Worcestershire Acute Hospitals NHS Trust

Guideline for Renal Replacement Therapy within Worcestershire Critical Care Units

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Key Amendments

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8th October 2019	Document extended with no changes as part of Disease Management section in critical care	Dr Nick Cowley/ Dr Andy Burtenshaw

INTRODUCTION

Acute Kidney Injury (AKI) may be broadly described as a rapid loss (days to weeks) of the functional ability of the kidneys to excrete the waste products of metabolism and to maintain fluid, electrolyte and acid-base homeostasis.

The incidence of AKI is 10–25% of critical care patients, with Renal Replacement Therapy (RRT) being required for approximately 3-5% of admissions.[1]

Patients in whom AKI is diagnosed, particularly those requiring RRT, have an increased mortality. In a large cohort study evaluating the RIFLE criteria for AKI the mortality rates for Class R, Class I and Class F AKI were 8.8%, 11.4% and 26.3% respectively compared to 5.5% for patients without AKI.2

Table 1: Risk, Injury, Failure, Loss, and End-stage kidney injury (RIFLE) classification:

Class		**Glomerular filtration rate criteria**	**Urine output criteria**
R	**Risk**	Serum creatinine × 1.5	< 0.5 ml/kg/hour × 6 hours
I	**Injury**	Serum creatinine × 2	< 0.5 ml/kg/hour × 12 hours
F	**Failure**	Serum creatinine × 3, or serum creatinine ≥ 300 μmol/L with an acute rise > 40 μmol/L	< 0.3 ml/kg/hour × 24 hours, or anuria × 12 hours
L	**Loss**	Persistent acute renal failure = complete loss of kidney function > 4 weeks	
E	**End-stage kidney disease**	End-stage kidney disease > 3 months	

[1] Standards and Recommendations for the Provision of Renal Replacement Therapy on Intensive Care Units in the United Kingdom. *Intensive Care Society.* January 2009

This document is a guide to effective provision of CRRT (Continuous Renal Replacement therapy) within the WAHT critical care directorate using the Gambro Prismaflex system for those patients who are considered likely to benefit. This includes indications for RRT. However, suitability of individual patients for advanced organ support, including RRT, is beyond the scope of this guideline.

Much of the information contained within the guideline is supplemented by more detailed explanation within the appendices.

INDICATIONS

The most common indications for commencing RRT are:

- Metabolic acidosis (Clinician free to decide degree of acidosis in context of clinical picture)
- Hyperkalaemia [K^+] > 6.5 mmol.L^{-1} (unresponsive to medical management or in the context of established AKI)
- Severe fluid overload adversely affecting organ function and unresponsive to medical management (e.g. pulmonary oedema)
- Symptomatic uraemia (e.g. vomiting, seizures, pericarditis)
- Anuria / oliguria anticipated to progress to one of the above four scenarios in spite of medical management
- As a potential adjunct in severe sepsis/Septic shock
- Removal of toxins following overdose

RRT MODE CHOICE

The default setting for the Prismaflex should be CVVHDF, with the dialysis flow set to zero. (This is essentially a CVVH filtration mode but permits a change to CVVHDF should this be required mid-cycle.)

VASCULAR ACCESS

The first choice for vascath length should be:

Internal Jugular	15cm
Subclavian	20 cm
Femoral	20 cm. (or 25 cm in selected cases where the benefit of access to the inferior vena cava rather than femoral / iliac vein is anticipated to overcome additional resistance of a longer line)

As a general guide, the largest gauge cannula possible should be inserted to permit high blood flow rates. High blood flow rates help reduce filter clotting.

All vascular devices must be inserted using the guidance encompassed in the 'Matching Michigan' initiative.

FLUID CHOICE

The default solution for RRT use is Prismasol 4. This is a bicarbonate buffered solution which also contains 4 mmol L^{-1} potassium.
Other replacement fluids are available but are not currently stocked in the department.

SELECTION OF FLUID "EXCHANGE RATE"

Standard: **25ml/kg/hr**

High Flow: **40 ml/kg/hr** For initial management of severe sepsis. Envisaged to be used for initial 24 hours only. Flows in excess of 40 ml/kg/hr are possible but not currently supported by evidence. They may be used in specific situations at the discretion of the critical care consultant. (For example to compensate for excessive filter down time)

Low flow: **15 ml/kg/hr** For patients requiring medium to long term RRT once gross metabolic derangement resolved and not in the presence of severe sepsis. Intermittent use of standard regimen is an alternative.

Standard (25 ml/kg/hr)	Pre-Blood Pump	8	ml/kg/hr
	Dialysis	0	ml/kg/hr
	Replacement	17	ml/kg/hr
	Pre-post setting	Post	

High Flow (40 ml/kg/hr)	Pre-Blood Pump	13	ml/kg/hr
	Dialysis	0	ml/kg/hr
	Replacement	27	ml/kg/hr
	Pre-post setting	Post	

Low Flow (15 ml/kg/hr)	Pre-Blood Pump	5	ml/kg/hr
	Dialysis	0	ml/kg/hr
	Replacement	10	ml/kg/hr
	Pre-post setting	Post	

POTASSIUM REPLACEMENT

1. No potassium replacement is required since Prismasol 4 contains 4mmol/L potassium.

MACHINE SETUP

1. Select filter set

Standard filter set: **ST100**
Surface area approximately 0.9 m^2

Alternative filter set: **ST150**
Surface area approximately 1.5 m^2
Indications for use: **Severe Sepsis**
Patient weight >100Kg

Both these sets are Surface Treated to reduce the risk of anaphylactoid reaction with ACE-Inhibitors. They also bond heparin to

the filter membrane which reduces the risk of filter clotting, promoting longer filter life and aids anticoagulant free filtration.

