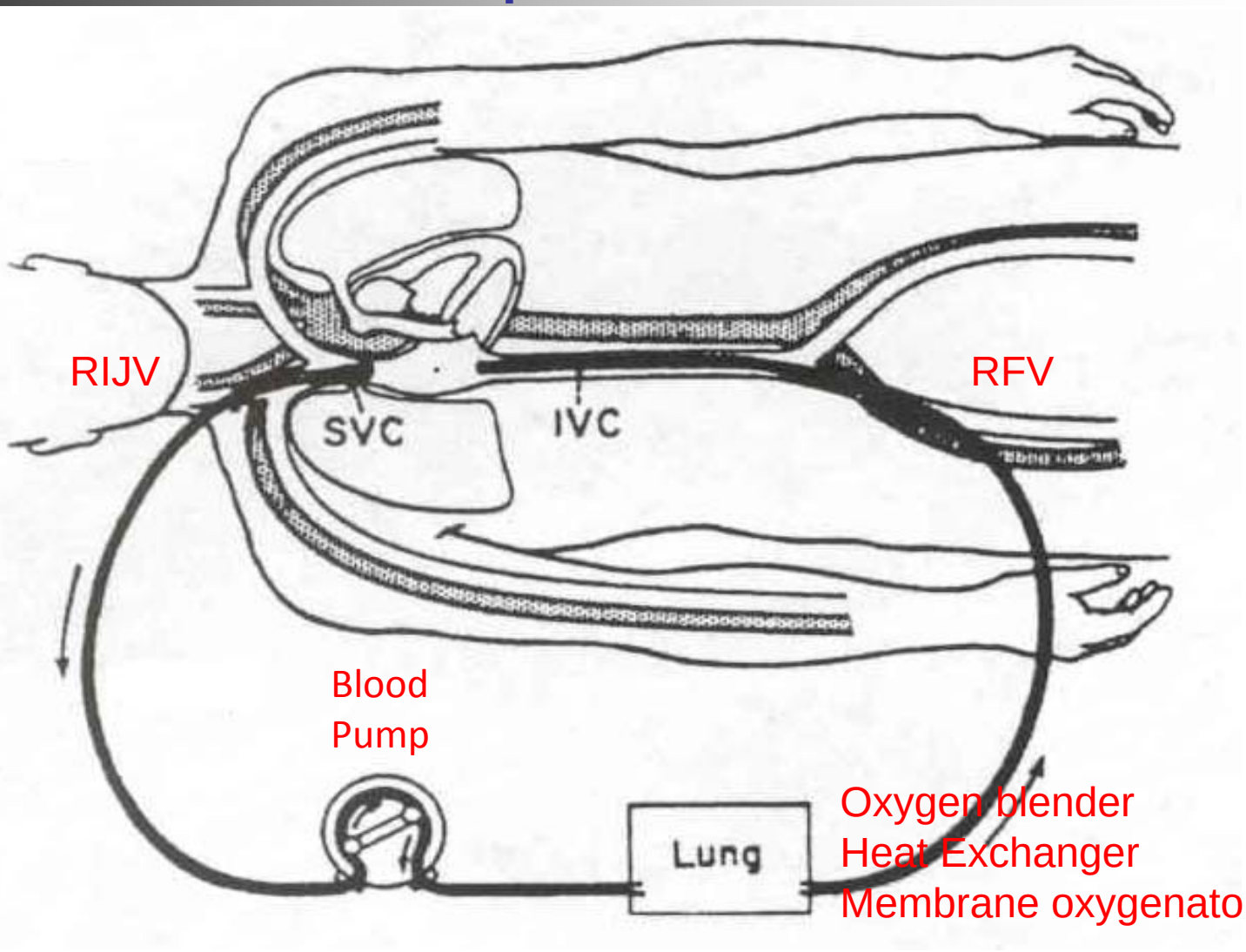
Paraquat poisoning (4)

- HVHF
  - Toxin removal
    - Serum toxin levels checked (results still pending)
  - To clear cytokines mediated injury
  - Renal replacement therapy
- N-acetylcysteine, steriod and cyclophosphamide
  - Decrease oxidative injury
  - Immune mediated injury

