Continuous renal replacement therapy (cRRT) Prescription, observations & record of therapy PLEASE, DO NOT RECORD this information anywhere else	Patient's Name			
	Date of birth		Gender (circle)	M / F
	St George's Hospital No.			
	NHS number			
PLEASE complete this form for **EVERY** cRRT **CIRCUIT** used. Keep completed forms with the ICU charts for the audit team.		PLEASE affix a patient's sticker if available		

1. Patient information – TO BE COMPLETD BY PRESCRIBING Dr

Height cm	measured? ☐ OR estimated? ☐	Actual body weight Kg	source?
Ideal body weight (IBW) Kg	use look up chart ***OR*** free smart phone app such as Qx calculate		

2. Indication(s) for cRRT - please tick ALL that apply **- TO BE COMPLETD BY PRESCRIBING Dr**

Hyperkalaemia ☐	**most recent** K^+	mmol/l	Time & date	rapidly rising? ☐
DEFINIITON: K^+ ≥6.5mmol/l *AND / OR* rising from 5.5 @ >0.25mmol/l/hr DESPITE continuous IV insulin + IV $NaHCO_3$ + enteral sodium zirconium cyclosilicate				
Acidosis ☐	**most recent** pH		Time & date	high dose vasoactive drugs in use? ☐
DEFINIITON: arterial pH<7.2 DESPITE medical Rx with continuous IV $NaHCO_3$ *AND* noradrenaline >0.2mcg/kg/min to maintain a MAP of 60-70mmHg				
Uraemia ☐	**most recent** urea	mmol/l	Time & date	rapidly rising? ☐
DEFINIITON: urea >40mmol/l *OR* rising by >12mmol/l/day				

Fluid overload ☐	DEFINIITON: urine output <0.3ml/kg/hr for >12 hours *AND* a negative furosemide stress test (FST) - *see notes on page 12* FST = 1.0 mg/kg IV bolus for loop diuretic naïve patients (1.5 mg/kg for patients with chronic loop diuretic exposure) Negative result = urine output <100ml/hr for 2 hours following bolus ***AND*** at least one of the following:
	☐ Hypoxaemia = PaO_2:FiO_2 ≤13.3kPa AND / OR dynamic compliance [Vt / (peak insp. Pressure - PEEP) < 30ml/cmH_2O DESPITE optimal ventilation strategy (including trail of prone positioning, if appropriate)
	☐ Acute cardiogenic shock from an acute reversible pathology with echocardiographic evidence of RV volume overload Dilated RV diameter / RV > LV with moderate to severe TR and septum moving towards the LV during diastole causing a D shape. CVP >12mmHg with sustained rise >4mmHg on fluid challenge (taking mean airway pressure into account) see https://www.123sonography.com/ebook/right-ventricular-volume-overload
	☐ Abdominal compartment syndrome
	☐ Hypertension refractory to medical Rx with acute end organ injury e.g. posterior reversible encephalopathy syndrome
Other ☐	*please describe*

☐ First episode of cRRT OR ☐ ongoing cRRT during a single ICU episode OR ☐ in place of chronic RRT (PD / iHD)

Decision to commence cRRT made by (print name)	Date and time of decision

3. Review of nutrition and drugs - during cRRT it may be advantageous to switch to a different enteral feeding regime **AND**, most drugs that are renally cleared, including antibiotics, should be given at full dose (i.e. as if the patient had normal renal function). Please review these aspects of the patients care and document any changes you make so that these changes can be reviewed as and when the patient is OFF cRRT. - **TO BE COMPLETD BY PRESCRIBING Dr**

Patient's name	MRN

4. cRRT STARTING prescription - current evidence suggests that 15ml/kg/hr over 24 hours is the minimum effective "dose" or "rate". To offset / mitigate against stoppages / loss of circuits etc it is recommended that patients be commenced at **20ml/kg/hr** BUT have the dose (efflutent rate) titrated to achieve pre-defined endpoints (see page 12).
All calculations should use ideal rather than actual body weight. - TO BE COMPLETD BY PRESCRIBING Dr FOR GUIDANCE SEE BACK PAGE

Size of "kidney": HF12 (small) ☐ **OR** HF19 (large) ☐	**Target blood pump speed** ml/min	**First fluid bag:** K^+ = 0 ☐ **OR** K^+ = 4.0mmol/l ☐
Dose / rate: 20ml/kg/hr ☐ 15ml/kg/hr ☐ OR other ml/kg/hr	ENTER **IBW** kg x **dose** ml/kg/hr =	ml/hr referred to below as ***A***