2. After switching machine on continue to "Choose Patient" screen, select "**New Patient**" and enter patient details, including weight. (Estimated if unknown.)
3. Continue to "mode select" screen and select "**CVVHDF**"
4. Continue to anticoagulation selection screen and select "**Syringe**". (N.B. This should be selected even if no anticoagulation is to be used and the syringe should be filled with 0.9% saline. This will allow heparin to be added in easily at a later stage if required. Standard anticoagulation will require a 20 ml syringe containing 1000 units/ml to be attached.)
5. Follow on-screen instructions to connect **Priming bag**, **Pre-Blood Pump (PBP) bag**, **Dialysate bag**, **Replacement bag** and **Effluent bag**.

Note: Priming solution should be 1L 0.9% saline containing 5000 units heparin. If the larger ST150 filter set is used then 2 of these will be required. If treatment is planned without anticoagulation, priming with heparin should still take place to permit heparin bonding EXCEPT for patients with Heparin Induced Thrombocytopenia (HIT) for whom 1 L 0.9% saline should be used with either an ST100 or ST150 set.)

Note: For standard CVVH there will be no dialysate flow. A 1 L bag of 0.9% saline can be attached in place of a dialysate bag. (This can be changed later if dialysate is later required as the machine will have been set in CVVHDF mode)

6. Install anticoagulant syringe as per on screen instructions and press "Prime".

Note: It is necessary to connect the machine to the patient within 30 minutes of priming. This is because ethylene oxide, which is used to sterilise the filter, may leach into the primed solution over time and can result in serious hypotension if distributed systemically. Delays longer than 30 minutes can be managed by re-priming the filter set within 30 minutes of patient connection using 0.9% saline (no further heparin required).

7. In all cases, wrap the filter return line in the heating element and turn heater on. This is required for all patients unless specifically indicated by the ITU consultant.
8. Check patency of vascular access cannula. This can be achieved by aspirating 5ml of blood and injecting onto gauze. If any clots are present repeat this process until no clots are evident. Attempt to aspirate 20 ml blood from each port. If this cannot be achieved in less than 6 seconds then adequate blood flow will not be achieved and the filter set will be at high risk of clotting. (This is equivalent to 200ml/min pump speed) The medical team should appropriately manage the vascular access until such flows can be achieved (on the access line as a minimum) before connection of the filter. Flush lines with 0.9% saline after patency check.
9. Confirm flow settings

Note: The fluid loss/gain limit should read approximately 400 ml (may vary slightly by weight entered) and the access range should be set to "-ve". (+ve refers to situations where high pressure access is encountered such as A-V fistulae (including Novalung circuit) or "piggy-backing" onto CPB or ECMO pumps.)

10. Enter flow settings. *Initial* settings should read:

Blood Flow	80-100	ml/minute
PBP	0	ml/minute

Dialysate	0	ml/minute
Replacement	0	ml/minute
Pre-Post	Post	
Patient Fluid removal	0	ml/minute

11. Set Anticoagulation syringe rate as per protocol, or set 0 ml/hr for no anticoagulation.
12. Review prescription and confirm settings
13. Administer bolus dose of heparin to patient as per anticoagulant protocol
14. Connect patient and press "Start"
15. Blood flow rate should be increased to as high as possible (dependent upon haemodynamic stability and vascular access) up to a maximum of 400 ml/minute (for ST100 set) or 450 ml/minute (ST150). Access pressure should ideally be at least -100mmHg (absolute limit -250 mmHg)
16. Once blood flow has been increased to at least 120 ml/minute, adjust PBP, Dialysate, Replacement and patient fluid removal settings according to prescription.

Note: Fluid removal should be prescribed as the total amount of fluid the patient is to lose per hour after adjustment for input and output. It will therefore require recalculation and adjustment on an hourly basis.

Note: A minimum fluid removal rate of 10 ml/hour is advised to allow for minor fluctuations in the scales.

Note: UFR post % of BFR (Ultrafiltration Rate as % of Blood Flow Rate) should not exceed 25% as this reflects the degree of concentration of blood in the filter and correlates with the likelihood of filter clot formation. If it is greater than 25% either increase the blood flow rate or increase the proportion of fluid replacement given as predilution. (i.e. increase PBP, decrease replacement)

PRESSURE DROP AND TRANSMEMBRANE PRESSURE

Pressure Drop is the pressure difference in the blood compartment across the membrane. It reflects the ease of passage of blood through the filter and increases significantly in the presence of blood clots. Heparin boluses may salvage a partially clotted filter. A pressure drop of 150-200 mmHg suggests a clotting filter which will soon require change if not resolved.

