renal replacement therapy [created by Paul Young 31/12/07]

general

- when acute renal failure is severe, resolution can take several days or weeks and during this time the kidneys cannot maintain homeostasis of fluid, potassium and waste products
- extracorporeal techniques of blood purification effectively prevent life threatening complications of acute renal failure

principles

(i) water removal
- the removal of unwanted solvent (water) is therapeutically as important as the removal of unwanted solutes (acids, uraemic toxins, potassium)
- during RRT water is removed through a process called ultrafiltration which is essentially the same as that performed by the glomerulus requiring a driving pressure to move fluid across a semi-permeable membrane. This pressure generated by generating a transmembrane pressure that is greater than the oncotic pressure (as in haemofiltration or intermittent haemodialysis) or by increasing the osmolarity of the dialysate (as in peritoneal dialysis)

(ii) solute removal
- the removal of unwanted solute can be achieved by
1. creating an electrochemical gradient across the membrane by using a flow past system with a toxin-free dialysate (diffusion) as in intermittent HD and PD
2. creating a 'solvent drag' driven by transmembrane pressure where solute moves together with solvent (convection) across a porous membrane, is discarded and then replaced with toxin-free replacement fluid (as in haemofiltration)
- the rate of diffusion of a given solute depends on its molecular weight, the porosity of the membrane, the blood flow rate, the dialysate flow rate, its binding to proteins and its concentration gradient across the membrane
- standard low flux cellulose based membranes do not allow middle molecules of greater than 500 daltons to be removed while synthetic high flux membranes have a cut off of 20-30 kDa

indications

- Oliguria (urine output: <200 ml/12 h)
- Anuria (urine output: 0–50 ml/12 h)
- [Urea] >35 mmol/l
- [Creatinine] >400 µmol/l
- [K+] >6.5 mmol/L or rapidly rising[b]
- Pulmonary oedema unresponsive to diuretics
- Uncompensated metabolic acidosis (pH <7.1)
- [Na+] <110 and >160 mmol/l
- Temperature >40°C
- Uraemic complications (encephalopathy/myopathy/neuropathy/pericarditis)
- Overdose with a dialyzable toxin (e.g. lithium)

[a] If one criterion is present, RRT should be considered. If two criteria are simultaneously present, RRT is strongly recommended.
[b] Be aware of differences between plasma vs. serum measurement in your laboratory.

anticoagulation during CRRT

- no anticoagulation may be appropriate if there has been recent surgery or endogenous coagulopathy & is this circumstance mean filter lives >24hrs can be achieved
- prostacyclin and heparinoids are used in HITTS

causes of filter clotting is often mechanical due to:
(i) inadequate access
(ii) kinking of the catheter
(iii) patient positioning
(iv) small catheters

- No anticoagulation
- Low-dose pre-filter heparin (<500 IU/h)
- Medium-dose pre-filter heparin (500–1000 IU/h)
- Full heparinization
- Regional anticoagulation (pre-filter heparin and post-filter protamine usually at a 100 IU : 1 mg ratio)
- Regional citrate anticoagulation (pre-filter citrate and post-filter calcium – special calcium-free dialysate needed)
- Low-molecular-weight heparin
- Prostacyclin
- Heparinoids
- Serine proteinase inhibitors (nafamostat mesylate)

	Advantages	Disadvantages
Systemic heparin (low to medium dose)	(i) easy to administer (ii) cheap (iii) may not have systemic anticoagulation (iv) effectively antagonized by protamine (v) physician familiarity	(i) anticoagulation is not always successful with this dose and higher doses may be needed increasing risk of bleeding (ii) need to monitor APTT (iii) risk of HITTs
Regional heparin (pre filter with post filter protamine)		(i) more complex to administer (ii) requires monitoring (iii) exposes patient to the risk of allergy to protamine
LMW heparin	(i) easy to use (ii) may decrease risk of HITTS	(i) may need to monitor Xa levels (ii) protamine cannot be used for reversal
Regional citrate (pre filter with post filter calcium)	(i) very effective (ii) can be used in HITTS	(i) clinician unfamiliarity (ii) need for special calcium free dialysate (iii) metabolic alkalosis (iv) hypocalcaemia (v) need for systemic DVT prophylaxis still
Prostacyclin	Useful if the patient has HITTS	(i) hypotension (ii) platelet dysfunction and risk of bleeding
Serine protease inhibitors (nafomostat)		(i) only available in Japan (ii) anaphylaxis (iii) agranulocytosis

