Continuous Veno Venous Haemofiltration (CVVH) and Continuous Veno Venous Haemodiafiltration (CVVHDF) within the paediatric critical care unit (PCCU)

Title of guideline (must include the word "Guideline" – not protocol, policy, procedure etc.)		Guideline for the use of CVVH and CVVHDF within PCCU
Contact name and job title (author)		Kate Peace, Paediatric Renal Critical Care Nurse Dusan Raffaj, Paediatric Intensivist Andrew Wignall, PCCU Lead Pharmacist
Directorate and speciality		Family health - PCCU
Date of submission		August 2022
Date on which guideline must be reviewed (this should be one to three years)		August 2025
Explicit definition of patient group to which it applies (e.g. inclusion and exclusion criteria)		Critically ill children who require CVVH/CVVHDF on PCCU
Abstract		This guideline discusses the principles of CVVH/CVVHDF, methods of anticoagulation, considerations prior and during treatment and potential problems
Keywords		CVVH, CVVHDF, Anticoagulation, citrate, flow rates
Statement of the evidence base of the guideline – has the guideline been peer reviewed by colleagues?		4 & 5
1a	Meta-analysis of randomised controlled trials (RCTs)	
1b	At least one RCT	
2a	At least one well designed controlled study without randomisation	
2b	At least one other type of well-designed quasi-experimental study	
3	Well-designed non-experimental descriptive studies (i.e. comparative/ correlation and case studies)	
4	Expert committee reports or opinions and/ or clinical experiences of respected authorities	
5	Recommended best practice based on clinical experience of guideline developer	
Consultation process		Discussion with colleagues on PCCU
Target audience		Staff working on PCCU
This guideline has been registered with the Trust. However, clinical guidelines are guidelines only. The interpretation and application of clinical guidelines will remain the responsibility of the individual clinician. If in doubt, contact a senior colleague or expert. Caution is advised when using guidelines after the review date.		

Document control

Version	Issue date	Author(s)	Updates/ notes
V1	August 2022	Kate Peace, Paediatric Renal Critical Care Nurse Dusan Raffaj, Paediatric Intensivist Andrew Wignall, PCCU Lead Pharmacist	Guideline rewritten due to citrate and new machines

Executive summary of guideline

Patient requires CVVH/CVVHDF

For **Peritoneal Dialysis** Liaise with renal team and refer to guideline: http://nuhnet/nuh_documents/Guidelines/Family%20Health/Children%27s%20Hospital%20-%20Renal/2118.pdf

First line **anticoagulation** on PCCU is **citrate**; consider using heparin and/or epoprostenol if contraindications present:

- Severe Liver Disease as the calcium-citrate complex is metabolised by the liver
- Patients with severe hepatic failure and INR >3.5
- Paracetamol hepatitis with gross elevation of AST, INR and with elevated lactate
- Clinical risk of bleeding considered too great for ANY CRRT anticoagulation
- Previous citrate accumulation, if organ dysfunction persists
- Additional citrate load e.g. on-going massive transfusion

You will need a **CVVHDF with citrate daily prescription and observation chart**. Use this in conjunction with **initiating CVVHDF** document which can be accessed using QR code on back of PrisMax

Prior to commencing therapy:

- Obtain a full set of bloods, paying particular attention to electrolytes
- Ensure appropriate size VasCath is insitu
- If possible have one unit of cross matched RBC available but do not delay urgent treatment
- Assemble PrisMax and all necessary equipment
- Complete prescription chart

The following groups of patients may require extra consideration:

- Low body weight
- Septic
- Hyperammonia

Prescribing checklist:

Heparin line lock
Priming fluid – Plasmalyte 148
Pre Blood Pump, Replacement and Dialysate fluid bags
Calcium Gluconate infusion
Flow rates
Fluid removal rate

Considerations during therapy:

General:
Haemodynamic stability
Fluid balance
Electrolytes, pay close attention to Mg^{++}, PO_4^- and K^+
Drug clearance
Temperature control

Monitoring:
Patient & filter blood gas 1hr after commencing
Filter iCa = 0.25-0.35
Patient iCa = 1-1.2
Full set of bloods after 6hrs then every 12hrs
T:i ratio every morning

Potential problems:
Fluid & electrolyte shift
Citrate accumulation
Hypothermia
Infection
Air embolism

Contents

1. Introduction and description of therapies

Continuous renal replacement therapy (CRRT) is a supportive therapy used for the management of fluid balance and metabolic derangement, with or without evidence of acute injury kidney injury (AKI), in critically ill patients.

Aims of the therapy include:

- Relieving hypervolaemia and maintaining fluid balance
- Removing excess urea & creatinine
- Correcting and maintaining metabolic and electrolyte balance
- Removing toxins

Indications for commencing treatment:

- Fluid overload
- Electrolyte imbalance
- Acute Kidney Injury (AKI)
- Inborn errors of metabolism
- Sepsis*
- Rhabdomyolysis
- Tumour lysis*
- Drug intoxications
- Optimising nutrition*
  (* other indication needed to support decision, not enough on its own)

In the EMEESY region, CRRT is utilised in the following forms; Peritoneal Dialysis (PD), Continuous Veno Venous Haemofiltration (CVVH) and Continuous Veno Venous Haemodiafiltration (CVVHDF). This guideline focuses on the use of CVVH and CVVHDF; these are both delivered using the PrisMax (Baxter) machine.

Using a dedicated double lumen vascath and an extracorporeal circuit, blood is continuously removed, and returned, to the patient. This continuous technique allows fluid and waste products to be removed gradually over a 24hr period. This provides more haemodynamic stability for critically ill children.

The extracorporeal circuit incorporates a blood pump and a filter containing a semi-permeable membrane. A pressure gradient within the circuit forces fluid and solutes across the membrane to form effluent fluid. Dialysis fluid can also be added to the other side of the filter, this causes molecules to move across with a concentration gradient. The processes utilised are ultrafiltration, convection and diffusion.