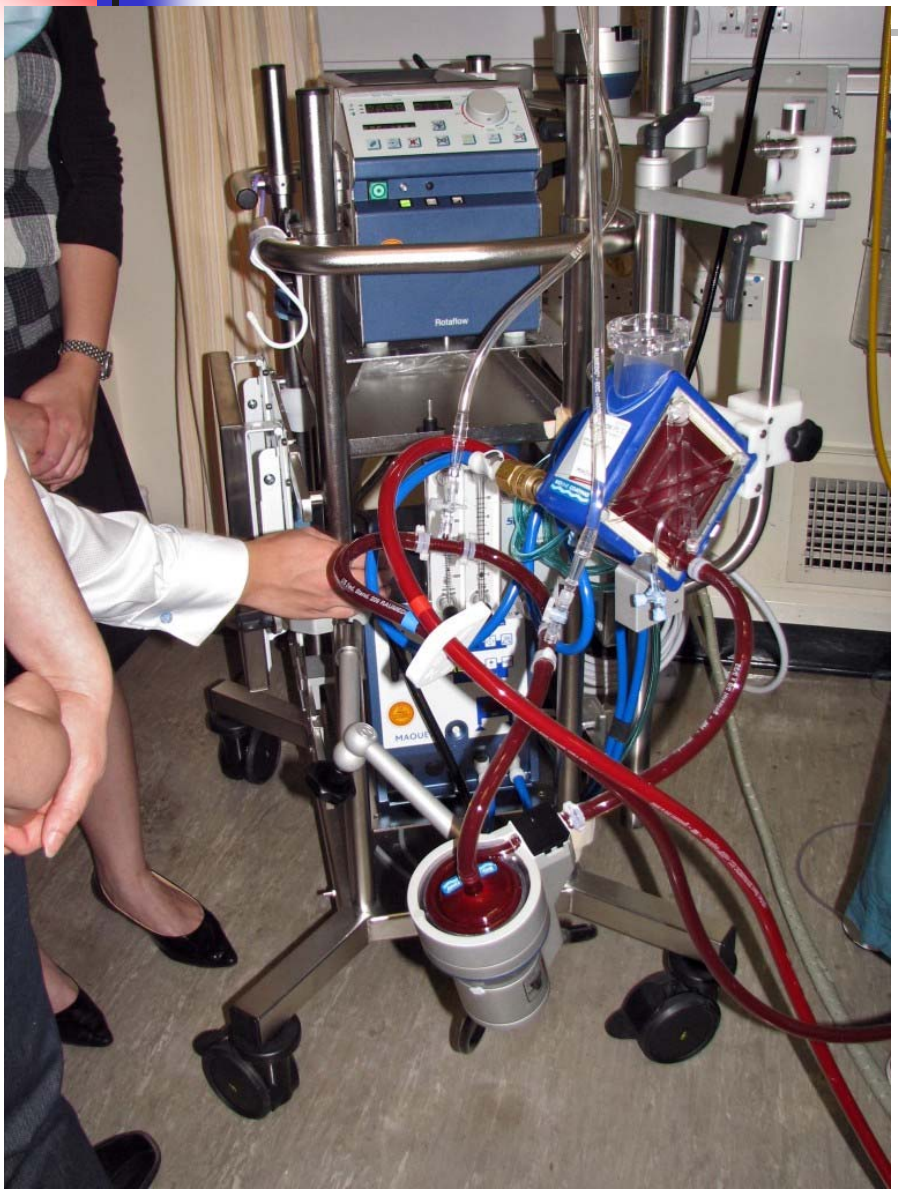
Mechanisms of toxicity

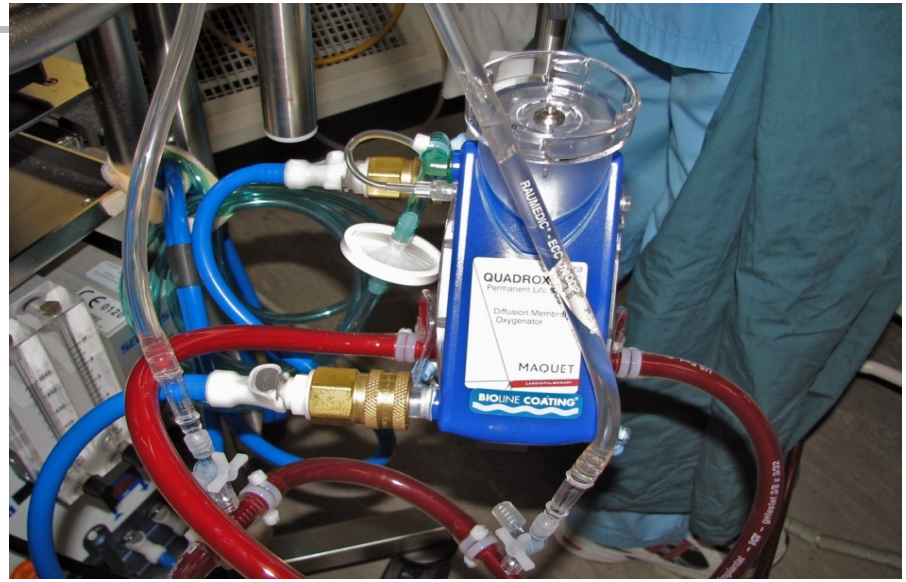


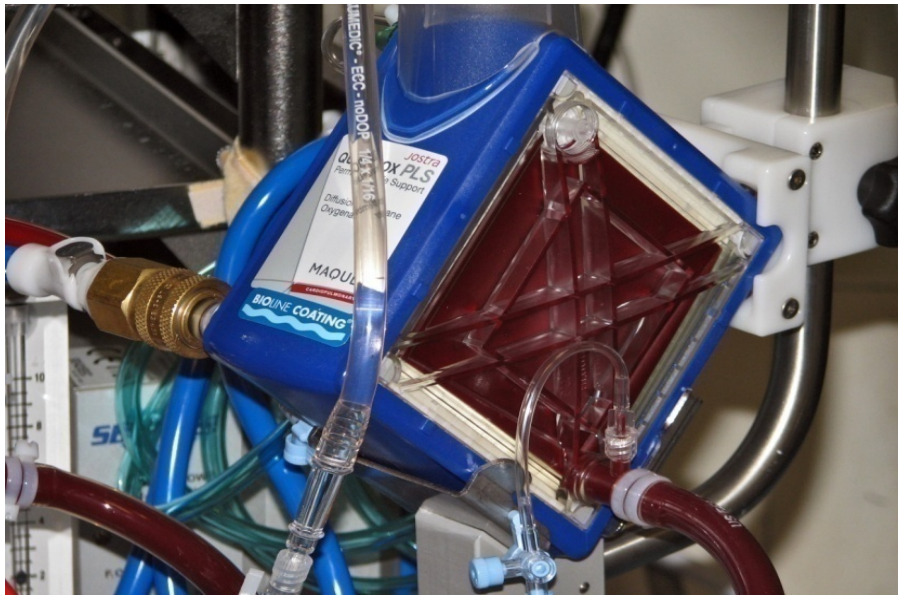