Mode	Standard starting settings	Value for this patient (ml/hr) ♦	Standard starting settings	Value for this patient (ml/hr) ♦
☐ CVVH(F)	Predilution = ***A*** ÷ 3		Post replacement = ***A*** ÷ 3 x 2	
☐ CVVHDF	Counter current = ***A*** ÷ 2		Post replacement = ***A*** ÷ 2	

Fluid removal: rate ml/hr ☐ ***OR*** fluid balance target (state + or -) ml ☐ by (date & time)

Anticoagulation **(refer to page 9)** **-** MUST be prescribed on Cerner (iCLIP)

Platelet count x10^9/L | HIT (score see table →)

☐ prime with heparin ☐ heparin infusion (target APTTr 1.5-2.0) ***OR***

☐ alternative strategy (detail AND reasoning below) e.g. therapeutic anticoagulation.

Category	0 point	1 point	2 points
Thrombocytopaenia	< 30% fall **OR** nadir < 10 x 10^9/L	30-50% fall **OR** nadir 10-19 x 10^9/L	>50% fall **OR** nadir ≥ 20 x 10^9/L
Timing of decrease in platelet count	< 4 days (no recent heparin)	> 10 days **OR** fall ≤ 1 day **AND** prior heparin ex-posure > 30 days ago	5-10 days **OR** ≤ 1 day but heparin in last 30 days
Thrombosis or other sequelae	None	Progressive / recurrent thrombosis **OR** non-necro-tizing skin lesions **OR** Possible thrombosis	Proven thrombosis **OR** Skin necrosis **OR** Anaphylaxis
Other causes of thrombocytopaenia	Definite	Possible	None evident

Set replacement fluid temp. to °C | **Prescribed by (PRINT and sign, date and time)**

♦ **You MAY wish to use an alternative calculation such as 90% predilution and 10% post replacement - see back page for guidance** ♦

Indication and prescription agreed by ICU consultant (PRINT name)

5. Record of review and changes to cRRT prescription - best practice is to review the effectiveness of the therapy at least daily and at most, 6 hourly. At each review you should aim to answer the follow questions and depending upon the answers, titrate the prescription accordingly. Additionally, the patient's clinical circumstance may warrant specific short-term changes such as a negative fluid challenge. Please document all short-term changes, problems and any interruptions (e.g. due to frequent alarms or temporary wash-back and re-circulation of the same circuit) in box 8 on page 7.

- Is the patient's K^+ 4.0-5.5mmol/l?
- Is the patient's arterial pH 7.20-7.40?
- Has the patient's urea fallen by 10-14mmol/l in 24 hours?
- Has the most recent fluid balance / fluid removal target been achieved?
- Are there vascular access or blood pump speed issues?
- Are there any clots in in the circuit or bleeding concerns in the patient?
- How much longer do you anticipate the current therapy session will last (maximum 80 hours per circuit)?

All calculations should use ideal rather than actual body weight. - TO BE COMPLETD BY PRESCRIBING Dr FOR GUIDANCE SEE BACK PAGE

Date and time of review	**Target blood pump speed** ml/min	**Fluid type:** K^+ = 0 ☐ **OR** K^+ = 4.0mmol/l ☐
Dose / rate: 20ml/kg/hr ☐ 15ml/kg/hr ☐ OR other ml/kg/hr	ENTER **IBW** kg x **dose** ml/kg/hr =	ml/hr referred to below as ***A***

Mode	Standard settings	Value for this patient (ml/hr) ♦	Standard settings	Value for this patient (ml/hr) ♦
☐ CVVH(F)	Predilution = ***A*** ÷ 3		Post replacement = ***A*** ÷ 3 x 2	
☐ CVVHDF	Counter current = ***A*** ÷ 2		Post replacement = ***A*** ÷ 2	

Fluid removal: rate ml/hr ☐ ***OR*** fluid balance target (state + or -) ml ☐ by (date & time)

Any other changes / comments:

Set replacement fluid temp. to °C | **Prescribed by (PRINT and sign, date and time)**

Prescription agreed by ICU consultant (PRINT name)