1.1 Ultrafiltration:

This is the movement of fluid through a semi-permeable membrane driven by a hydrostatic pressure gradient. On the PrisMax a positive pressure is generated by the blood pump on the blood side of the semi-permeable membrane and a negative pressure by the effluent pump on the other side. This results in the movement of fluid from the positive pressure side (blood side) to the negative pressure side.

1.2 Convection:

This occurs when large volumes of fluid crossing the semi-permeable membrane down the hydrostatic pressure gradient results in solvent drag across the membrane. Large molecules can be moved efficiently if the flow is fast enough. Pre blood pump and replacement fluid is added to the circuit to increase the flow across the semi-permeable membrane.

1.2 Diffusion:

This is the movement of solutes across a semi-permeable membrane caused by a concentration gradient. Solutes move from an area of higher concentration to an area of lower concentration. On the PrisMax this is achieved by the addition of dialysate fluid on the other side of the semi-permeable membrane, this is run counter-currently to the blood flow to ensure the concentration gradient is maintained the whole length of the filter.

The movement of molecules in CRRT are driven by the above processes but are limited by the size of the solute particles. The PrisMax filters have pores that allow passage of molecules up to 35,000 Daltons. This allows for free movement of small ions and molecules (e.g. urea, creatinine, ammonia) across the membrane as well as some larger molecules such as myoglobin (17,200 Daltons), insulin (active) and interleukins (varies). Small molecules are more efficiently removed by diffusion and larger molecules by convection.

Some molecules are removed in CRRT by adherence to the artificial semi-permeable membrane; this is the process by which inflammatory markers are thought to be removed. High levels of these molecules can cause the filter to clog and become less effective.

On PCCU the Baxter PrisMax machine is used and has several different modes. The two main modes are Continuous Veno Venous Haemofiltration (CVVH) and Continuous Veno Venous Haemodiafiltration (CVVHDF). Slow Continuous Ultrafiltration (SCUF) is used on some units as a rest mode to assess if a patient is ready to stop treatment however this is currently not used on PCCU.

1.4 CVVH

This mode of CRRT utilises the principles of ultrafiltration and convection and is ideal for removing middle and large molecules.

- Biochemistry is controlled by removing large volumes of filtrate and replacing it with electrolyte containing fluid (replacement fluid). The more filtrate you remove and replace the more efficient haemofiltration is in controlling biochemical disturbance.

- As most solutes are distributed within the extracellular and intracellular fluid compartments (total body water), the volume of filtration (replacement) necessary to control biochemistry relates to total body water. Clinical experience has shown that a replacement of approximately 50% of bodyweight (1kg = 1litre) is usually adequate for solute and electrolyte removal.

1.5 CVVHDF

This mode of CRRT utilises the principles of ultrafiltration, convection and diffusion; using both convective and diffusive transport systems will optimise the clearance of molecules of varying sizes.

- The addition of dialysate flow with CVVHDF will improve the efficiency of acid base, waste and control of electrolyte balance. Waste and electrolytes diffuse from the patient's blood into the dialysate fluid surrounding the fibres. The "saturated" dialysate fluid (effluent) is removed from the filter and discarded.

- Diffusion is a two way process, molecules that are at a low concentration in the blood and high in the dialysate fluid will diffuse into the blood and vice versa (e.g. bicarbonate).

- Convective transport systems utilised in CVVH are limited by the blood flow achieved. If higher replacement rates are indicated, but not achievable, adding in dialysate flow will optimise clearance. Reasons for not achieving desired replacement rates could be due to patient stability or issues with access limiting the blood flow rates.

- This is practically important when treating children with inborn errors of metabolism, for overdose of drug or therapeutic agents and for patients with a high lactate.

- Increasing dialysate flow will at least theoretically improve clearance; however this is limited by the relatively low dialysate flow rates generated by CRRT equipment.

1.6 Which therapy?

***CVVHDF** should always be selected when setting up the PrisMax.*

When performing filtration with heparin anticoagulation it is possible to switch between CVVH and CVVHDF whilst treatment is running depending on the patient's clinical condition.

*However, when using citrate anticoagulation **CVVHDF** will always be the therapy of choice.* This is due to the additional benefits of running dialysate with citrate, such as off-loading citrate into the effluent bag which can help prevent citrate accumulation and reducing high bicarbonate levels in the patient's blood. If therapy is proving to be too efficient you can move the patient down a weight bracket (see table on page 21).

2. Coagulation

As with any extracorporeal circuit, the circuits used for CRRT require the administration of anticoagulation to prevent the development of clots and keep the blood flowing in the circuit. Historically, the commonest anticoagulant used for CRRT within PCCU was heparin, which is run as an infusion into the circuit. In recent years there has been a shift to use regional citrate anticoagulation. This is more beneficial than heparin as it can be used in patients that are at an increased risk of bleeding and have contraindications to heparin. It has also been shown to increase the life of the circuit, resulting in fewer interruptions to treatment and ensuring a more efficient treatment for the patient. Regional citrate will be the anticoagulation of choice on PCCU and therefore the focus of this guideline.

For information on heparin and epoprostenol anticoagulation please see Appendix Two and Three.

2.1 What is citrate?

Citrates are a family of compounds, but in relation to anticoagulation for CRRT trisodium citrate and citric acid are the two relevant compounds.

The citrate solution used on PCCU is Prismocitrate 18/0; this contains trisodium citrate 18mmol/L and 0mmol/L of citric acid.

Trisodium citrate is a salt of citric acid sometimes referred to as sodium citrate. It is metabolised in the liver to bicarbonate. Trisodium citrate also binds with ionised calcium and magnesium.

Sodium citrate is widely used in blood collection tubes and for the preservation of donated blood products. It is now becoming an increasingly popular alternative to heparin for the anticoagulation of the extracorporeal circuits used in CRRT.