VV -ECMO setup -1



ECMO setup: membrane oxygenator

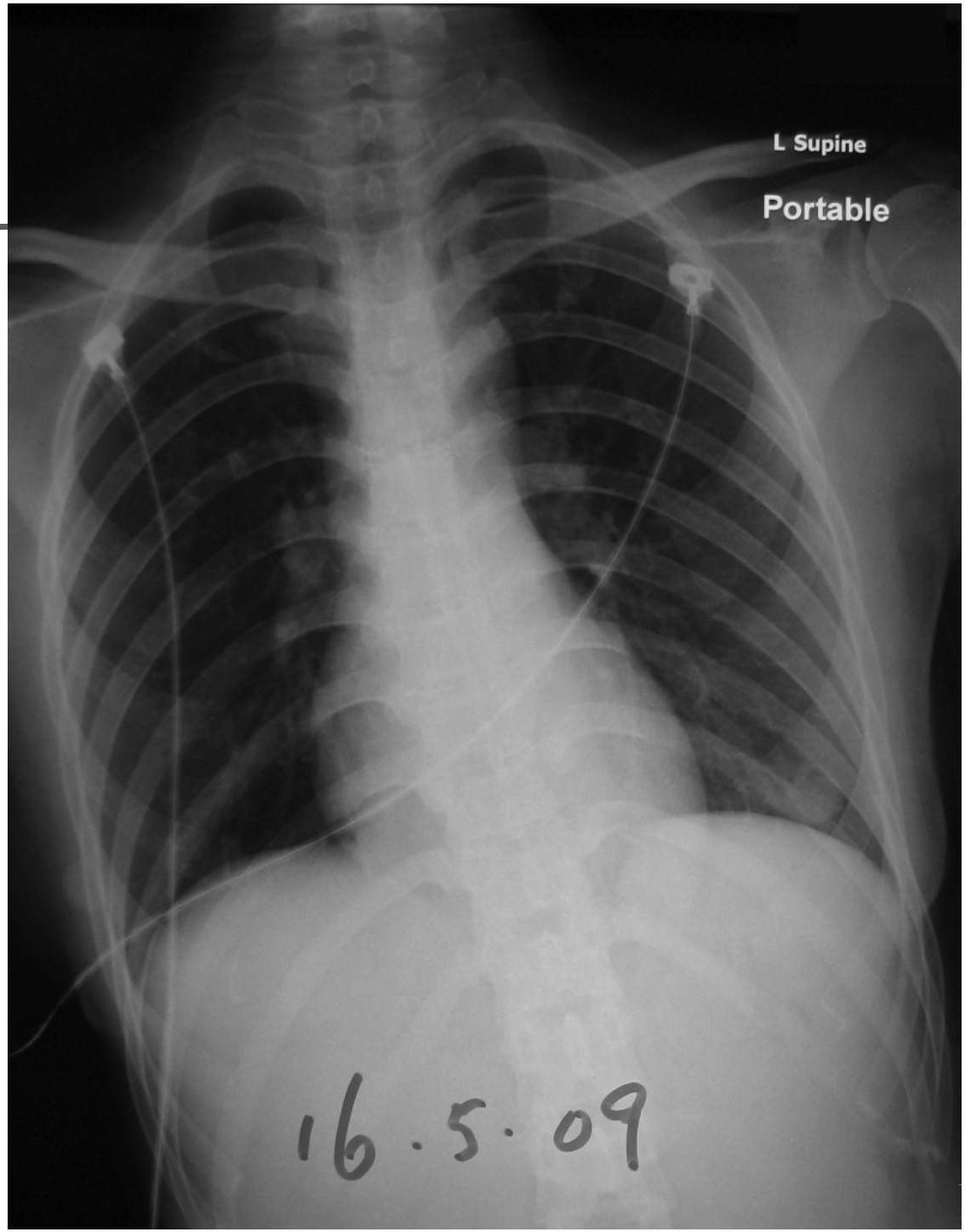


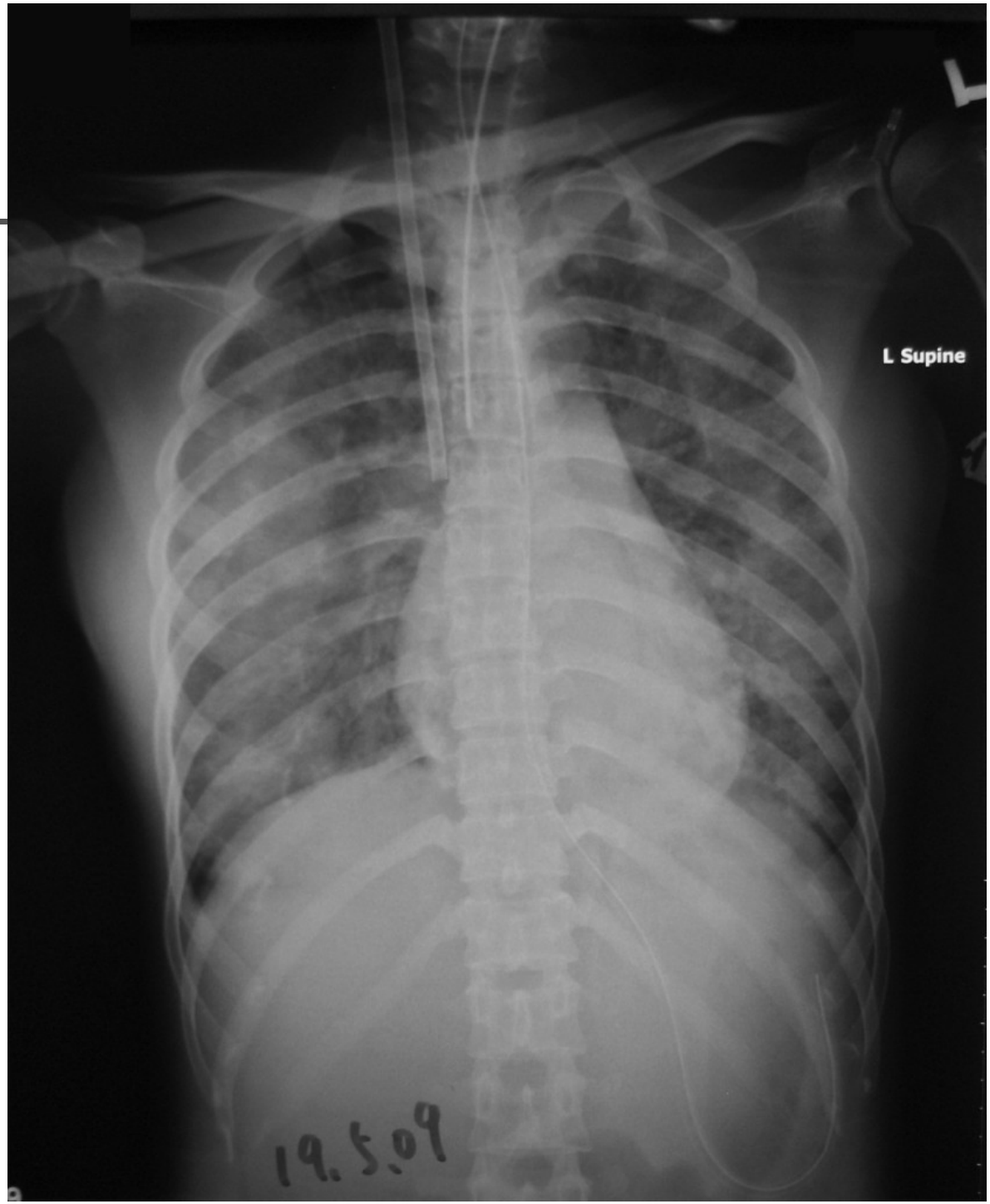




Paraquat poisoning (5)

- Lung continued to deteriorate
- Oxygenation totally dependent on VV-ECMO
- Developed secondary sepsis, DNR and died on day 15