Patient's name	MRN

Date and time of review		**Target blood pump speed** ml/min	**Fluid type:** K+ = 0 ☐ **OR** K+ = 4.0mmol/l ☐	
Dose / rate: 20ml/kg/hr ☐ 15ml/kg/hr ☐ OR other ml/kg/hr		ENTER **IBW** kg x **dose** ml/kg/hr = ml/hr referred to below as ***A***		
Mode	**Standard settings**	**Value for this patient (ml/hr)**	**Standard settings**	**Value for this patient (ml/hr)**
☐ CVVH(F)	Predilution = ***A*** ÷ 3		Post replacement = ***A*** ÷ 3 x 2	
☐ CVVHDF	Counter current = ***A*** ÷ 2		Post replacement = ***A*** ÷ 2	
Fluid removal: rate ml/hr ☐ ***OR*** fluid balance target (state + or -) ml ☐ by (date & time)				
Any other changes / comments:				
Set replacement fluid temp. to °C	**Prescribed by (PRINT and sign, date and time)**			
Prescription agreed by ICU consultant (PRINT name)				

Date and time of review		**Target blood pump speed** ml/min	**Fluid type:** K+ = 0 ☐ **OR** K+ = 4.0mmol/l ☐	
Dose / rate: 20ml/kg/hr ☐ 15ml/kg/hr ☐ OR other ml/kg/hr		ENTER **IBW** kg x **dose** ml/kg/hr = ml/hr referred to below as ***A***		
Mode	**Standard settings**	**Value for this patient (ml/hr)**	**Standard settings**	**Value for this patient (ml/hr)**
☐ CVVH(F)	Predilution = ***A*** ÷ 3		Post replacement = ***A*** ÷ 3 x 2	
☐ CVVHDF	Counter current = ***A*** ÷ 2		Post replacement = ***A*** ÷ 2	
Fluid removal: rate ml/hr ☐ ***OR*** fluid balance target (state + or -) ml ☐ by (date & time)				
Any other changes / comments:				
Set replacement fluid temp. to °C	**Prescribed by (PRINT and sign, date and time)**			
Prescription agreed by ICU consultant (PRINT name)				

Date and time of review		**Target blood pump speed** ml/min	**Fluid type:** K+ = 0 ☐ **OR** K+ = 4.0mmol/l ☐	
Dose / rate: 20ml/kg/hr ☐ 15ml/kg/hr ☐ OR other ml/kg/hr		ENTER **IBW** kg x **dose** ml/kg/hr = ml/hr referred to below as ***A***		
Mode	**Standard settings**	**Value for this patient (ml/hr)**	**Standard settings**	**Value for this patient (ml/hr)**
☐ CVVH(F)	Predilution = ***A*** ÷ 3		Post replacement = ***A*** ÷ 3 x 2	
☐ CVVHDF	Counter current = ***A*** ÷ 2		Post replacement = ***A*** ÷ 2	
Fluid removal: rate ml/hr ☐ ***OR*** fluid balance target (state + or -) ml ☐ by (date & time)				
Any other changes / comments:				
Set replacement fluid temp. to °C	**Prescribed by (PRINT and sign, date and time)**			
Prescription agreed by ICU consultant (PRINT name)				

Patient's name	MRN

6a. Pre-treatment checklist - Vascath - there are 3 sizes of vascaths available, a 15cm for RIGHT IJ/subclavian, a 20cm for LEFT IJ/subclavian and a 24cm for femoral use. You MUST ensure the correct size is used at the correct site. Dialysis lines with a THIRD, small, central lumen (for drug administration in longterm term patients) are also available. To assess the adequacy of flow you MUST be able to easily withdraw AND inject 20mls of blood in <3s without interruption to flow. **NURSE**

Site	**Type / make**	**Length**	**Inserted on**
Locked with 5,000units/ml heparin ☐ **on (date & time)**		**Flow adequate in RED lumen** ☐ **& BLUE lumen** ☐ **both aspiration and return**	

6b. Pre-treatment checklist - Filter - Stop time should be the connection time. NOTE RED to BLUE & BLUE to RED connection MAY dramatically reduce treatment efficacy as treated blood is recirculated **- NURSE**

Priming AND recirculation for >20 mins with 10,000units of heparin in 1L of 0.9%NaCl ☐ ***OR*** (details)	**Start time**	**Stop time**
Connection: RED to RED & BLUE to BLUE ☐ ***OR*** RED to BLUE & BLUE to RED ☐ if the latter then why?		