Transmembrane pressure reflects the pressure across the filter membrane between the blood and filtrate compartments. In contrast to pressure drop, TMP reflects the degree of "clogging" of membrane pores. Once TMP exceeds 300-350 mmHg consideration should be given to changing the filter set, particularly in the context of severe sepsis where removal of inflammatory mediator molecules may have become saturated.

Ideally, in the absence of evidence of filter "clotting", a clogged filter should be washed back before changing the set in order for the patient to avoid unnecessary blood loss.

PRISMAFLEX PRESSURE RANGES

Normal ranges for pressure measurement are shown in the table below. This information is also written on a card on the side of the machine and on the quick reference chart.

	Normal	Limit
Access	-30 to -150	-250
Filter	+80 to +400	+500

Effluent	+50 to -150	
Return	+50 to +250	+350

(All pressures measured in mmHg)

END OF TREATMENT

- Please remember to download the treatment data to the memory card at the end of each treatment whether stopped temporarily or permanently.
- Unless clotted, the filter set should be washed back using 250 ml 0.9% saline and following the on-screen instructions.
- Unless specifically contra-indicated, the vascath should be “hep-locked” with 1000 units/ml heparin according to the lumen volume printed on the vascath.

STANDARD

A bolus of heparin is required prior to commencement of filtration. A dose of 40 units/kg is usually appropriate but can be reduced according to clinical requirement (No anticoagulation or 10 units/kg in the context of pre-existing coagulopathy or risk of clinically significant haemorrhage, at the clinician's discretion)

Unfractionated heparin (UFH) infusions should be made up to the Trustwide standardised concentration of 1000 units/ml by diluting 20,000 units into 20ml 0.9% saline.

The UFH infusion should then be commenced at a rate of 10 units/kg/hr and an initial APTT ratio checked four hours after commencing therapy. The infusion rate should then be adjusted to aim for an APTT ratio of 1.5-2.5 which will usually require a UFH infusion rate of between 5-20 units/kg/hr. Audit of filter set duration identified APTT ratio as the only statistically significant determinant of premature loss of filter sets. Therefore, in the absence of a perceived additional risk, maintenance of the APTT range between 2.0 and 2.5 should be preferentially sought.

Weight	**Bolus Dose** (40 U/Kg)	**Initial Rate** (10 U/Kg/Hr)	
Kg	*Units*	*Units/hr*	*ml/hr*
50	2000	500	0.5
55	2200	500	0.5
60	2400	600	0.6
65	2600	600	0.6
70	2800	700	0.7
75	3000	700	0.7
80	3200	800	0.8
85	3400	800	0.8
90	3600	900	0.9
95	3800	900	0.9
100	4000	1000	1

(the syringe pump in the prismaflex can be set to only the nearest 0.1 ml/hr)

APTT ratio should then be checked at a maximum interval of every 8 hours.

(N.B. A degree of clinical interpretation may sometimes be necessary in adjusting the infusion rate or target range for some patients. Patients may exhibit heparin resistance due to low antithrombin levels and heparin binding to drugs and acute phase proteins and it is clear that APTT ratios do not always accurately reflect the anticoagulant effect of UFH.)

EXCEPTIONS

a) NO ANTICOAGULATION

Anticoagulation should be omitted entirely in the following circumstances:

1. INR ≥ 2.0

2. APTT ratio ≥ 2.0
3. Platelet count < 60 x 10^3/mm^3
4. High risk of clinically significant haemorrhage or less than 12 hours post-op.

(where anticoagulation has been omitted because of a high risk of serious bleeding maintenance of a clot free filter may be encouraged by the use of a larger venous access catheter, higher blood flow rates and the use of predominantly, or exclusively, pre-dilutional haemofiltration.)

B) EPOPROSTENOL

Indications:

1. Evidence of heparin induced thrombocytopaenia (HIT)
2. Patient at high risk of serious haemorrhage (e.g. Sub-arachnoid haemorrhage) in whom anticoagulant free CRRT has failed.

The trust Epoprostenol monograph should be consulted for dosage guidance.

REFERRAL TO NEPHROLOGY

The nephrology team should be notified of all patients with acute kidney injury requiring renal replacement therapy within the critical care unit.

Appendix A: List of Abbreviations

ADQI	Acute Dialysis Quality Initiative
AKI	Acute Kidney Injury
ARF	Acute Renal Failure
CRRT	Continuous Renal Replacement Therapy
CVVH	Continuous Veno-Venous HaemoFiltration
CVVHD	Continuous Veno-Venous HaemoDialysis
CVVHDF	Continuous Veno-Venous HaemoDiaFiltration
HIT	Heparin Induced Thrombocytopenia
HVHF	High Volume HaemoFiltration
LMWH	Low Molecular Weight Heparin
RIFLE	Risk, Injury, Failure, Loss, End-Stage Kidney Disease
RRT	Renal Replacement Therapy
SCUF	Slow Continuous UltraFiltration
TPE	Total Plasma Exchange
UFH	UnFractionated Heparin

Appendix B: Definition of Acute Kidney Injury

In 2006 the Acute Dialysis Quality Initiative published a new definition and classification scheme for renal failure known as RIFLE.[2] RIFLE describes five stages of renal impairment as shown in table 1. The RIFLE classification was introduced in recognition that there was no uniform means of classifying different degrees of renal impairment and that this made comparison and application of research findings to patient populations difficult.