L Supine
Portable
16.5.09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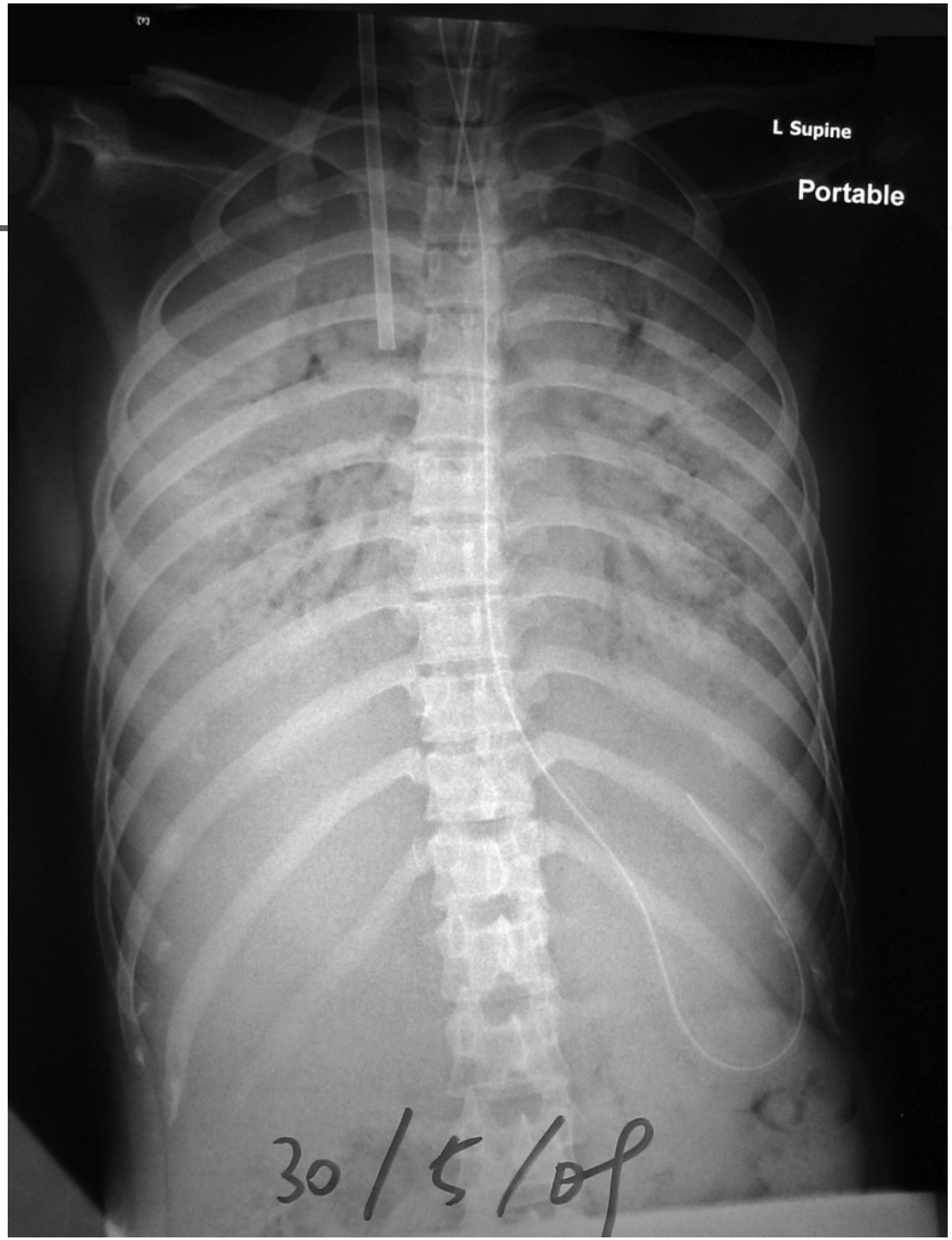