7. Record of replacement fluid type / mixing / checking / administration. NOTE use K^+ free bags if serum K^+>5.5mmol/l. PLEASE document bags DOWN then across **- NURSE**

Date	Time	K^+ in fluid		Mixed by	Checked by	Given By	Date	Time	K^+ in fluid		Mixed by	Checked by	Given By	Date	Time	K^+ in fluid		Mixed by	Checked by	Given By
		0	4.0						0	4.0						0	4.0			
		☐	☐						☐	☐						☐	☐			
		☐	☐						☐	☐						☐	☐			
		☐	☐						☐	☐						☐	☐			
		☐	☐						☐	☐						☐	☐			
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		☐	☐						☐	☐						☐	☐			
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		☐	☐						☐	☐						☐	☐			
		☐	☐						☐	☐						☐	☐			
		☐	☐						☐	☐						☐	☐			
		☐	☐						☐	☐						☐	☐			
		☐	☐						☐	☐						☐	☐			

8a. Filter observation chart - FIRST 24 HOURS OF TREATMENT - NURSE

Hours	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
Time																								
BPS																								
AP																								
RP																								
TMP																								
Hep																								
aPTTr																								
FF%																								
FR%																								
Fluid loss																								

KEY - **BPS** = blood pump speed, **AP** = access pressure, **RP** = return pressure, **TMP** = transmembrane pressure, **Hep** = heparin ***OR*** alternative anticoagulation infusion rate in ml/hr, **FF%** = filtration fraction % (found in the MORE screen option), **FR%** = filtration ration % (found in the MORE screen option, **Fluid loss** = fluid loss total as displayed on screen. **NOTE** if totals reset at any stage, detail this as a CHANGE see next page and restart entries at 0.

8b. Filter observation chart - SECOND 24 HOURS OF TREATMENT - NURSE

Hours	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48
Time																								
BPS																								
AP																								
RP																								
TMP																								
Hep																								
aPTTr																								
FF%																								
FR%																								
Fluid loss																								

KEY - **BPS** = blood pump speed, **AP** = access pressure, **RP** = return pressure, **TMP** = transmembrane pressure, **Hep** = heparin ***OR*** alternative anticoagulation infusion rate in ml/hr, **FF%** = filtration fraction % (found in the MORE screen option), **FR%** = filtration ration % (found in the MORE screen option, **Fluid loss** = fluid loss total as displayed on screen. **NOTE** if totals reset at any stage, detail this as a CHANGE see next page and restart entries at 0.

8c. Filter observation chart - THIRD 24 HOURS OF TREATMENT - NURSE

Hours	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71	72
Time																								
BPS																								
AP																								
RP																								
TMP																								
Hep																								
aPTTR																								
FF%																								
FR%																								
Fluid loss																								

KEY - **BPS** = blood pump speed, **AP** = access pressure, **RP** = return pressure, **TMP** = transmembrane pressure, **Hep** = heparin ***OR*** alternative anticoagulation infusion rate in ml/hr, **FF%** = filtration fraction % (found in the MORE screen option), **FR%** = filtration ration % (found in the MORE screen option, **Fluid loss** = fluid loss total as displayed on screen. **NOTE** if totals reset at any stage, detail this as a CHANGE see next page and restart entries at 0.

8d. Filter observation chart - UP TO MAXIMUM FILTER CIRCUIT LIFE - NURSE

Hours	73	74	75	76	77	78	79	80																
Time																								
BPS																								
AP																								
RP																								
TMP																								
Hep																								
aPTTr																								
FF%																								
FR%																								
Fluid loss																								

KEY - **BPS** = blood pump speed, **AP** = access pressure, **RP** = return pressure, **TMP** = transmembrane pressure, **Hep** = heparin ***OR*** alternative anticoagulation infusion rate in ml/hr, **FF%** = filtration fraction % (found in the MORE screen option), **FR%** = filtration ration % (found in the MORE screen option, **Fluid loss** = fluid loss total as displayed on screen. **NOTE** if totals reset at any stage, detail this as a CHANGE see next page and restart entries at 0.

9. Record any relevant notes and minor prescription changes here- NURSE OR PRESCRIBING Dr

Date & time	Conclusion of review. Record of changes and rationale. Decided by (PRINT name)

10. Cessation of cRRT, post cRRT considerations and checklist - NURSE

Date & time Rx stopped / circuit failed	Circuit washed back YES ☐ NO ☐	If **NO, CONSIDER** if the patient requires a check full blood count AND pRBC transfusion
Reason for cRRT cessation (as much detail as possible)		
Post cRRT considerations and checklist		
Give patient time off cRRT? What are the indications to restart cRRT? Could the patient have intermittent haemodialysis or haemodiafiltration?		
Is the vascath a problem? If so, what is the solutuion? "Lock" and label the vascath with 5000units per ml unfractionated heparin?		
Does the patient need a change to, OR plan for, anticoagulation therapy OR VTE prophylaxis?		
What is the target fluid balance for the next period of time? Are any changes to fluid or nutrition therapy required to achieve this?		
Are any changes to drug dosing or frequency of administration needed?		
What is the long term renal plan?		

