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# Great Ormond Street Hospital for Children



NHS Trust

## Renal Replacement Therapy & Plasmapheresis

Quen Mok, July 2006

Updated: St Mary's Hospital March 2007 –Claudine de Munter

**Associated clinical guidelines/protocols:**

- Guidelines for PD
- Guidelines for CVVH
- Plasmafiltration trial protocol
- Trial protocol for Early CVVH in ARDS post BMT

**Fundamental Knowledge:**

*List of topics relevant to PIC that will have been covered in membership examinations.*

**They will not be repeated here.**

- Osmolarity, osmolality, diffusion of molecules across membranes
- Anatomy of abdominal wall (including the inguinal region) Landmarks for suprapubic and peritoneal lavage catheters

## Information for Year 1 ITU Training (basic):

### Year 1 ITU curriculum

**Peritoneal dialysis:**

- Indications, contra indications and complications (including respiratory complications)
- Understand the effect of dwell time and type of dialysate on the clearance of molecules.
- Insertion of PD catheter.

**Continuous veno-venous haemofiltration:**

- Indications, contra indications and complications (hypotension, drug level interference, bleeding)
- Vascular access requirements
- Basic principles of fluid and electrolyte control

## Curriculum Notes for Year 1:

**General Indications for renal replacement therapy (RRT)**

- Renal failure
- Fluid overload
- Severe electrolyte imbalance
- Manipulation of metabolic environment
- Tumour lysis syndrome
- Drug intoxication
- Rhabdomyolysis
- ?Inflammatory mediator removal in sepsis

The specific therapy used depends on available expertise in the unit, the child's size and clinical condition. Also studies show that early dialysis leads to a better outcome with a lower mortality and a shorter length of stay than starting dialysis late [1]

### Transport mechanisms and solute clearance

Dialysis – small molecules easily removed by diffusion

Haemofiltration – as fluid is removed, the solute is cleared by convection (solvent drag). Solute clearance is therefore dependent on sieving coefficient of solute and ultrafiltrate removal, which is dependent on the hydrostatic pressure gradient either side of the membrane. This will depend on blood flow, filter surface area and ultrafiltration rate (% filtration fraction). Hence middle sized and small molecules can be removed.

Osmosis – movement of water from a higher to lower water concentration

### Peritoneal dialysis

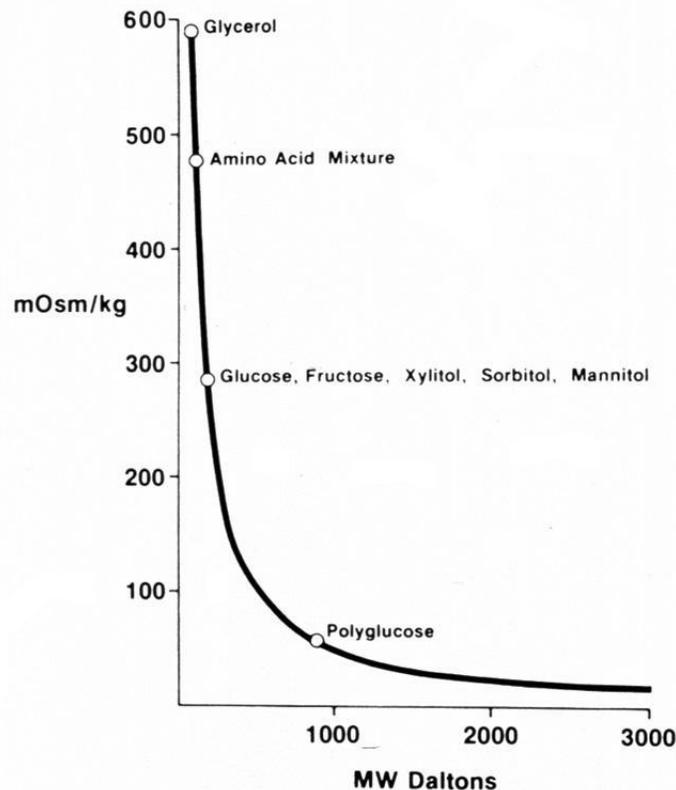
Removal of solutes is by diffusion due to an osmotic pressure gradient across the semi-permeable peritoneal membrane. Removal of fluid is achieved with the use of dialysate solutions containing hypertonic glucose or other osmotically active particles (see figure 2-10 below).