Table 1: Risk, Injury, Failure, Loss, and End-stage kidney injury (RIFLE) classification:

Class	Glomerular filtration rate criteria	Urine output criteria
Risk	Serum creatinine × 1.5	< 0.5 ml/kg/hour × 6 hours
Injury	Serum creatinine × 2	< 0.5 ml/kg/hour × 12 hours
Failure	Serum creatinine × 3, or serum creatinine ≥ 300 μmol/L with an acute rise > 40 μmol/L	< 0.3 ml/kg/hour × 24 hours, or anuria × 12 hours
Loss	Persistent acute renal failure = complete loss of kidney function > 4 weeks	
End-stage kidney disease	End-stage kidney disease > 3 months	

*RIFLE class is determined based on the worst of either glomerular filtration criteria or urine output criteria. Glomerular filtration criteria are calculated as an increase of serum creatinine above the baseline serum creatinine level. Acute kidney injury should be both abrupt (within 1–7 days) and sustained (more than 24 hours). When the baseline serum creatinine is not known and patients are without a history of chronic kidney insufficiency, it is recommend to calculate a baseline serum creatinine using the Modification of Diet in Renal Disease equation for assessment of kidney function, assuming a glomerular filtration rate of 75 ml/min/1.73 m^2. When the baseline serum creatinine is elevated, an abrupt rise of at least 40 μmol/L to more than 300 μmol/L is all that is required to achieve class Failure.*2

[2] RIFLE criteria for acute kidney injury are associated with hospital mortality in critically ill patients: a cohort analysis. Hoste EAJ, Clermont G, Kersten A et al. Critical Care 2006, 10:R73

Appendix C: Indications for RRT

Indications for commencing RRT are:[3]

- Metabolic acidosis
- Hyperkalaemia [K^+] > 6.5 mmol.L^{-1} (unresponsive to medical management or in the context of established AKI)
- Severe fluid overload adversely affecting organ function and unresponsive to medical management (e.g. pulmonary oedema)
- Symptomatic uraemia (e.g. vomiting, seizures, pericarditis)

Other factors which may provoke consideration of RRT but are not absolute indications include:

- Anuria / oliguria anticipated to progress to established AKI and not responding to medical management (despite not yet reaching above triggers)
- MODS, SIRS or severe sepsis/septic shock
- Severe dysnatraemia ([Na^+] < 115 mmol.L^{-1} or [Na^+] > 160 mmol.L^{-1})
- Drug intoxication amenable to RRT
- Severe hyperthermia refractory to other methods of treatment
- Severe hypothermia refractory to other methods of treatment (limited benefit)

REFERENCES

Standards and Recommendations for the Provision of Renal Replacement Therapy on Intensive Care Units in the United Kingdom. *Intensive Care Society.* January 2009

[1] RIFLE criteria for acute kidney injury are associated with hospital mortality in critically ill patients: a cohort analysis. Hoste EAJ, Clermont G, Kersten A et al. Critical Care 2006, 10:R73

[1] Core Topics in Critical Care Medicine. Cambridge University Press. (April 2010)
All references should be 'Harvard' referenced, eg,

[3] Core Topics in Critical Care Medicine. Cambridge University Press. (April 2010)

Appendix D: Complications of RRT

The following are potential complications associated with RRT:

1. Central venous access associated complications:
   1.1. Haematoma formation / arterial puncture
   1.2. Pneumothorax
   1.3. Line infection / sepsis
   1.4. Line thrombosis or thromboembolism
   1.5. Poor blood flow through cannula (cannula against vessel side wall or kinked)
   1.6. Line disconnection
   1.7. Air embolism
   1.8. Subclavian stenosis associated with subclavian lines
   1.9. Lower limb DVT may be associated with femoral venous catheterisation

2. Machine problems:
   2.1. Clotting of circuit
   2.2. Machine malfunction

3. Clinical problems:
   3.1. Allergic reactions
   3.2. Hypothermia (discomfort, shivering, coagulopathy & masking of pyrexia)
   3.3. Cardiovascular instability (particularly on initiation of therapy)
   3.4. Electrolyte imbalance / disequilibrium syndrome / hypophosphataemia.
   3.5. Adverse effects of anticoagulation (e.g. gastrointestinal bleeding) including those associated with over or under anticoagulation.
   3.6. Unpredictable drug concentrations (e.g. effect upon antibiotic efficacy, effect on vasoactive drug concentrations)
   3.7. Nutrient losses
   3.8. Metabolic acidosis and lactate rise in situations where lactate cannot be adequately metabolised

Appendix E: Modes of RRT

Fundamentally, the principle aims of RRT are to remove waste products from the circulation and to maintain fluid, electrolyte and acid-base balance. RRT may also be used to assist in the removal of toxins including sepsis mediators and some drug overdoses.

These aims are achieved by transport of water and solute molecules across a semi-permeable membrane through the mechanisms of ultrafiltration, convection and diffusion.