2.2 How it works

In the blood, calcium circulates primarily either in a free form or bound to plasma protein. The free portion, termed ionized calcium (iCa), is the form of calcium which is key to the activation of the coagulation cascade. Through binding and forming a complex with iCa, citrate prevents coagulation in the extracorporeal circuit.

Citrate anticoagulation is referred to as regional anticoagulation as it is delivered to the circuit and filter without anticoagulating the patient, offering a significantly reduced risk of bleeding. However, it is still vital that iCa levels in both the circuit and the patient are closely monitored to ensure adequate anticoagulation of the circuit and minimise risk to the patient.

Citrate solution is delivered to the patient's blood pre-filter, on the pre-blood pump (PBP) scale; this ensures that both the filter and circuit are anti-coagulated. The concentration of citrate added to the patient's blood before entering the filter depends on the blood flow rate and citrate infusion (PBP) flow rate. The amount of citrate is expressed, as citrate dose, in mmol/L blood. On PCCU the starting citrate dose will be 4mmol/L. A filter iCa concentration of 0.25-0.35mmol/L is required for optimum anticoagulation of the circuit.

Blood flow rates and citrate infusion rates determine the ionised calcium level in the circuit; if the blood flow rate is adjusted the citrate infusion rate will automatically be altered by the PrisMax. This synchronization of the blood flow rate and PBP citrate flow rate is necessary to maintain the citrate dose at the desired level.

Citrate also non-specifically binds to positively charged ions such as magnesium and so a reduction in serum magnesium levels is to be expected. Magnesium levels should be checked daily whilst patient is on the filter.

Most of the citrate infused into the circuit is cleared by the filter and lost in the effluent. Consequently, only a portion of the infused citrate is delivered to the patient. Based on the citrate infusion rate and the rate of citrate loss in the effluent, the amount of citrate delivered to the patient can be calculated. This is called the 'patient citrate load'. Citrate will be rapidly metabolised by the patient so will not have any anticoagulation effect, however if this citrate is not metabolised this can lead to citrate accumulation, please refer to the 'Citrate accumulation' section for more details on how to deal with this.

2.3 Precautions (please discuss with consultant)

- Severe Liver Disease as the calcium-citrate complex is metabolised by the liver
- Patients with severe hepatic failure and INR >3.5
- Paracetamol hepatitis with gross elevation of AST, INR and with elevated lactate
- Clinical risk of bleeding considered too great for ANY CRRT anticoagulation
- Previous citrate accumulation, if organ dysfunction persists
- Additional citrate load e.g. on-going massive transfusion

3. Calcium Gluconate infusion

A certain percentage of citrate in the blood in the circuit is cleared by the filter and lost in the effluent. This citrate is bound to some of the patient's ionised calcium so in order to avoid systemic ionised hypocalcaemia, a separate infusion of calcium is required, being adjusted to maintain patient ionized calcium levels between 1.0-1.2mmol/L. This infusion is delivered via the PrisMax syringe pump directly to the patient via a **central** line, not into the circuit. If central access is problematic then this infusion can be delivered via the return lumen.

Based on the estimated calcium loss in the effluent, the PrisMax calculates the amount of compensatory calcium to be delivered by the machine syringe pump. This calculation takes into account the concentration of the calcium solution in the syringe.

Calcium compensation is expressed in % and can be modified during treatment. Complete replacement of the calcium lost in the effluent corresponds to a calcium compensation of 100%. The range of calcium compensation is variable, with a minimum of 5% and a maximum of 200%.

The PrisMax software calculates the syringe flow rate based on the calcium compensation selected, CRRT dose, patient body weight and calcium concentration in the syringe. The syringe flow rate cannot be set directly. The same applies for the calculation of the calcium rate i.e. the amount of calcium administered per hour.

On PCCU calcium gluconate will be used for the calcium infusion, see prescription chart for details.

3.1 Calcium gluconate concentration

For all patients
40ml of Calcium Gluconate 10% with 10ml Sodium Chloride 0.9% (9mmol/50ml or **0.18mmol/ml**)

Calcium syringe needs to be changed every 24 hours and calcium syringe lines every 72 hours.

Calcium gluconate must be administered centrally, if separate central access is not available then run on return line using a 3-way tap. Monitor Vas Cath closely for signs of clotting and keep filter iCa in lower end of range, discuss with renal critical nurse if any issues.

4. Citrate, Dialysate and replacement solutions

The fluid bag required for each scale (Pre blood pump, Dialysate and Replacement) will depend on the type of anticoagulation used.

For heparin, the fluid bags will either be Prismasol 4 (if patient's potassium <6mmol/L) or Hemosol BO (if patient's potassium >6mmol/L)

Prismasol 4 (all values in mmol/L)									
Sodium	Potassium	Calcium	Magnesium	Chloride	Phosphate	Lactate	Bicarbonate	Glucose	Citrate
140	4	1.75	0.5	113.5	0	3	32	6.1	0

Hemosol BO (all values in mmol/L)									
Sodium	Potassium	Calcium	Magnesium	Chloride	Phosphate	Lactate	Bicarbonate	Glucose	Citrate
140	0	1.75	0.5	109.5	0	3	32	0	0

For citrate the following fluid bags will be used:

The Citrate solution used on PCCU will be Prismocitrate 18/0 and will be used on the Pre Blood Pump scale:

Prismocitrate 18/0 (all values in mmol/L)									
Sodium	Potassium	Calcium	Magnesium	Chloride	Phosphate	Lactate	Bicarbonate	Glucose	Citrate
140	0	0	0	86	0	0	0	0	18

The Dialysate solution will be Prism0cal B22; calcium-free solutions should be used on the dialysate scale to prevent restoration of ionized calcium levels and coagulation in the filter.

Prism0cal B22									
Sodium	Potassium	Calcium	Magnesium	Chloride	Phosphate	Lactate	Bicarbonate	Glucose	Citrate
140	4	0	0.75	120.5	0	3	22	6.1	0

Phoxilium will be the first line fluid for the replacement scale. The use of Phoxilium will aid in the restoration of phosphate lost during filtration. Contains no glucose so close monitoring is essential. Phoxilium contains calcium so the return line should be closely observed for signs of clotting.