Generally use 10-20 ml/kg volumes with ½ - 1 hour cycles.

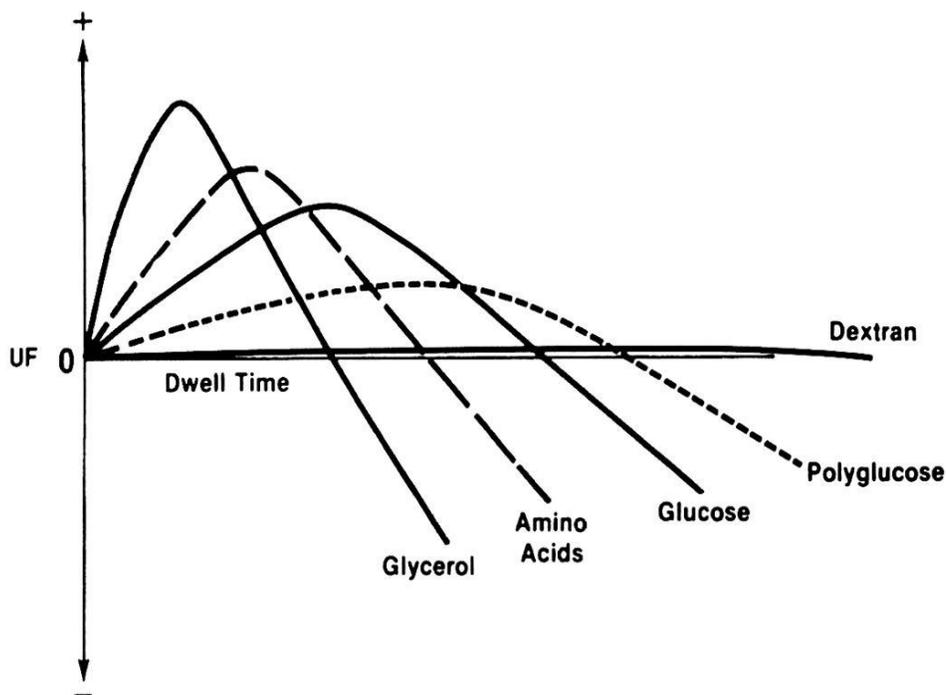
Increased clearance by

- Increased dwell time, to a degree
- Increased dialysis volume
- Increased osmolality of dialysis solution

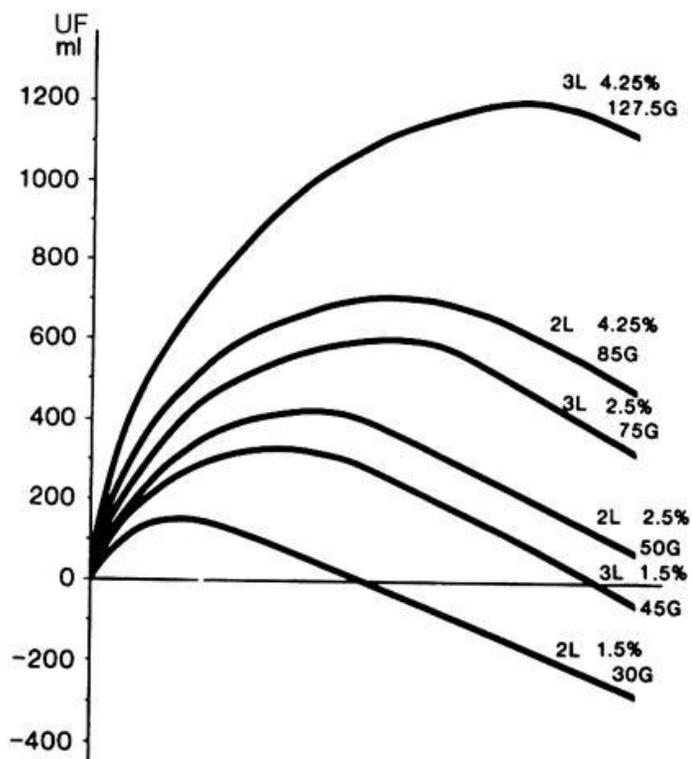
(see figures below)