"WHY DO WE HAVE THIS CHART?"

1. **cRRT is our most expensive therapy, in terms of consumables (circuit PLUS replacement fluid).**
2. **Current data suggest our circuit life is on average only 15 hours - it should be between 48 and 80 hours.**
3. **We don't know why we appear to be so poor at keeping filters going because we don't record a diagnosis of the failure.**
4. **We have no idea have effectively we deliver this therapy.**
5. **We should document why we start therapy as there appears to be significant variability in the threshold for doing so.**
6. **We don't appear to titrate the therapy to any pre-defined endpoints.**
7. **We don't clearly prescribe what we want.**
8. **We don't record what changes we make and why.**
9. **We don't know how many blood products, especially pRBCs we use as a consequence of unplanned filter loss.**
10. **We are inconsistent at dose adjusting antibiotics and other drugs during and after cRRT**
11. **We are inconsistent at VTE drug prophylaxis during and after cRRT**

Decision tree for circuit anticoagulation for cRRT

Is the patient actively bleeding?

AND / OR

Is the patient very hypocoaguable (on TEG)?

AND / OR

Is the patient very high risk of bleeding with likely catastrophic consequences?

YES

Postpone cRRT

unless

- rapidly rising K^+
- "toxic" acidosis
- Severe pulmonary oedema (fluid overload)

THEN CONSIDER iHD in preference to cRRT
*If cRRT **ONLY** option then*

HIT score

0-3

1. Prime with 10,000 units unfractionated heparin in 1L 0.9% NaCl
2. Recirculate for >20 minutes

4-8

CALL Haematology*

Prime with 1L 0.9% NaCl

- Use "SMALL" HF12 size kidney
- Use high blood pump speed (>250ml/min)
- 90% predilution: 10% post replacement
- ≥20ml/kg/hr total replacement fluid dose

If clots develop in bubble trap and / or return pressure gradually rises

- Ensure there is NO AIR in bubble trap
- Consider disconnection and recirculation and / or Wash-back before circuit fails.
- Check Vascath flows
- Re-consider need for cRRT and / or postpone re-starting
- Depending upon HIT score commence heparin (or alternative) with target aPTTr **1.5-2.0**

NO

HIT score

0-3

Use unfractionated heparin protocol

4-8

CALL Haematology*

Use argatroban protocol

Heparin induced thrombocytopaenia (HIT) score
Circle score for each category.

Category	0 point	1 point	2 points
Thrombocytopaenia	< 30% fall **OR** nadir < 10 x 10^9/L	30-50% fall **OR** nadir 10-19 x 10^9/L	>50% fall **OR** nadir ≥ 20 x 10^9/L
Timing of decrease in platelet count	< 4 days (no recent heparin)	> 10 days **OR** fall ≤ 1 day **AND** prior heparin ex-posure > 30 days ago	5-10 days **OR** ≤ 1 day but heparin in last 30 days
Thrombosis or other sequelae	None	Progressive / recurrent thrombosis **OR** non-necro-tizing skin lesions **OR** Possible thrombosis	Proven thrombosis **OR** Skin necrosis **OR** Anaphylaxis
Other causes of thrombocytopaenia	Definite	Possible	None evident

*HIT score 4-8 **IMPLIES** thrombosis hence patient requires therapeutic anticoagulation with argatroban

Standard Protocol for unfractionated heparin in cRRT circuit

Is therapeutic anticoagulation required AND is the patient NORMOcoaguable / UNLIKELY to be RESISTANT to heparin?
IF HYPERcoaguable / LIKELY to be RESISTANT to heparin THEN use the ENHANCED / HIGH DOSE protocol

Refer to the ENHANCED / HIGH DOSE UFH protocol for definitions of HYPERcoaguable state and heparin resistance

YES

IF possible / practical
establish patient on systemic UFH infusion
AND
achieve reliable therapeutic range aPTTr of 1.5-3.0
BEFORE
starting cRRT

1. Check baseline aPTTr. Alert doctor if >2.0
2. Prepare syringe. Add **25,000** units unfractionated heparin to 50ml normal saline = **500** units/ml.
3. Start heparin **INTO PATIENT**
4. Give 5,000 unit IV bolus then commence infusion @ 2ml/hr (1,000units/hr)