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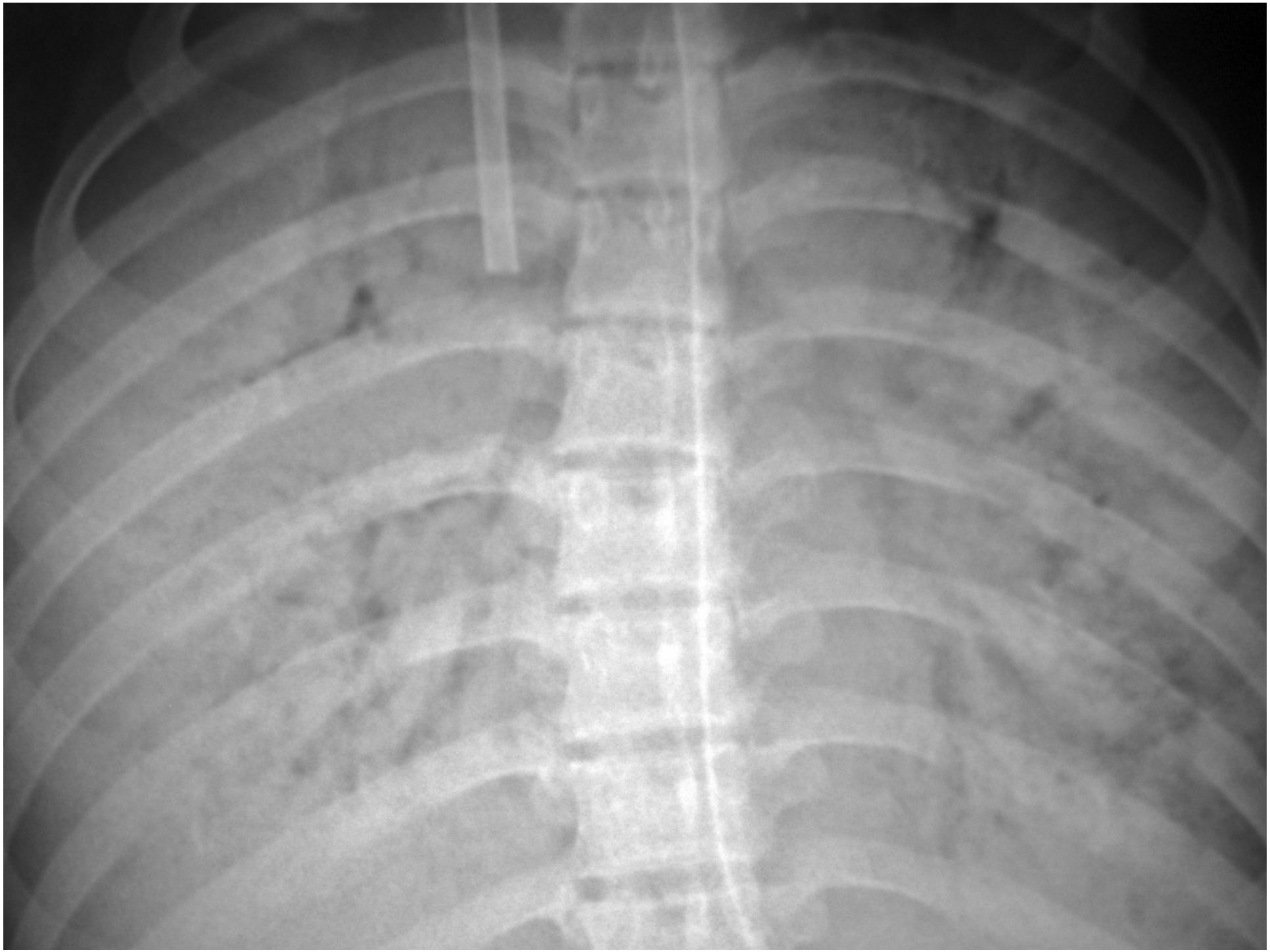
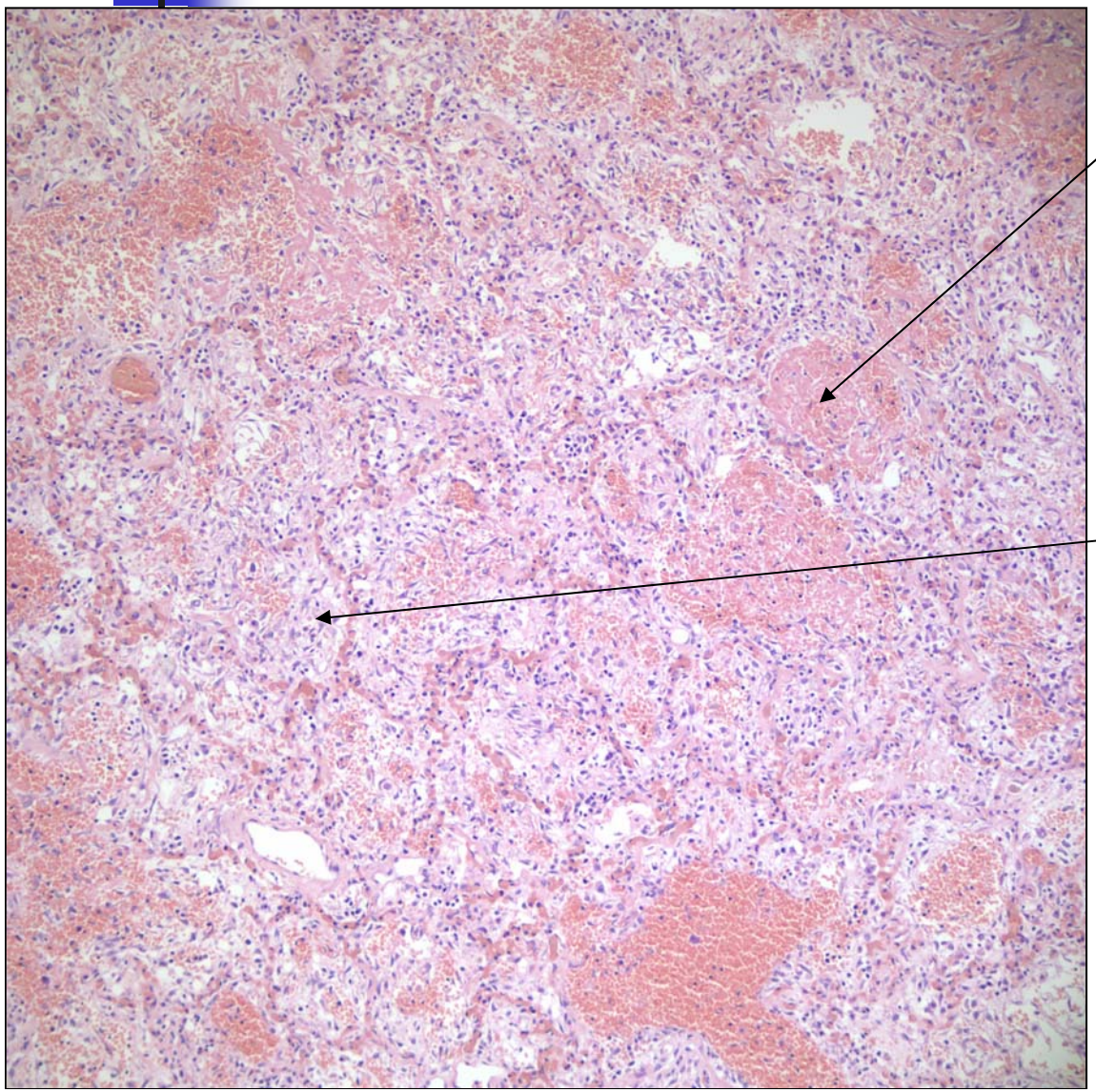
30/5/08