Ultrafiltration is the flow of small molecules through a semi-permeable membrane under the influence of hydrostatic pressure, whilst the membrane holds larger molecules back. The rate of ultrafiltration can be controlled by the pressure difference across the semi-permeable membrane and the blood flow past the membrane.

Convection is the movement of a solute in a moving stream of ultrafiltrate across a membrane and is therefore intrinsically related to ultrafiltration. The rate of convection is influenced by the direction and force of the ultrafiltrate current and the size of the membrane pores. This is the predominant mechanism of water and solute removal in “haemofiltration” and is a more effective means of moving medium sized molecules (e.g. inflammatory mediators in sepsis) across a membrane than diffusion.

Diffusion is the flow of molecules across a semi-permeable membrane from a region of high concentration to a region of low concentration which tends towards the development of equal concentrations each side. Diffusion is the principle mode of action occurring in haemodialysis. A large number of factors influence the rate of diffusion including the size and electrical charge of the molecules, the concentration each side of the membrane, characteristics of the membrane (thickness, surface area, pore size, material used), and the rate and direction of blood and dialysate flows each side of the membrane. A setup in which the blood and dialysate flows are in opposite directions (countercurrent flow) allows much more efficient diffusion across the membrane than if the flows are in the same direction by essentially preventing the equalisation of concentrations each side of the membrane and maintaining a concentration gradient along the entire length of the membrane. Because small molecules more rapidly diffuse than larger molecules, dialysis, which mainly utilises diffusion as its mechanism of action, is much more effective for managing electrolyte disturbances than it is for removing larger molecules such as sepsis mediators.

The following modes of RRT are possible on the PRISMA machines:

CVVH – Continuous Veno-Venous HaemoFiltration

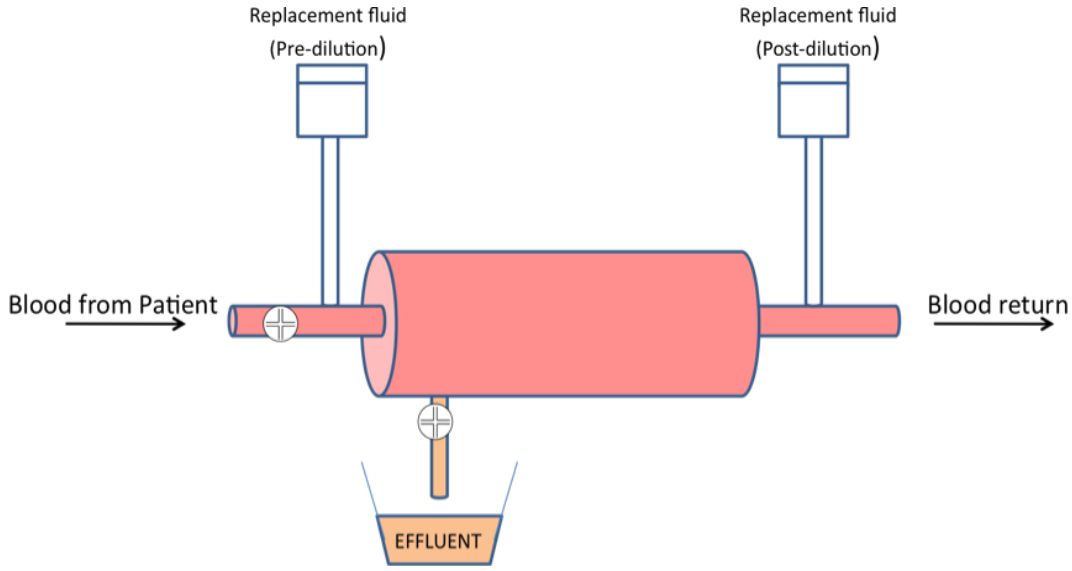

Figure 1: CVVH3

Blood is delivered under pressure over a semi-permeable membrane through which water, electrolytes and medium sized molecules will pass. Because the ultrafiltrate volume produced is large this fluid must be replaced to avoid rapid fluid depletion. Fluid replacement constituents are discussed later. This replacement fluid may be introduced before the blood passes in to the filter in which case it will dilute it before filtration (pre-dilution). This reduces the likelihood of blood clot formation (because the haematocrit is reduced) within the filter at a cost of reduced filter efficiency (because molecules to be removed have been diluted). Alternatively the replacement fluid can be replaced after the filter (post-dilution). In this case the efficiency of the filter is much better because concentrated waste products are filtered, but the increase in haematocrit as the fluid is removed increases the tendency for the filter to clot. Pre-dilution with ultrafiltrate volumes up to 2L per hour are associated with a reduction in urea clearance of approximately 15%, whilst volumes of 4.5L/hour result in a loss of urea clearance of approximately 36%. The Prismaflex machine allows the proportion of pre- or post-dilution to be controlled.

CVVH commonly uses ultrafiltrate rates of 15-60 ml/minute and blood flow rates 100-250 ml/minute. There is limited evidence that high volumes of haemofiltration (>35 ml/kg/hr) may have beneficial effects in severe sepsis.