Phoxilium									
Sodium	Potassium	Calcium	Magnesium	Chloride	Phosphate	Lactate	Bicarbonate	Glucose	Citrate
140	4	1.25	0.6	115.9	1.2	0	30	0	0

Please discuss any patients with high potassium levels with consultant before commencing treatment.

Fluid bags need to be changed every 24 hours.

5. Considerations prior to commencing therapy

5.1 Adding electrolytes to fluid bags

With the exception of sodium, no additives should be added to any of the fluid bags.

If the patient requires additional phosphate then please discuss this with the consultant and pharmacist. This should then be given as a direct correction to the patient.

In cases of hypernatraemia in patients requiring CRRT it may be necessary to add sodium to replacement/dialysis fluids to ensure sodium correction does not occur too rapidly. The sodium content of Prism0cal B22 and Phoxilium is 140mmol/L, so without the addition there is a significant risk the patients' serum sodium could drop too quickly.

If an addition is required this must be clearly documented on the patients CVVH/CVVHDF Daily Prescription and Record Chart and the patient's serum sodium must be closely monitored. If the patient's plasma sodium is greater than 150mmol/L follow the guidance below for adding sodium (sodium should **NOT** be added to the citrate 18/0 fluid bag):

Target Na^+ (mmol/L)	Addition to 5 litre bag (Prism0cal B22/Phoxilium)	
150	10mls of sodium chloride 30%	Remove same volume from replacement/dialysate bag before addition (e.g. for target 150mmol/L remove 10mls from Prism0cal B22/Phoxilium, then add 10mls sodium chloride 30%)
155	15mls of sodium chloride 30%	
160	20mls of sodium chloride 30%	
165	25mls of sodium chloride 30%	
170	30mls of sodium chloride 30%	
175	35mls of sodium chloride 30%	
180	40mls of sodium chloride 30%	
185	45mls of sodium chloride 30%	
190	50mls of sodium chloride 30%	

For patients on heparin please see Appendix Two for more information on adding electrolytes.

5.2 Access

Temporary central venous lines are used for CRRT within PCCU. Follow the guideline for insertion of CVL in PCCU. The use of ultrasound guidance when inserting CVL's should strictly be adhered to.

Weight	Type	Size	Line lock
<10kg	**Braun or similar**	2 x 18G (green) peripheral cannula	0.2ml 1.3ml with connection Heparin 100units/ml
	Gam Cath	6.5Fr x 7.5cm	Lock using volume of line plus 0.2ml Heparin 100units/ml Prescribe on front of CVVHDF chart
		6.5Fr x12.5cm	
10-20kg	**Gam Cath**	8Fr x 10cm	
		8Fr x12.5cm	
>20kg	**Gam Cath**	11Fr x15cm	
		11Fr x 20cm	

Heparin line lock MUST be aspirated and discarded before connection to patient.

5.3 Prior to connecting

Obtain baseline bloods: to include ABG, FBC, U+E, LFT, magnesium, phosphate, total calcium and clotting.

Check the patient's iCa and magnesium levels are within normal limits:

- iCa >1.2 start calcium compensation at 90%
- iCa 1.0-1.2 start calcium compensation at 100%
- iCa <1.0 start calcium compensation at 110%

If patients iCa level is very low consider giving a correction prior to commencing treatment. Also if the patient already has a calcium infusion running then keep this going whilst filtration is established. Once patient's iCa levels are at desired level the calcium infusion **not** being delivered by the PrisMax can be stopped.

- Magnesium levels <0.7 should be corrected (if arrhythmias present then <1mmol/l). This should be done according to unit policy. Discuss with consultant and pharmacist before replacing.

With citrate, effectiveness of anticoagulation is monitored by taking iCa levels from the filter so Activated Clotting Times (ACTs) are not required prior to or during treatment.

5.4 Equipment required:

- PrisMax circuit HF20/ST60/ST100 (see prescription for size guide)
  If patient requires more efficient treatment next size up filter can be used, discuss with Paediatric Renal Critical Care Nurse prior to commencing.
- Dedicated calcium infusion line (CA250)
- TherMax disposable if using ST circuits
- 50mL luer lock syringe
- 5 litre bag Prismocitrate 18/0 to be used on the pre blood pump scale
- 5 litre bag Prism0cal B22 to be used on the dialysate scale
- 5 litre bag Phoxilium to be used on replacement scale
- 1 litre bag Plasmalyte 148 for priming
- Calcium Gluconate 10%
- Ensure at least one adult unit of packed red cells is available in blood bank

To set up the Prismax for citrate anticoagulation please refer to the initiating CVVHDF with citrate document which can be found on back of PrisMax

5.5 Priming

Plasmalyte 148 is now the priming fluid of choice; this will be suitable for the majority of patients. If the patient has a high potassium level then 0.9% sodium chloride can be used instead. With citrate a heparin prime is no longer necessary; just one prime with Plasmalyte 148 is all that is required.

A 4.5% HAS prime can be considered if required, please discuss with consultant.

Blood priming should **not** be routinely practised; however there might be an occasion when this is necessary such as in very low weight babies. Please discuss with sif a patient requires blood please run a **transfusion** prior to or during commencement of therapy.

5.6 Starting parameters

- Always set up in CVVHDF
- Initial starting citrate dose 4mmol/L, only change after discussion with consultant or renal critical care nurse.
- If patient's iCa within normal range start calcium compensation at 100%
- Due to the blood pump speed being considerably slower than previously used, there is no need to commence treatment at half the blood pump speed for patients <50kg.
- For patients >50kg you may want to start at a lower blood pump speed and build up when the patient is haemodynamically stable.