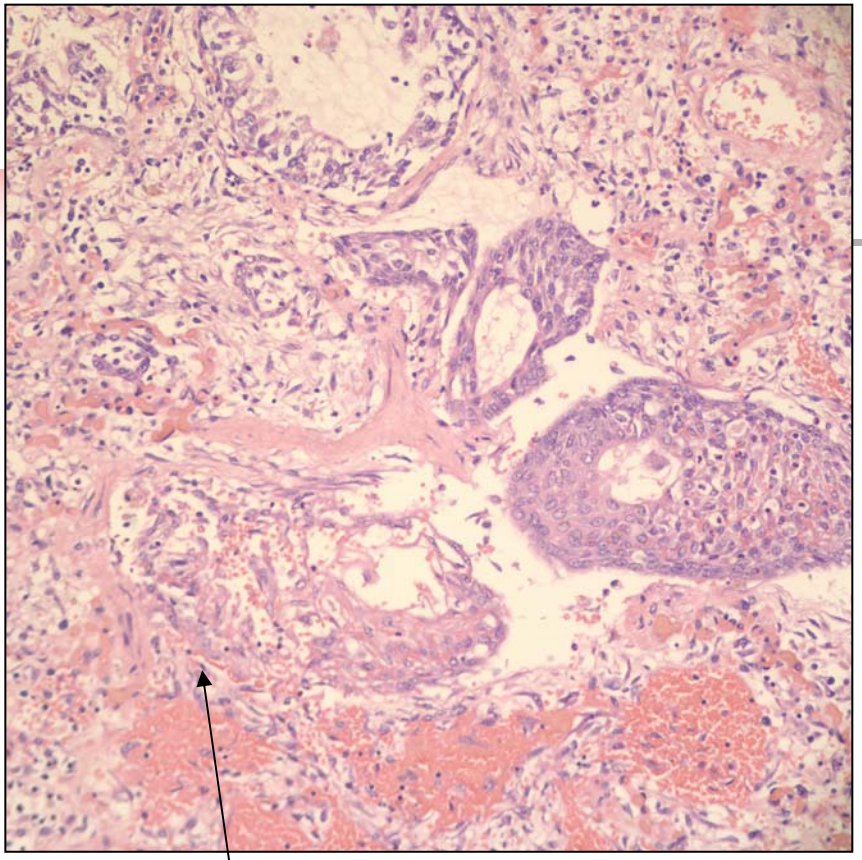
Pathological changes of Lungs

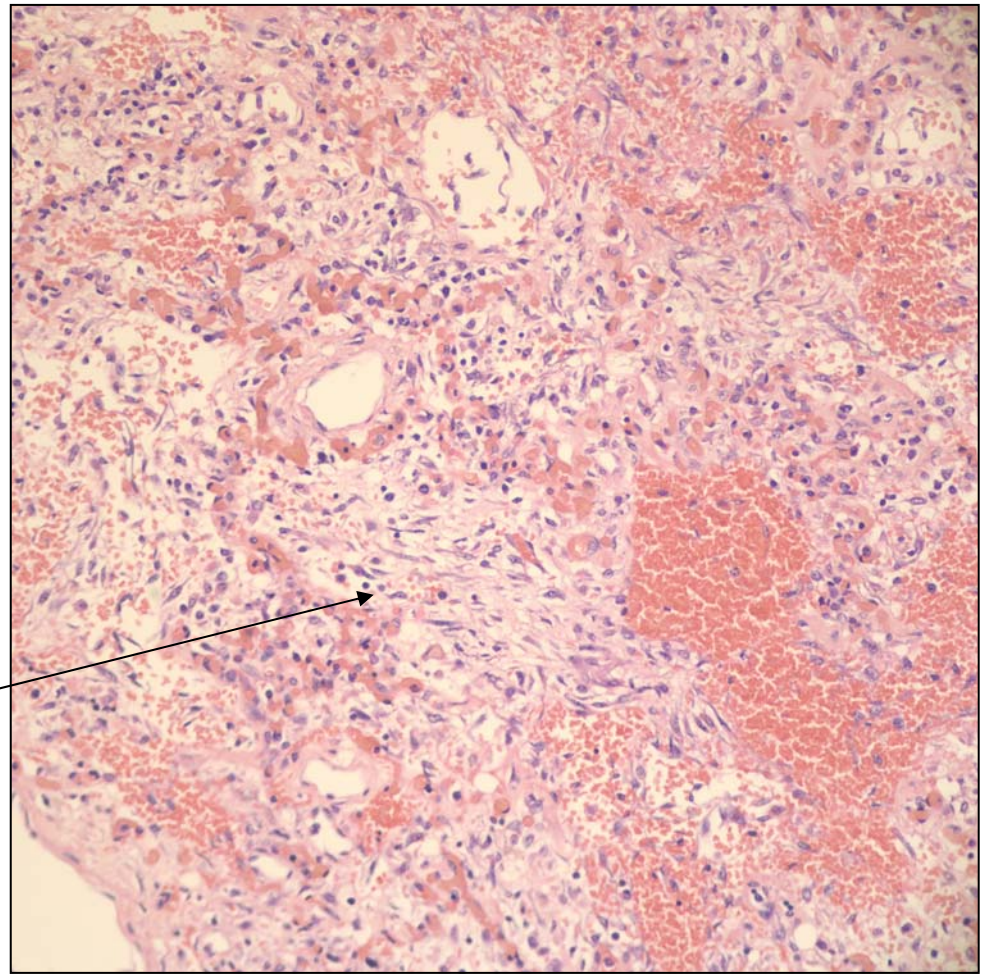
- Acute to subacute lung injury with diffuse alveolar damages, evidenced by
  - Alveolar haemorrhage
  - e and hyaline membrane formation, signifying acute injury
  - Early organization with fibroblastic proliferations in both alveolar space and interstitium
  - Well establish fibrosis was not present
- Overall changes could be explained by lung injury induced by chemicals (Paraquat)