**Fig. 2-10.** Calculated solution osmolality (mOsm/kg) of the same concentration (5 percent) of solutes of different molecular weight. (From Twardowski et al,<sup>3</sup> with permission.)



**Fig. 2-11.** Representative ultrafiltration patterns with the same concentration (5 percent) of osmotic agents of different molecular weight. (From Twardowski et al,<sup>3</sup> with permission.)



Indications – child <2kg as difficulties with adequate vascular access for haemofiltration  
 Contraindications – diaphragmatic hernia, omphalocele, gastroschisis, possibility of intra-abdominal catastrophe, recent abdominal surgery, multiple adhesions, peritonitis, presence of VP shunt

**Complications**

- Splinting of diaphragm and increased respiratory compromise
- Leak of fluid from insertion site
- Obstruction of catheter by omentum
- Peritonitis
- Peritoneal fibrosis

**CVVH**

This utilizes a blood pump to circulate blood through the filter for continuous removal of toxins and fluid by convection. Thus CVVH is the ideal RRT for ICU patients and is associated with a lower mortality than HD [2], although this is not confirmed on other studies.

Indications – continuous RRT in the ICU setting, especially if patient will not be able to tolerate big fluid shifts.

Contraindications – serious bleeding risk (consider regional anticoagulation), recent intracranial infarct or bleed.

Access

Vascath or Gamcath inserted in ICU using Seldinger technique. Size of line depends on size of child. Length of line depends on size and site of access. Once the line is inserted, it must be flushed with pure heparin (volume is equal to the priming volume of the lines).

Avoid using the subclavian for insertion of the vascath as this may cause subclavian stenosis and this route then cannot be used when the patient needs long term RRT. Consider insertion of permacath by surgeons or interventional radiologists if there is a possibility of long term RRT.

	Size	Length	Priming Volume
Child <10 kg	6.5Fr	10cms	A 0.75, V 0.78 mls
	6.5Fr	15cms	A 0.81, V 0.84 mls
Child <20 kg	8Fr	10cms	A 0.80, V 0.82 mls
	8Fr	15cms	A 0.88, V 0.90 mls
Child >20 kg	11Fr	15cms	A 1.04, V 1.10 mls
	11Fr	25cms	A 1.36, V 1.42 mls

The circuit needs to be primed with blood if extracorporeal volume >10% of intravascular blood volume. As extracorporeal volume of paediatric lines and filter is about 100ml, children <10 kg will all generally need a blood prime.

When the patient is considered haemodynamically unstable, the circuit can be primed with 4.5% HAS. Blood can be transfused separately.

### Replacement solution

Fluid and solutes removed must be replaced by replacement fluid to maintain fluid homeostasis. This replacement can be done pre- or post-filter. We tend to replace our solutions pre-filter as it results in increased effective filter life.

We prefer to use potassium free replacement solutions so that we can add the desired amount of potassium as required, although there are commercially available solutions containing different concentrations of potassium.

### Lactate based

- Monosol (30mmol/l lactate)
- Haemofiltrisol (45 mmol/l lactate)

Lactate free – needs bicarbonate as buffer, which is added at time of use. In the newer solutions a standard amount may already be provided in a separate compartment

- Accusol
- Edwards Bicaflac
- Hospal Hemasol
- Normocarb
- Baxter LF10

Lactate free solutions are ideal for patients with liver dysfunction and for neonates where the immature liver is unable to convert lactate to bicarbonate. We would also use lactate free solutions for patients with significant acidosis or inborn errors of metabolism. Different solutions have different concentrations of sodium depending on how much sodium bicarbonate is added.