5.7 Unintended patient fluid loss or gain limit

This is the difference between the fluid removal measured on the machine and the set fluid removal rate over the last 3 hours. Once this limit has been reached the PrisMax will stop and treatment will not be able to continue. The default limit is 60-400mls over 3 hours, but should be set based on patient's weight, clinical condition and haemodynamic stability.

5.8 Flow rates

Initial Treatment Settings						
	<5kg	5-11kg	11-18kg	18-30kg	30-50kg	>50kg
Blood flow rate	20ml/min	30ml/min	50ml/min	3ml/kg/min		
PBP citrate	Starting dose: 4mmol/L. Adjust during treatment according to algorithm.					
Dialysate	Commence at 10ml/kg/hr (can increase to 50ml/kg/hr)					
Replacement	20ml/hr	30ml/hr	50ml/hr	100ml/hr	150ml/hr	200ml/hr
Calcium syringe	Initially start at 100% if patient calcium normal. Adjust during treatment according to algorithm.					
Set patient gain/loss limit	This is set at 10ml/kg over 3 hours, once set this limit cannot be changed during treatment.					

These are initial flows for commencing treatment and can be altered depending on patient's condition. For example: if patient has hyperammonia then start dialysis rate at 50ml/kg/hr and titrate rate according to ammonia level. If patient has high sodium then you can slow down the flow rates. Please see **Appendix One** for clearance table, to increase efficiency go up the weight brackets and to decrease efficiency then go down the weight brackets

6. Patient fluid removal rate

This is calculated on an hourly basis depending on actual patient fluid balance, desired fluid balance and condition and stability of the patient. Individual prescription depends on input (i.e. nutrition, IV fluids, drugs) and output (i.e. urine, gastric, drain losses). The PrisMax will continue to run at the set hourly rate until changed by staff. The rate **must** be reviewed every hour. Beware of removing fluid too quickly.

If a negative balance is required this needs to be prescribed in ml/hr. Net fluid removal rate refers to desired net removal (e.g. 0ml/hr would mean a neutral balance to the patient, 10ml/hr would mean -10ml/hr to the patient). Net fluid removal rate and hourly actual fluid balance both need to be added together to work out patient fluid removal rate to be programmed (e.g. total hourly amount of IV fluids and infusions is 45ml/hr and 10ml/hr net removal prescribed = 55mls/hr needs to be programmed into the machine). Do not remove fluid bolus given to support blood pressure or intravascular loss. Blood products which have **not** been administered for volume should be added to the programed fluid removal rate.

If the machine shows a minus number that means that it has gained that amount of fluid. This may occur when treatment is first commenced, but should readjust itself after a few minutes.

Deciding exactly how much fluid to remove from the patient is complex as it depends on many clinical factors including urine output, insensible loss, hypervolaemia/hypovolaemia and clinical observations.

EXTREME CAUTION should be used when setting the patient fluid loss rate, as the PrisMax will try to remove that fluid; it has no way of assessing the effect on the patient. It will continue to remove fluid even when the patient is **HYPOVOLAEMIC.** In low body weight children extra caution is advised in assessing and programming fluid removal rates. No Paediatric CRRT equipment is accurate ml for ml and there may be some discrepancies in what the machine actually achieves.

Always treat the patient NOT the machine.

7. Considerations during therapy

7.1 Care and clinical monitoring of patient

- Continuous monitoring of cardiovascular and respiratory parameters should be undertaken.
- Ensure cardiovascular observations are recorded on PCCU chart hourly or half hourly depending on stability of patient.
- All patients who are receiving CVVH/CVVHDF should have central/peripheral temperature*, heart rate and arterial blood pressure (*central temperature does not have to be a rectal temperature).
- Fluid balance needs careful monitoring because of the large volumes of fluid being removed/infused. Weigh patient on daily basis.
- There are inherent errors in all the measures of fluid balance therefore it is wise to assess the following factors before deciding upon the hydration status of the patient in relation to CRRT:
    - Fluid balance
    - Clinical examination (HR,ABP,CVP, etc..)
    - Biochemistry
    - Haematocrit
    - Weight (preferably use a bed with weighing scales inbuilt)

Always treat the patient NOT the machine.

7.2 Pharmacological considerations

Drug removal by haemofiltration/haemodiafiltration depends on molecular weight, albumin binding, water solubility and volume of distribution, therefore some drugs' handling properties are changed by the therapy. Filtration will remove non-protein bound, water soluble drugs, which are available in the circulation. Adding dialysate flow will cause more efficient drug removal by diffusion. Drug dose changes should be checked with a pharmacist.

*Contrast is efficiently removed by filtration

*IVIG does not pass through the haemofilter most commonly used on PCCU

7.3 Temperature control

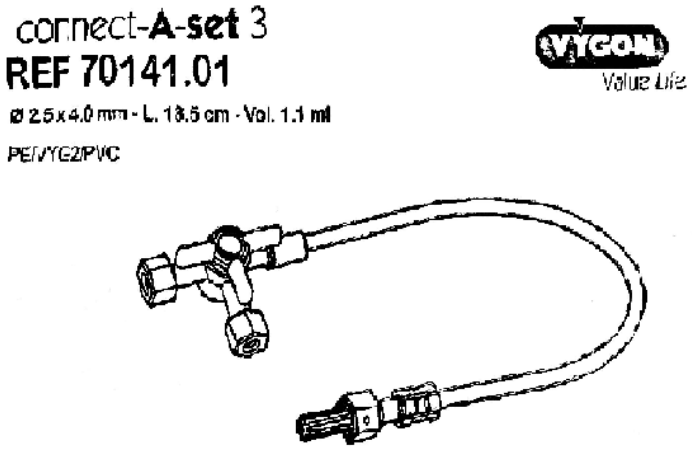
As the patient's blood is removed from their body and pumped through the circuit it significantly cools down so it is essential that a blood warming device is used during treatment. There are two options to heat the patient's blood, the TherMax for ST circuits and the Prismacomfort for HF20 circuits.