- **Target aPTTr 1.5-3.5**

Monitoring frequency
- Send aPTTr sample 4 hours after initiation and every dose change or any other circuit change
- If stable, send aPTTr sample every 12 hours

1. Prime filter with 10,000 units unfractionated heparin in 1L 0.9%NaCl
2. Recirculate for >20 minutes

aPTTr	ACTION
< 1.2	BOLUS 0.8ml (400units) ***AND*** increase by 0.8ml/hr (400units/hr)
1.2 - 1.4	increase by 0.4ml/hr (200units/hr)
1.5 - 3.5	**NO CHANGE**
3.6 - 4.1	reduce by 0.1ml/hr (50units/hr)
4.1 - 4.6	reduce by 0.2ml/hr (100units/hr)
4.7- 5.2	reduce by 0.4ml/hr (200units/hr)
5.3- 5.9	reduce by 0.6ml/hr (300units/hr)
≥ 6.0	stop for 1 hour, reduce by 1.0ml/hr (500units/hr)

NO

1. Prime filter with 10,000 units unfractionated heparin in 1L 0.9%NaCl
2. Recirculate for >20 minutes
3. Check baseline aPTTr. Alert doctor if >2.0
4. Prepare syringe. Add **10,000** units unfractionated heparin to 50ml normal saline = **200** units/ml.

Start heparin **INTO FILTER CIRUIT**
Give 2,500 unit bolus then commence infusion @ 5ml/hr (1,000units/hr)

- **Target aPTTr 1.5-2.0**

Monitoring frequency
- Send aPTTr sample 4 hours after initiation and every dose change or any other circuit change
- If stable, send aPTTr sample every 12 hours

aPTTr	ACTION
< 1.2	BOLUS 0.8ml (400units) ***AND*** increase by 0.8ml/hr (400units/hr)
1.2 - 1.4	increase by 1.0ml/hr (200units/hr)
1.5 - 2.0	**NO CHANGE**
2.1 - 2.5	reduce by 0.5ml/hr (100units/hr)
2.6 - 3.1	reduce by 1.0ml/hr (200units/hr)
3.2- 4.3	reduce by 1.5ml/hr (300units/hr)
4.4- 4.9	reduce by 2.0ml/hr (400units/hr)
≥ 5.0	stop for 1 hour, reduce by 3.0ml/hr (600units/hr)

Troubleshooting – part 1
If filter circuit clots despite aPTTr >1.5-2.0
- Use "SMALL" HF12 size kidney
- Use high blood pump speed (>250ml/min)
- 90% predilution: 10% post replacement
- ≥20ml/kg/hr total replacement fluid dose
- **Consider** increasing target aPTTr to 2.0-3.0

&

Troubleshooting – part 2
If clots develop in bubble trap and / or return pressure gradually rises
- Ensure there is NO AIR in bubble trap
- Consider disconnection and recirculation and / or Wash-back before circuit fails.
- Check Vascath flows
- Re-consider need for cRRT and / or postpone re-starting
- **Consider** increasing target aPTTr to 2.0-3.0

ENHANCED / HIGH DOSE Protocol for UFH in cRRT circuit

INDICATIONS & DEFINITIONS

Pathologies commonly associated with high risk of a HYPERcoaguable state +/- heparin resistance (HS+/-HR)

- ***COVID-19 / polytrauma / burns / acute severe pancreatitis***

Pre treatment clotting results (NOT including standard VTE prophylactic dose LMWH or UFH) suspicious for HS+/-HR

- ***platelet count ≥450 x10^9/L / fibrinogen ≥4.8g/L / D-dimer ≥3000ng/mL***
- ***citrated kaolin (CK) TEG R ≤4.6min / K ≤0.8min / angle ≥78° / MA ≥69mm / LY30 =0%***
- ***citrated functional fibrinogen (CFF) TEG MA ≥32mm***

4 hours post UFH bolus then infusion (EITHER standard protocols) tests highly suggestive of HS+/-HR

- ***lab aPTTr ≤1.3 / citrated rapid TEG (CRT) ACT ≤150s / ratio of CK R time to CKH R time ≤1.3***

Very highly suggestive of HS+/-HR

- ***Loss of 1 (or more) cRRT circuits due to clots in circuit (most commonly in bubble trap) DESPITE good flows via vascath [DEFINED AS able to tolerate RED-RED & BLUE-BLUE connection with blood pump speed ≥250ml/min without frequent pressure alarms]***

↓

IF possible / practical establish patient on systemic UFH infusion
AND
achieve reliable therapeutic range aPTTr of 2.0-4.5 ***BEFORE*** starting cRRT

↓

1. Prepare syringe. Add **25,000** units unfractionated heparin to 50ml normal saline = **500** units/ml.
2. Start heparin **INTO PATIENT**
3. Give 5,000 unit IV bolus then commence infusion @ 4ml/hr (2,000units/hr)
4. Perform an aPTTr every 4 hours aiming for a target of 2.0-4.5.