### Anticoagulation

The requirement for anticoagulation depends on the condition of the haemostatic system, which in critically ill acute renal failure patients may show a reduced procoagulant potential, an activated coagulation or a combination of both [3]. Anticoagulation of the circuit can be with heparin (standard or low molecular weight), prostacyclin or citrate. No anticoagulant may be required if the patient is already coagulopathic. However if the filter clots frequently, consider regional anticoagulation of the filter using LMW heparin or citrate.

- Standard unfractionated heparin – catalyses inactivation of thrombin, fXa and fIXa by antithrombin. Generally used and monitored with ACT at the bedside, keeping ACT between 180-200. Regular lab APTR may be necessary.
- LMW heparin (dalteparin) - adequate anticoagulation monitored using anti-Factor Xa levels. This is done daily and will need to be arranged with the coagulation lab.
- Prostacyclin at 5ng/kg/min to reduce platelet aggregation. Heparin sparing effect but very expensive and effects on BP can be difficult to control in haemodynamically unstable patients.
- Citrate – causes chelation of calcium, thus depleting necessary co-factor for several steps in coagulation cascade. Anticoagulation restricted to extracorporeal circuit as citrate is metabolized to bicarbonate in the liver. Many USA centers are using citrate, but most of the replacement solutions in the UK contain calcium and this will bind with citrate and precipitate. If using citrate then this needs to be infused separately from the replacement solution which will need to be infused post filter. Monitor ionized calcium levels in the patient and in the circuit. Problem of metabolic alkalosis and citrate toxicity with ionized hypocalcemia, and high anion-gap metabolic acidosis. Almost as expensive as prostacyclin.

### Complications of CVVH

- Bleeding
- Excessive fluid removal from loss of autoregulation

- Clearance of drugs especially if low protein binding
- Hypotension from excessive fluid loss or clearance of inotropes
- Malnutrition from clearance of many amino acids – this may be reduced if nutrition is optimized during RRT.

**Other sources of information:**

**Websites:**

Peds CRRT website [www.pcrct.com](http://www.pcrct.com)

Acute Dialysis Quality Initiative group website [www.ADQI.net](http://www.ADQI.net)

**References:**

1. Quan A and Quigley R. Renal replacement therapy and acute renal failure. *Curr Opin Pediatr* 2005; 17:205-9
2. Kellum JA, Angus DC, Johnson JP et al. Continuous versus intermittent renal replacement therapy: a meta-analysis. *Intensive Care Med* 2002; 28: 29-37
3. Schetz M. Anticoagulation for continuous renal replacement therapy *Curr Opin Anaesthesiol* 2001; 14:143-9

**Information for Year 2 ITU Training (advanced):**

**Year 2 ITU curriculum**

**Continuous veno-venous haemofiltration:**

Complete understanding of

- Indications, contra indications and complications
- Principles of fluid and electrolyte control: flow rate, % filtration fraction and fluid balance.

**Plasmapheresis:**

- Indications, contraindications and complications
- Need to replace immunoglobulin

**Haemodialysis:**

- Indications, contra indications and complications
- Haemodynamic effects.

**Curriculum Notes for Year 2:**

**CVVH**

Increased solute clearance by

- Bigger filters with larger membrane surface area
- Increased blood flow rate  $Q_b$  through filter
- Increased ultrafiltration rate  $Q_f$
- Addition of countercurrent dialysis (CVVHD), to a certain extent

The comparison of CVVH with CVVHD or CVVHDF (CVVH with countercurrent dialysate flow or continuous veno-venous haemodiafiltration) shows that all are equally effective [4,5]. We tend to use CVVH in PICU as we have managed effective solute clearance with large filters and by adjusting blood flows and filtration fractions. Higher ultrafiltration rates (35 or 45 ml/kg/h compared to 20 ml/kg/h) improved survival significantly [6]. Early institution of RRT

before >10% excess volume overload and before the BUN is higher than 80 mg/dl is associated with better outcome and survival [5,7,8]

To increase potential clearance of inflammatory mediators from blood by CVVH various modifications to the technique have been attempted. This includes high volume HF [9], haemodiafiltration, high flux filters [10], frequent membrane changes to allow for adsorptive removal [11], high permeability membranes [12], and plasmfiltration (see below). At present there is a lack of randomised trials and the available studies show an absence of benefit.