- Follow on screen instructions when setting up PrisMax as the screen will guide you through set up of both devices
- The Prismacomfort should be set 1-2^{o}C above the desired patient temperature and attached to the Return line.
- As the heater sleeve covers the Return line it is essential that a portion of the line is left exposed next to the patient's catheter so any air will be visible.
- The TherMax should be set at 37°C
- Additional warming devices may be required (e.g. overhead heater, Bair hugger).
- Beware of both blood warming devices masking pyrexia.

8. Low body weight patients (<4kg)

8.1 Access

For very small patients if siting a 6.5fg or 8fg double lumen central venous catheter is not possible, we advise two 18G cannulas in separate sites. A short connection line with a 3-way tap (see below) will need to be attached to these cannulas prior to connecting the CRRT circuit. If the cannula needs to be used as a point of access in an emergency then the blood pump must be stopped.



8.2 Temperature Control

As hypothermia is a serious complication of CRRT, particularly within this group of patients, additional warming devices will be required. Both access and return limbs of the circuit should be actively heated with original heating sleeves provided by manufacturer. Close monitoring of the patient's temperature is paramount.

9. Considerations for septic patients

9.1 Calcium infusion

Many of the septic patients on PCCU will already be on a calcium infusion due to their inotropic requirements. If this is the case, still continue to run this infusion whilst treatment via the PrisMax is commenced. Once the patient's iCa is within normal range then the calcium infusion being delivered via the Alaris syringe pump can be turned off. The calcium infusion being delivered via the Prismaflex can be used to maintain optimum patient iCa levels.

Please be aware that if the PrisMax is discontinued for any reason then the patient won't be receiving any calcium. If treatment is going to be stopped for a while then please recommence a calcium infusion on the Alaris syringe pump as soon as possible to prevent a decrease in the patient's iCa. This is only applicable if patient was on a calcium infusion for inotropic support pre CVVHDF.

9.2 Transmembrane pressure (TMP)

TMP is the hydrostatic pressure gradient across the filter membrane i.e. the difference in pressure between the blood compartment and the dialysate compartment. This is the driving force that causes ultrafiltration. A rise in TMP suggests that there is clogging occurring in the filter. This is a natural occurrence during treatment and can occur more frequently in septic patients, thought to be due to the adsorption of inflammatory markers to the filter membrane. Unfortunately once the TMP starts to rise there isn't much that can be done to resolve the issue. Making the PrisMax work less by reducing the patient fluid removal or replacement rate may stop TMP rising too quickly but this will mean treatment is less effective. So ultimately the only solution is to effectively stop treatment and set up a new circuit.

9.3 High flow replacement

When using heparin for anticoagulation it was possible to increase the flow rates to achieve a more efficient treatment. However this is more complicated with citrate anticoagulation, mainly due to not being able to manually change the pre blood pump flow rate. If a more efficient treatment is required then this can be achieved by moving the patient up the weight brackets until desired treatment is achieved (see Appendix One). When doing this change blood pump, dialysate and replacements flow rates simultaneously.

10. Monitoring

10.1 iCa – post filter and patient

Within the first hour after treatment has been commenced, the iCa level of the filter and the patient need to be checked. Take a blood sample from the blue port on the circuit and another blood sample from the patient's arterial line. Compare the results to the table below and alter the citrate dose and/or calcium compensation accordingly. After initial blood samples repeat both again 1 hour later even if first results in the normal range. If the second set of levels remain in the normal range then you can monitor 4 hourly.

	Filter Ca^{2+} >0.35	**Filter Ca^{2+} 0.25-0.35**	**Filter Ca^{2+} <0.25**
Patient Ca^{2+} <1.0	Increase citrate dose by 0.5mmol/L blood Increase calcium compensation by 10%	Increase calcium compensation by 10%	Decrease citrate dose by 0.5mmol/L blood
Patient Ca^{2+} 1.0-1.2	Increase citrate dose by 0.5mmol/L blood	**Normal Ideal Values - no change needed.**	Decrease citrate dose by 0.5mmol/L blood
Patient Ca^{2+} >1.2	Decrease calcium compensation by 10%	Decrease calcium compensation by 10%	Decrease calcium compensation by 10% Decrease citrate dose by 0.5mmol/L blood

- Changes must be documented and checked by two nurses and signed for on prescription chart.
- After adjustments to citrate dose and calcium compensation are made, iCa must be checked in both the patient and the filter after 1 hour.
- Check post filter and patient iCa hourly until ideal values have been established, then 4 hourly.
- Increased requirements for calcium compensation could indicate citrate accumulation, so check *Total Calcium/iCa patient ratio (see below).*
- If the citrate dose is reduced, pre blood pump and total effluent will reduce. If total effluent falls below 30mL/kg/hr, gradually increase replacement flow rate until a dose of 30mL/kg/hr is achieved.

10.2 Total Calcium/iCa patient ratio (calcium T:I ratio)

Perform blood total calcium with morning bloods the morning after treatment has been commenced. Divide patient's total calcium by the patient's iCa and then action as below. If stable repeat daily. Inform renal critical care nurse if ratio >2.5.

Calcium T:I ratio	Action
<2.5	No change needed. Check daily
>2.5	Aim for post filter iCa 0.35-0.4mmol/L by decreasing citrate dose in 0.5mmol/L increments until range achieved, check calcium T:I ratio after 1hour See *Citrate Accumulation* section if calcium T:I ratio still >2.5 after 1mmol/L decrease in citrate dose

10.3 pH acid/base balance

Aim for pH 7.35-7.45

Metabolic acidosis (pH <7.35, BE <4mmol/L, HCO_3 <22mmol/L)

Most patients with AKI have some degree of metabolic acidosis on commencement of treatment. This should improve over the first few hours of treatment.