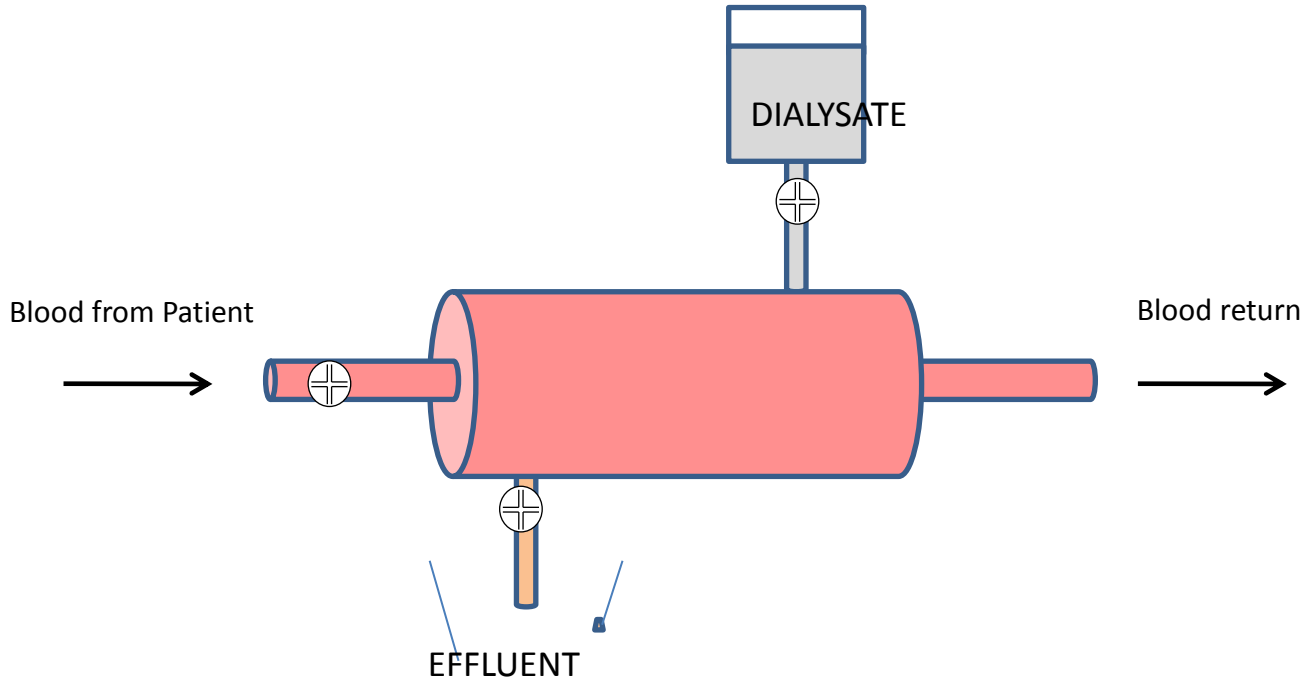

Figure 2: CVVHD3

In CVVHD blood is passed one side of a membrane with a fluid (referred to as dialysate fluid) passed in the opposite direction on the other side. Molecules tend towards equilibration across the membrane and in doing so, high concentrations of waste products (e.g. urea, potassium) are removed from the blood. Small alterations in the transmembrane pressure (contolled by the rollers pumping blood and dialysate) control any quantities of fluid which are also to be removed. In contrast to CVVH, large fluid shifts do not take place.

This mode of RRT most closely replicates native renal function and is used in stable patients with end stage renal failure unaccompanied by other organ failure. It is ineffective at removing larger molecules or large volumes of fluid and is not a commonly used RRT mode within the critical care setting.

Higher blood flow rates improve efficiency (up to 250ml/minute in the critical care setting) and dialysate flow rates of 15-60 ml/minute are commonly used. Because the ultrafiltration rate is low, fluid replacement is not necessary.