PLEASE NOTE patients with a HS+/-HR are likely to have elevated fVIII levels which adversely affect the aPTTr assay and MAY result in falsely low ratios / shortened times.

ONCE 2 successive 4 hourly tests are STABLE at the same infusion rate [ideally 2.5 +/- 0.5], request aPTTr with routine morning bloods and roughly every 12 hours. Make note of this infusion rate as it should be used as the starting infusion rate for the next cRRT session.

↓

1. Prime filter with 10,000 units unfractionated heparin in 1L 0.9%NaCl
2. Recirculate for >20 minutes

↓

aPTTr	ACTION
< 1.3	BOLUS 5.0ml (2,500units) ***AND*** increase by 2.0ml/hr (1,000units/hr)
1.3 - 1.9	increase by 2.0ml/hr (1,000units/hr)
2.0 – 4.5	**NO CHANGE**
4.6 – 6.0	reduce by 1.0ml/hr (500units/hr)
≥ 6.0	stop for 1 hour, reduce by 1.0ml/hr (500units/hr)

1. If the target aPTTr is achieved with <1,000units/hr revert to the standard UFH protocol, therapeutic arm
2. If an aPTTr 2.0-4.5 cannot be reliably achieved despite an infusion rate of 4,000units/hr THEN switch to systemic Argatroban using the 2.0mcg/kg/min dose (HS+/-HR) arm [as opposed to 0.5mcg/kg/min HIT with MOF arm]

Protocols for using Argatroban

HIT score 4-8 / confirmed Dx of HIT AND high risk of bleeding / HYPOcoaguable CKH TEG	HIT score 0-3 AND HYPERcoaguable +/- heparin resistant

IF possible / practical establish patient on systemic Argatroban infusion
AND
achieve reliable therapeutic range aPTTr of 1.5-3.0 ***BEFORE*** starting cRRT

- Usual presentation is a **MULTI-DOSE** vial of Argatroban containing 250mg in 2.5ml. [Exembol Multidose 100 mg/ml concentrate for solution for infusion]
- For infusion rates ***less than 9.0ml/hr:*** Withdraw 0.5ml (50mg) and dilute in 50ml of cystalloid in a 50ml syringe to make a solution with a concentration of 1mg/ml. ***YELLOW***
- Place the opened vial in the drug fridge having written on the box the date first opened. Storage for 28 days is allowed.
- For infusion rates ***greater than 9.0ml/hr:*** Dilute 250mg (2.5mL) with 250mL NS or D5W (1mg/mL). ***BLUE***

Argatroban 250mg in 2.5ml multi use vial	***Syringe***	**Default:** 0.5mcg/kg/min **Maximum:** 10mcg/kg/min	Dilute 50mg (0.5mL) with 50mL NS, D5W or Hartmanns (1mg/mL)	Use only the multidose vial. Once opened, store in the fridge up to 28 days.
Argatroban 250mg in 2.5ml multi use vial	***Volumatic pump required***	**Default:** 0.5mcg/kg/min **Maximum:** 10mcg/kg/min	Dilute 250mg (2.5mL) with 250mL NS or D5W (1mg/mL)	Use Uncommon Volumat Pump Make a bag only if more than 10mL/hour is required See protocol for dosing guidelines If no uncommon pump, MUST calculate rate in mL/hr Give via Drug X

Start infusion at 0.5mcg/kg/min

aPTTr	ACTION
< 1.5	increase by 0.1mcg/kg/min
1.5 - 3.0	NO CHANGE
≥ 3.0	stop for 2 hours then restart infusion at 50% of the previous infusion rate

Start infusion at 2.0mcg/kg/min

aPTTr	ACTION
< 1.5	increase by 0.5mcg/kg/min
1.5 - 3.0	NO CHANGE
≥ 3.0	Reduce infusion rate by 50%