If there is a failure to improve BE/HCO_3 towards normal, consider:

- Decreasing dialysate rate by 50% from baseline, therefore more citrate will reach the patient
- Increasing blood flow rate which will increase citrate delivery
- Giving systemic sodium bicarbonate to the patient (consider respiratory acidosis contribution in first instance, so ventilation is optimised)

These will have different effects on clearance, potential for citrate toxicity and cardiovascular status and should be discussed with consultant and renal critical care nurse.

Metabolic alkalosis (pH >7.45, BE >+4mmol/L, HCO3 >25mmol/L)

This occurs due to the metabolism of citrate into bicarbonate (1mmol citrate converts to 3mmol bicarbonate), plus the addition of bicarbonate via the dialysate fluid. May also indicate citrate accumulation so check calcium T:I ratio. Consider:

- Doubling baseline dialysate flow, this will increase citrate clearance
- Decreasing blood flow (min 20mL/min) which will reduce citrate intake
- Be aware of other reasons for the alkalosis and gain ensure ventilation is optimised

These options will have differing effects on clearance, potential for citrate toxicity and cardiovascular status and should be discussed with consultant and renal critical care nurse.

10.4 What bloods to take and when

Calcium monitoring – timing summary	**Initially**	**And then**
Post filter ionised Ca (blood gas from ***blue*** port in circuit Target 0.25-0.35mmol/L	Within the first hour after commencing then 1 hour after initial levels	4 hourly once stable
Patient systemic iCa (blood gas from patient) Target 1.0-1.2mmol/L		
Post filter gas and patient gas must be taken at the same time		
Patient total calcium (not corrected calcium) Target 2.2-2.5mmol/L	With morning bloods the day after commencing	Daily once stable
Calcium ratio (total Ca/patient systemic iCa) Target ratio <2.5		
Blood sampling and frequency		
Arterial blood gas Pay particular attention to pH, lactate, bicarbonate, sodium, potassium, glucose, iCa	Within the first hour after commencing then 1 hour after initial levels	4 hourly once stable
U's & E's, plus magnesium and phosphate	6 hours after commencing	12 hourly once stable
Clotting	Every 12 hours	
FBC	Daily	

11. Potential problems whilst undergoing treatment

11.1 Emergency Disconnection

In some circumstances emergency disconnection is required such as when lines have clotted, technical failure or evacuation of the unit. In these circumstances wash back should be considered if possible. CVVH/CVVHDF catheter should then be flushed and locked with heparin or at least with sodium chloride 0.9%.

11.2 Cardiac Arrest

In the event of cardiac arrest while the patient is undergoing CVVH/CVVHDF, treatment should be stopped and the line aspirated, flushed and locked as time allows. It may be an option to wash back the blood in the circuit to the patient, if deemed necessary. In some circumstances continuing filtration may be appropriate (e.g. if being used for life threatening electrolyte disturbance like HYPERKALEMIA). Haemofiltration catheters are central venous access and can be used instead of standard central lines in an emergency.

11.3 Air Embolism

In the event of the patient having an air embolism, attempt to aspirate air using the central line. To do so, put the patient on their left side with their head down. Summon emergency assistance.

11.4 Citrate Accumulation

When more citrate is being infused than can be cleared by either metabolic or dialysis pathways, the calcium-citrate complex remains in the patient's circulation. As most of this complex is metabolised by the liver, citrate accumulation is more likely to occur in patients with liver failure. The citrate molecule itself is not toxic however the aim is to avoid the secondary effects which are hypocalcemia and acidosis

The main indicator for citrate accumulation is an increasing total calcium with decreasing patient iCa and a calcium T:I ratio of >2.5. If this ratio remains high despite steps taken in *Total Calcium/iCa patient ratio* section consider the following actions to resolve the problem:

- Reduce the citrate to 2mmol/L
- Repeat ratio after 30mins
- If ratio remains >2.5, double the baseline dialysate flow, this will increase citrate clearance
- Decreasing blood pump speed (min 20mls/min), will also decrease the total administered citrate
- If improvement seen, restart citrate at 70% of previous citrate dose
- Monitor the iCa of the circuit hourly to ensure adequate anticoagulation of the circuit.

If despite these actions the calcium T:I ratio remains high do not restart citrate and discuss converting to alternative anticoagulation with consultant.

Appendix One - **Clearance table**

To increase clearance move patient up weight brackets

To decrease clearance move patient down weight brackets

Weight	BFR	Dialysate	Replacement	Effluent dose
80	200	800	200	46
70	200	700	200	51
60	180	600	200	54
50	150	500	150	54
45	135	450	150	54
40	120	400	150	54
35	105	350	150	55
30	90	300	100	54
25	75	250	100	55
20	60	200	100	56
18	50	180	50	50
16	50	160	50	55
14	50	140	50	62
12	50	120	50	70
11	50	110	50	76
10	30	100	30	43
9	30	90	30	58
8	30	80	30	64
7	30	70	30	84
6	30	60	30	82
5	30	50	30	97
4	20	40	20	82
3	20	30	20	107
2	20	20	20	155

Appendix Two - **CVVH/CVVHDF with heparin anticoagulation**

In the rare event that citrate is contraindicated for a patient e.g. in citrate accumulation, heparin can still be used for anticoagulation of the circuit.

Properties

Heparin inhibits coagulation by preventing the conversion of prothrombin to thrombin and fibrinogen to fibrin. Heparin displays almost immediate action following intravenous administration. The clotting time then returns to normal within 2-6 hours after the infusion is discontinued. It binds extensively to plasma proteins and is activated in the liver and excreted in the urine.

The action of heparin can be reversed with Protamine Sulphate. The dose is dependent on the heparin rate - see the BNFC for more information. The protamine dose should be based on the cumulative heparin dose given over the previous 2 hours.

Administration and dosage

Heparin is administered into the dedicated heparin infusion line on the access side of the PrisMax circuit.

The initial bolus (if appropriate) should be given as blood reaches the pre filter port; this is then followed by a continuous infusion. The aim is to raise the patient's clotting time sufficiently to prevent clotting in the filter and lines, while not increasing the risk of bleeding to the patient.