mode of renal replacement therapy

general:
- techniques of RRT may be judged on the basis of:
(i) haemodynamic side effects
(ii) ability to control fluid status
(iii) biocompatability
(iv) risk of infection
(v) uraemic control
(vi) avoidance of cerebral oedema
(vii) ability to allow full nutritional support
(viii) ability to control acidosis
(ix) absence of specific side effects
(x) cost
- haemodialysis or CRRT techniques should be considered for serious toxic ingestions of:
(i) alcohol
(ii) chloral hydrate
(iii) barbiturates
(iv) ethylene glycol (significant ingestion, >2.5mg/dL, ARF, CRF)
(v) methanol
(vi) lithium (>4.0mmol/L, ARF, CRF, failure to decrease 20% at 6 hours)
(vii) salicylates (>120mg% initially, >100mg% at 6 hours)

trials:
- a 2006 RCT published by a French group in Lancet compared IH 48hrly with CVVHD in patients with MOD. This study showed no significant difference between these modalities in terms of mortality or complications includinghypotension; hypothermia was more common in the CVVHD group

continuous renal replacement therapy:
- no matter what technique is used, the following outcomes are predictable:
(i) continuous control of fluid status
(ii) haemodynamic stability
(iii) control of acid base status
(iv) ability to provide protein rich nutrition which achieving uraemic control
(v) control of electrolyte balance including phosphate and calcium balance
(vi) prevention of swings in intra-cerebral water
(vii) minimal risk of infection
(viii) high level of biocompatibility
- several biosynthetic membranes on the market have excellent biocompatability (AN69, polyamide, polysulfone, cellulose triacetate) but no controlled studies have been undertaken to show that one of them confers any benefit over the others
- AN69 is the most commonly used CRRT membrane in Australia
- The issue of membrane size is controversial as no studies have compared different membrane surface sizes. For AN69 membrane there is no increase in price up to asize of 1.2m2 thus there is no reason to use a smaller membrane in adults; high volume haemofiltration requires a membrane surface of 1.6-2.0m2

intermittent haemodialysis:
- the major differences are that standard IHD uses high dialysate flows (300-400ml/min), generates dialysate by using purified water and concentrate and is applied for short periods of time (3-4 hours) usually every 2nd day
- important considerations in the critically ill include:
(i) hypotension due to poor tolerance of removal of volume in a short period of time
(ii) repeated hypotensive episodes may delay renal recovery
(iii) episodic solute removal translates into inferior uraemic control and acid-base control which may impose limitations on nutritional support
(iv) rapid solute shifts increase brain water content and raise ICP
(v) bioincompatable membranes may be proinflammatory

peritoneal dialysis:
- used uncommonly in adults with ARF but may be an adequate technique in developing countries or in children when alternatives are too expensive, too invasive or not available
- several major shortcomings make PD relatively unsuited to the treatment of ARF:
(i) limited and sometimes inadequate solute clearance
(ii) high risk of peritonitis
(iii) unpredictable hyperglycaemia
(iv) fluid leaks
(v) protein loss
(vi) interference with diaphragm function

haemoperfusion:
- during haemoperfusion, blood is circulated through a circuit similar to the one used for CVVH; however, a charcoal cartridge is perfused with blood instead of a dialysis membrane
- charcoal microcapsules effectively remove molecules of 300-500 daltons in size including some lipid soluble and protein bound substances
- problems include:
(i) the large priming volume of the cartridge (260ml) can cause hypotension of the patient is hypovolaemic
(ii) glucose absorption is significant and hypoglycaemia is common
(iii) thrombocytopenia can be common
(iv) the need for heparinisation to prevent filter clotting
- no trials demonstrate a benefit for haemoperfusion; however it is useful in serious overdoses of:
(i) theophylline (acute >440mcmol/L, chronic >330mcmol/L; lower threshold if age >60, IHD, seizure)
(ii) barbiturates
(iii) phenytoin
(iv) carbamazepine

plasmapharesis or plasma exchange:
- plasma is removed and exchanged with FFP and mixture of colloid and crystalloid solutions
- a plasmafilter (a filter that allows passage of molecules up to 500kDa is used instead of a haemofilter in the CVVH circuit & the plasma is discarded