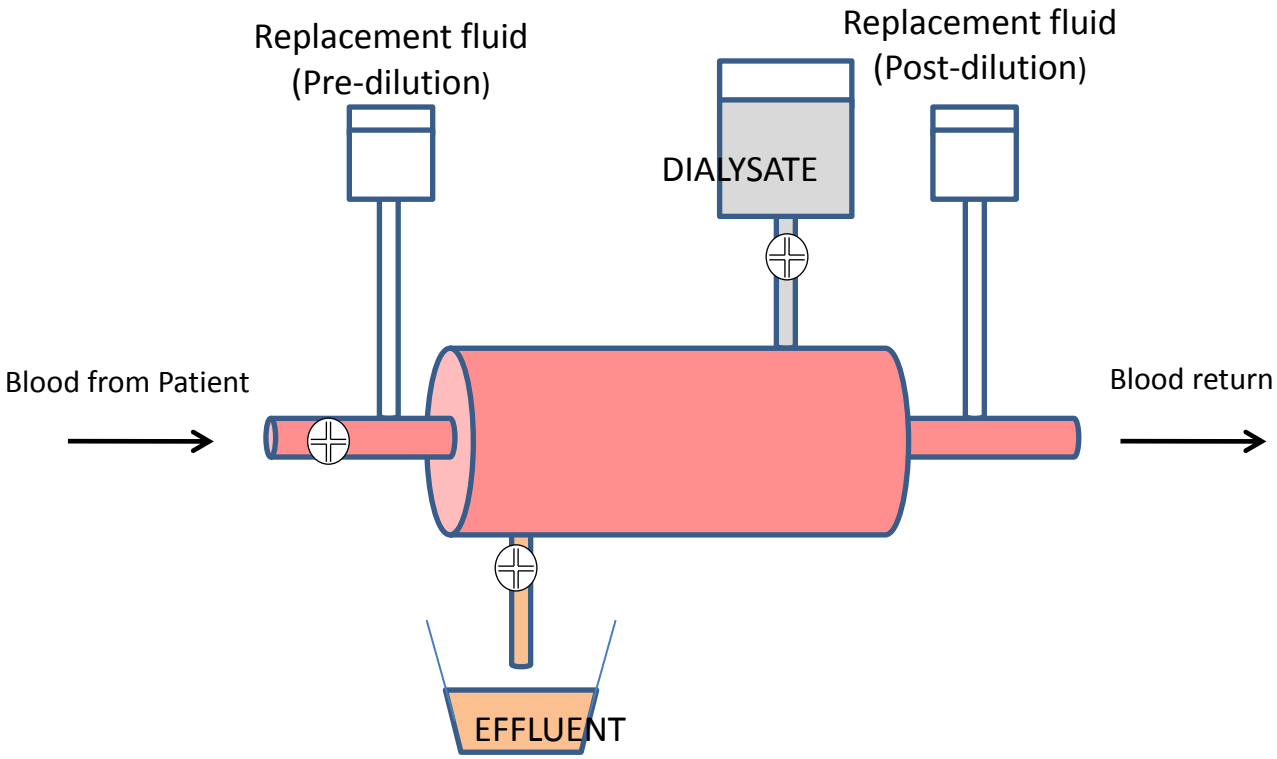

Figure 3: CVVHDF3

CVVHDF is a hybrid of CVVH and CVVHD, utilising ultrafiltration, convection and diffusion mechanisms in its action to produce a RRT mode which is an efficient means of removing electrolytes and small molecules whilst also being an effective way to remove larger volumes of fluid together with larger molecules seen in the context of the critically ill patient.

Blood and dialysate flow in opposite directions as with CVVHD to produce a dialysis effect (diffusion), whilst a transmembrane pressure also drives fluid (ultrafiltrate) through the membrane at the same time, taking with it more molecules (convection). The effluent is a combination of dialysate fluid passed along one side of the membrane and the ultrafiltration fluid. Because large volumes of ultrafiltrate are produced, a replacement fluid is required as with CVVH.

Blood flow rates of 100-250ml/minute are used together with a combination of an ultrafiltrate flow of 15-60 ml/minute and a dilaysate flow of 15-60 ml/minute.

Other potential modes of RRT available but not currently in use in WAH NHS trust include:

SCUF – Slow Continuous Ultrafiltration

This technique is highly efficient where fluid removal is required without manipulation of solute concentration. As volume overload in the absence of renal failure is rare, SCUF is seldom used within critical care.

Plasmapheresis and Total Plasma Exchange (TPE)

Standard filters allow the passage of molecules up to about 50 KiloDaltons. Membranes that allow the passage of much larger molecules (usually 100,000 to 1,000,000 KD) permit the removal of large volumes of plasma which is then replaced with fresh frozen plasma (FFP) or albumin solution. This is potentially useful to rapidly remove harmful autoantibodies in conditions such as Guillain-Barré syndrome, Goodpasture's syndrome, myasthenia gravis, Lambert-Eaton myasthenic syndrome and thrombotic thrombocytopenic purpura.

In addition to the complications of RRT, plasmapheresis and TPE are associated with severe immunosuppression (because of indiscriminate removal of antibodies) and reactions to blood products.

Haemoperfusion

Blood may be passed over a filter containing charcoal powder that allows removal of certain solutes by adsorption to the charcoal molecules. This is of particular use for lipid soluble drugs occasionally seen in poisoning or overdose patients.

High Volume HaemoFiltration (HVHF)

This technique utilises high blood flow and ultrafiltration rates through highly permeable membranes with the aim of increasing the removal of systemic inflammatory mediators. Filtration volumes are in the region of 40-85ml/kg/hr. This therapy is not yet commonplace in the treatment of sepsis and is not currently supported by a strong evidence base.

Appendix F: Fluid Replacement

A balanced salt solution is required either to replace that lost through ultrafiltration or to pass across a membrane as a dialysate. If left unchecked, bicarbonate loss would rapidly result in severe metabolic acidosis. Bicarbonate can be replaced either by lactate containing solutions (relying upon subsequent hepatic metabolism to bicarbonate) or by bicarbonate itself. However, bicarbonate containing solutions have a short shelf life and are more expensive than lactate containing solutions.

Solutions in regular use at WAHT ICU's are Hemolactol (lactate buffered) and Prismasol 4 (bicarbonate buffered).