The following table should be used when making up the heparin infusion; this should now be made up in a 50ml syringe.

Pre-treatment ACT	Bolus loading dose	Maintenance infusion	Strength dilution	Dose range
Normal: ACT <180	25-50 units/kg	100 units/kg in **40ml** sodium chloride 0.9%	2ml/hr = 5 units/kg/hr	2-10ml/hr
Abnormal: ACT 180-200	12.5 units/kg	50 units/kg in **40ml** sodium chloride 0.9%	2ml/hr = 2.5 units/kg/hr	2-10ml/hr
Abnormal: ACT >200	No bolus	50 units/kg in **40ml** sodium chloride 0.9%	2ml/hr = 2.5 units/kg/hr	2-10ml/hr

The level of anticoagulation is monitored by measuring the activated clotted time (ACT); this is measured using an Actalyke MINI machine.

A clotting time that is taken pre-filtration and is not heparinised, such as at initial insertion of haemofiltration catheter must always be taken. This is essential because each individual will respond differently to the same dose of heparin; therefore, their reaction to it (the

increase in the clotting time following heparin administration) will be different. The initial ACT should be 100-130 seconds.

Once commenced on treatment you will need to check an ACT within one hour. Further ACTs should be taken 1-2 hourly. The aim is to maintain the patients clotting time within the pre-determined limits on the prescription chart. **The maximum concentration of heparin should be 100 units/kg/40ml with a maximum rate of 10ml/hr (25 units/kg/hr).** Should the ACTs remain low on this maximum rate the target range needs to be reviewed, amended and documented on the prescription chart.

If the ACT is low, thrombosis and clotting may occur – in the circuit and patient

If the ACT is too high, bleeding may occur – in the patient

The patient's clotting must also be monitored closely via laboratory bloods; should the patients clotting become deranged the ACT target range may need to be reviewed and reduced.

Contraindications

- Active bleeding
- Imminent or recent surgery
- Coagulopathies such as thrombocytopenia, especially in septic and oncology patients
- Heparin Induced Thrombocytopenia (H.I.T)
- Disseminated Intravascular Coagulation (D.I.C)
- Liver disease
- Haemophilia
- Diabetes
- Pericarditis

CVVH/CVVHDF may be carried out in the above circumstances with minimal or no heparin or with an alternative such as Epoprostenol (Appendix Three).

Flow rates for heparin

Blood Flow Rates Affected by vascular access and patient's condition
Standard blood flow rate = 6-9ml/kg/min, 12-15ml/kg/min in low weight babies Minimum flow rate 30ml/min Blood flow rates will not affect clearances There is no such thing as too much blood flow (other than max limit set by filter size). In patients >30kg aim for a blood pump speed of 180-240mL/min, rates above this are not always achievable or necessary. Blood flows should be adjusted in high flow CRRT to compensate for excessive haemoconcentration of the filter

Replacement rate = ultrafiltration & convection medium and large molecule clearance (e.g. products of inflammation/cytokines)
Standard replacement rate = 30ml/kg/hr On PrisMax this is programmed as 10ml/kg/hr for Pre Blood Pump and 20ml/kg/hr for Replacement Higher rates can be used in sepsis and hyperammonia up to 100ml/kg/hr (this should be increased incrementally and patient response closely monitored) Increasing % pre-dilution may be required when having problems with the filter. Majority pre-dilution may be needed in certain patients (**Max 90% pre, 10% post.**)

Dialysate rates = diffusion Small molecule clearance (e.g. urea/ammonia)
Standard dialysate rates = 20ml/kg/hr can be increased up to 50ml/kg/hr (this should be increased incrementally and patient response closely monitored)

In AKI no evidence exists to support one mode over another. A combination of convection and diffusion to optimise the removal of small and medium sized molecules may be preferred

Typical starting prescription for fluid overload, oliguria would be 30ml/kg/hr convection (replacement), with the addition in SIRS/Sepsis of 20ml/kg/hr diffusion (dialysis).

Adding electrolytes to fluid bags

Additives are always prescribed to be added per litre of fluid and as a total dose. Care needs to be taken when making up the fluid as a result. When additives are required more frequent blood sampling will be required.

Electrolyte	Indication	Additive
Phosphate	Serum Phosphate <2mmol/L	Sodium glycerophosphate 1mmol/L (5mmols added to 5 litre bag)
Glucose	Serum glucose <6mmol/L	Glucose 1.1 grams/L (6mmol/L) (5.5 grams glucose to 5 litre bag of Hemosol BO,11mls of 50% glucose).

Management of hypernatraemia

This is the same as with citrate anticoagulation, the only difference being sodium chloride can be added to all fluid bags.

Appendix Three - **CVVH/CVVHDF with epoprostenol anticoagulation**

If patient has contraindications to citrate and heparin then Epoprostenol can be used as an anticoagulant. It can also be used in combination with heparin or citrate if these are proving inadequate running on their own. Epoprostenol is used to anticoagulate the patient and therefore the blood that is traveling through the circuit.

When administering Epoprostenol it must be delivered directly to the patient, not through the PrisMax machine. Use a dedicated central line for administration. If struggling with access add a 3-way tap on to return line of circuit.

Contraindications

- Treat any hypovolaemia before commencing infusion.
- Avoid sudden withdrawal due to the potential for rebound pulmonary hypertension.
- Contraindicated in severe left ventricular dysfunction and pulmonary veno-occlusive disease.
- Inhibition of platelet aggregration can cause unwanted bleeding, therefore monitor coagulation status carefully, particularly if on other anticoagulants.
- Vasodilator effect may augment or be augmented by other vasodilators.
- Caution if patient has abnormal coagulation.

Please see pharmacopeia for more information:

http://nuhnet/nuh_documents/Guidelines/Family%20Health/Children%27s%20Hospital%20-%20PICU/2560.pdf

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