### **Haemodialysis (HD)**

This is an extracorporeal therapy where toxins and fluid are removed by diffusion across an artificial semi-permeable membrane of the dialyzer into the dialysate fluid. HD is performed by the dialysis team from the renal unit, and a treatment cycle is usually done over 3-4 h, and on alternate days. There is evidence that daily HD results in improved control of uraemia and BP, a more rapid resolution of ARF and a lower mortality compared to alternate day HD [3]

Indications – rapid removal of small molecules e.g. severe hyperkalaemia >7mmol/l or massive tumour lysis. However in our unit CVVH may be more readily available out of hours.  
Contraindications – cardiovascular instability due to rapid fluid removal

#### Complications

- Haemodynamic instability
- Disequilibrium syndrome due to rapid solute clearance and large fluid shifts especially across cell membranes leading to raised ICP and seizures
- Anaphylactoid reactions (chest pain, dyspnoea, hypotension) from bioincompatible dialysis membrane (cuprophane cellulose)

### **Plasmapheresis**

Plasma exchange – plasma is removed and replaced by donor plasma

Plasmapheresis – plasma is removed and replaced with fluid other than plasma, usually albumin

Can be done by centrifugation or by filtration (plasmfiltration).

Can be done by renal team or ICU team, and in most cases the “course” of therapy consists of 4-5 cycles.

#### Indications

Large molecules including proteins, inflammatory mediators and bacteria are removed non-selectively, thus this is theoretically a useful technique in vasculitides and septic shock.

Immune mediated – acceptable “standard” therapy

- Severe acute polyneuropathy (Guillain-Barre)
- Myasthenia gravis
- Goodpasture’s and other vasculitides
- TTP
- HUS
- Acute poisoning or overdose with certain drugs

Many other conditions where conventional therapy is tried first as inadequate evidence available of its efficacy in randomized trials

- SLE
- Dermatomyositis
- Juvenile idiopathic arthritis
- Autoimmune haemolytic anaemia
- Sepsis

A randomized study has shown no benefit on mortality in adults with septic shock [13], while two others showed a tendency to improved outcome [14,15]. There was a trend towards improvement in children in the Australian study [13] and there is therefore an ongoing trial of

plasmafiltration in children with septic shock. It is unclear if the beneficial effect of plasma therapies is due to the removal of inflammatory mediators or to the replacement with fresh frozen plasma of immunoglobulins and coagulation factors and inhibitors

#### Complications

- Allergic reaction to bioincompatible membrane
- Concomitant removal of albumin, immunoglobulins and clotting factors
- Bleeding
- Fluid or electrolyte imbalance

#### Other sources of information:

##### Websites.

Peds CRRT website [www.pcrct.com](http://www.pcrct.com)

Acute Dialysis Quality Initiative group website [www.ADQI.net](http://www.ADQI.net)

#### References.

1. Quan A and Quigley R. Renal replacement therapy and acute renal failure. *Curr Opin Pediatr* 2005; 17:205-9
2. Kellum JA, Angus DC, Johnson JP et al. Continuous versus intermittent renal replacement therapy: a meta-analysis. *Intensive Care Med* 2002; 28: 29-37
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12. Morgera S, Rocktaschel J Haase M et al. Intermittent high permeability hemofiltration in septic patients with acute renal failure. *Intensive Care Med* 2003; 29: 1989-95

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15. Busund R, Koukline V, Utrobin U, Nedashkovsky E. Plasmapheresis in severe sepsis and septic shock: a prospective, randomised, controlled trial. *Intensive Care Med* 2002; 28: 1434-9