Constituents:	*Hemolactol*	*Prismasol 4*
Na^+ (mmol/L)	140	140
K^+ (mmol/L)	4.0	4.0
Ca^{2+} (mmol/L)	1.75	1.75
Mg^{2+} (mmol/L)	0.75	0.5
Cl^- (mmol/L)	109	113.5
Lactate (mmol/L)	40	3
Bicarbonate (mmol/L)	-	32
Osmolarity (mOsm/L)	301	301
Glucose (mmol/L)	4.4	6.1

Most patients will demonstrate a rise in serum lactate level when a lactate-based buffer is used. This does not indicate intolerance to the solution, but a higher equilibrium point between production / absorption and metabolism. However, some patients are intolerant of additional lactate and develop a more severe lactate rise. Patients at high risk of this include those with severe liver disease, profound tissue hypoperfusion or pre-existing lactic acidosis.

The default solution for RRT use is Hemolactol.

Indications for commencing RRT with Prismasol 4 are:
1. Pre-existing lactate ≥ 8 mmol/L with a pH ≤ 7.2, or a rise in lactate level ≥ 5 mmol/L from previously recorded baseline with a drop in pH
2. Evidence of severe liver dysfunction

A rise in lactate level ≥ 5 mmol/L with a drop in pH during RRT treatment with Hemolactol is an indication to change to Prismasol 4.

Appendix G: Anticoagulation

Contact between the blood and the extracorporeal circuit activates inflammatory and coagulation cascades. Partial filter clotting results in reduced performance of the filter whilst complete circulation clotting results in the loss of the filter and circuit, interruption of therapy and the loss of the patient's blood trapped within the system.

Many factors contribute to filter clotting such as poor vascular access, slow flow rates, excessive haemoconcentration during filtration, inadequate anticoagulation and a procoagulant state.

Alternative anticoagulant strategies:

Low Molecular Weight Heparin (LMWH)
LMWHs are not routinely used in our critical care units for two reasons. Firstly their effect is not readily measured and secondly their action is longer and less easy to reverse.

Although not currently used, their use may increase with time as evidence suggests that their activity may be more predictable in the context of the critically ill patient.

Epoprostenol
Epoprostenol (a prostacyclin analogue) is a naturally occurring potent inhibitor of platelet aggregation which prevents/reduces clot formation. It should be reserved for use in patients with evidence of heparin induced thrombocytopaenia (HIT). It may also have a lower risk of bleeding than unfractionated heparin and may therefore be preferable in patients at higher clinical risk of haemorrhage such as subarachnoid haemorrhage if anticoagulant free CRRT cannot be achieved.

Epoprostenol is more expensive than heparin and is also a potent vasodilator. This may result in hypotension (half life of hypotensive effect thought to be much shorter than the half life of anticoagulant effect) and has potential for causing hypoxia predominantly through amelioration of hypoxic pulmonary vasoconstriction.

Citrate anticoagulation
Regional citrate anticoagulation (i.e. CRRT circuit only) has been shown to be an effective means of preventing filter clotting but has a number of potential complications, which mean that very strict protocols are required. At present this is not undertaken within WAHT critical care department.

Other forms of anticoagulation
There are a number of other potential anticoagulant agents available such as Fondaparinux, Nefamostat, Argatroban, Hirudin and Danaparoid. However, there is currently no evidence to suggest superiority or adequate safety of these drugs for this use.

Appendix H: Potassium replacement

Prismasol 4 has a potassium concentration of 4mmol/L resulting in a tendency towards a safe equilibrium during CRRT.

Appendix I: Temperature management

Extracorporeal blood flow exposes the patient's blood to room temperature and results in a cooling effect. An important complication of this is that pyrexia indicative of early sepsis can be easily masked. Indeed, many clinicians would regard normothermia in a patient receiving CRRT as indicative of masked pyrexia.

Prismaflex Quick Reference Charts

Filter Choice:

Standard filter set: **ST100**
Surface area of approximately 0.9 m^2

Alternative filter set: **ST150**
Surface area of approximately 1.5 m^2
Indications for use: **Severe Sepsis**
Patient weight >100Kg

Initial pump settings:

Blood Flow	80-100	ml/minute
PBP	0	ml/minute
Dialysate	0	ml/minute
Replacement	0	ml/minute
Pre-Post		Post
Patient Fluid removal	0	ml/minute

Fluid "Exchange Rate" settings: (once blood flow > 150 ml/minute, preferably higher):

Standard (25 ml/kg/hr)	Pre-Blood Pump	8	ml/kg/hr
	Dialysis	0	ml/kg/hr
	Replacement	17	ml/kg/hr
	Pre-post setting	Post	

High Flow (40 ml/kg/hr)	Pre-Blood Pump	13	ml/kg/hr
	Dialysis	0	ml/kg/hr
	Replacement	27	ml/kg/hr
	Pre-post setting	Post	

Low Flow (15 ml/kg/hr)	Pre-Blood Pump	5	ml/kg/hr
	Dialysis	0	ml/kg/hr
	Replacement	10	ml/kg/hr
	Pre-post setting	Post	

Initial Heparin Anticoagulation:

Weight	**Bolus Dose** (40 U/Kg)	**Initial Rate** (10 U/Kg/Hr)	
Kg	*Units*	*Units/hr*	*ml/hr*
50	2000	500	0.5
55	2200	500	0.5
60	2400	600	0.6
65	2600	600	0.6
70	2800	700	0.7
75	3000	700	0.7
80	3200	800	0.8
85	3400	800	0.8
90	3600	900	0.9
95	3800	900	0.9
100	4000	1000	1