Acute to Subacute Lung Injury



- Diffuse alveolar damage with alveolar hemorrhage and focal fibrin deposition.
- Early organization with loose fibroblasts proliferation in the alveolar spaces and interstitium





- Loose fibroblastic proliferation in the interstitium, could progress to fibrosis

Paraquat poisoning (6)

- Learning points
  - > 40mg/kg universally fatal
  - Even with aggressive methods
    - Elimination
      - ? Removal of paraquat by HVHF
    - Organ support
  - Prevention
    - Ban the sales of concentrated paraquat solution
    - 24% paraquat, 40mg/kg == 8 ml for 50kg person

Star fruit intoxication

Star fruit intoxication

- 76 year-old woman with chronic renal impairment, secondary to diabetic nephropathy ([creatinine] ~290 umol/l)
- Presented with sudden onset of seizures and drowsiness at mid-day.
- Patient was perfectly normal hours before
- Developed another seizure attack at the A&ED, generalised tonic-clonic for 10 mins, self aborted
- GCS(E4V1M3), BP207/140, pulse 125
- Afebrile, no neck stiffness, spontaneous movement of all 4 limbs, normal tendon reflexes
- CT scan brain showed old right internal capsular infarct and otherwise normal

Star fruit intoxication (2)

- GCS deteriorated to E1V1M2 8 hours after admission
- WBC 11.4, Hb10.5, platelet 372
- [urea] 14.1, [creatinine] 319
- Electrolytes normal
- LP done, CSF normal biochemistry and cell count
- MRI brain
  - No radiological evidence of brain, brainstem lesion, or meningoencephalitis

Star fruit intoxication (3)

- History from son
  - Taken two star fruits on the day of admission
- Diagnosis: star-fruit poisoning with severe neurotoxicity
- Supportive care
  - Intubation and IPPV
  - Inotropic support

Star fruit intoxication (4)

- 8 hour charcoal haemoperfusion followed by 30 hours CVVH (33ml/min)
- Her GCS gradually improved back to normal 15/15
- No recurrence of her neurological symptoms upon cessation of CVVH
- Extubated on next day
- Well afterward

Star fruit intoxication (5)

- No consensus on the exact neurotoxin
  - ? Oxalate
  - Neurotoxin (AcTx)
    - <500D
    - Excreted largely by kidney
    - Lipophilic, cross BBB, accumulate in the brain
    - Moderate volume of distribution
    - Can be redistributed in different body compartments

Studies	Region	No. of patients Symptoms	Tx modality	Outcome
Chang et-al Am J Kidney Dis 2000;35:189-193	Taiwan	10, all with impaired consciousness	Intensified HD	8 Deaths, 2 survivors
Hosp Authority Unpublished, 2001	Hong Kong	1, impaired consciousness	CAPD	Death
Neto et-al Nephrol Dial Transplant 2003;18:120-125	Brazil	7, all with seizures	Symptomatic(2) CAPD (1) CAPD+2-hour HD (1) IPD (1) IPD+CAVHD (1) HD+15h-CVVHD+daily HD (1)	Death Death Death Death Death in 10 days Survived, needed 8 days
Tse et-al Intern Med J 2003;33:314-316	Hong Kong	1, impaired consciousness	Daily HD	Survived
Chen et-al Clin Toxicol (Phila) 2005;43:197-199	Taiwan	1, hearing impairment, impaired consciousness, coma	2 sessions HD + charcoal HP	Survived, regained consciousness within 1 day after HP
Wu et-al Am J Kidney Dis 2007;49:e1-5	Taiwan	2, hiccups, impaired consciousness, status epilepticus (1)	2 sessions HD + charcoal HP	Survived, regained consciousness within 16-20 hours after HP
Chan et-al Hong Kong Med J 2009;15:149-152	Hong Kong	1, seizures, impaired consciousness, coma	Charcoal HP + 30h CVVH	Survived, regained consciousness within 2-30 hours after HP

Star fruit intoxication (7)

- Learning points
  - Toxicology should be one of ddx for unexplained coma
  - History is important
  - Anything can be toxic, dependent on circumstances
  - Extracorporeal elimination is life saving in some condition
    - Should be considered in life threatening condition with unknown diagnosis

Summary

- Haemodialysis (low flux)
- Haemoperfusion (charcoal / resin)
- Haemodialysis (high flux)
- Haemofiltration (CVVH / CVVHDF)
- High volume haemofiltration
- Superhigh flux haemofiltration
- MARS
- Prometheus
- Single pass albumin dialysis
- Coupled plasma filtration adsorption
- Plasmapheresis
- Extracorporeal life support
  - VV-ECMO
  - VA-ECMO

Thank you for your attention