DOSE (mcg/kg/min)	0.5	1.0	1.5	2.0	2.5	3.0	3.5	4.0
Actual body weight (kg)	*Infusion Rate (ml/hr) using dilution of 1mg/ml*							
50	1.5	3.0	4.5	6.0	7.5	9.0	10.5	12.0
60	1.8	3.6	5.4	7.2	9.0	10.8	12.6	14.4
70	2.1	4.2	6.3	8.4	10.5	12.6	14.7	16.8
80	2.4	4.8	7.2	9.6	12.0	14.4	16.8	19.2
90	2.7	5.4	8.1	10.8	13.5	16.2	18.9	21.6
100	3.0	6.0	9.0	12.0	15.0	18.0	21.0	24.0
110	3.3	6.6	9.9	13.2	16.5	19.8	23.1	26.4
120	3.6	7.2	10.8	14.4	18.0	21.6	25.2	28.8
130	3.9	7.8	11.7	15.6	19.5	23.4	27.3	31.2
140	4.2	8.4	12.6	16.8	21.0	25.2	29.4	33.6
150	4.5	9.0	13.5	18.0	22.5	27.0	31.5	36.0

Protocols for using Argatroban

HIT score 4-8 / confirmed Dx of HIT
AND
high risk of bleeding / HYPOcoaguable CKH TEG

- **CONTINUE** systemic Argatroban whether ON or OFF cRRT as it is a specific therapy for HIT
- When condition stabilises consider switch to warfarin

HIT score 0-3
AND
HYPERcoaguable +/- heparin resistant

- **CONTINUE** systemic Argatroban UNTIL off cRRT for ≥48hours with decision NOT to restart cRRT again in the next 48 hours
- **STOP** Argatroban and re-commence enhanced dose UFH s/c BD regime for VTE prophylaxis – titrate dose against anti Xa levels
- **UNLESS** therapeutic anticoagulation required, in which case continue Argatroban
- When condition stabilises consider switch to warfarin

- **Pharmacodynamics:** Argatroban, a synthetic L-arginine derivative, is a direct thrombin inhibitor that binds reversibly to thrombin. Argatroban exerts its anticoagulant effect independently of antithrombin III and inhibits fibrin formation; activation of coagulation factors V, VIII and XIII; activation of protein C; and platelet aggregation.
- **Pharmacokinetics:**
  - Steady-state levels typically achieved within 1-3 hours following initiation.
  - Anticoagulation parameters return to baseline generally within 2 to 4 hours after discontinuation of infusion. There is no reversal agent.
  - Predominantly inactivated by hepatic metabolism. Use with caution / dose reduce in severe hepatic impairment.
  - No significant clearance on RRT
- **NOTE:**
  - Argatroban will result in an elevated INR but this should not be used to titrate therapy.
  - Argatroban interferes with the Fibrinogen lab assay resulting in falsely low levels. If assessment of Fibrinogen required during therapy perform a TEG as the functional fibrinogen (CFF) assay should not be affected.

GUIDANCE NOTES

MEDICAL MANAGEMENT OF ACUTE OLIGO / ANURIC RENAL FAILURE

- Optimise renal perfusion (intravascular volume, cardiac output, renal perfusion pressure)
- Actively manage fluids, electrolytes and drugs to avoid iatrogenic / preventable injury
  - Avoid indiscriminate / untargetted fluid boluses
  - Avoid maintenance fluids in excess of needs / losses
  - Avoid excessive loading of Na, Cl, K and PO_4
  - Consider the effects of altered drug pharmacokinetics
- Manage hyperkalaemia with a 2unit BOLUS of insulin (actrapid) followed immediately by a **CONTINUOUS** infusion staring at 2units/hr together with a continuous infusion of dextrose (20-50mls of 10% peripherally OR 10-30ml of 20% via a central venous line).
  - **DO NOT** give a "one off" infusion of 10-15units of insulin in 50ml of 50% dextrose as this results in **REBOUND** hyperkalaemia within 30-60minutes and frequently causes problematic dysglycaemia.
  - In the event of ECG changes, give 10mls of 10% (6.8mmol) of $CaCl_2$ OR 30mls of 10% (2.2mmol) calcium gluconate. Repeat as necessary.
  - CONSIDER the use of adjunctive medical therapies such as IV sodium bicarbonate 1.4% (peripherally) or 8.4% (centrally)
  - CONSIDER sodium zirconium cyclosilicate 10g 8 hourly PO or NG.
- To manage worsening renal acidosis (bicarbonate loss) give IV sodium bicarbonate 1.4% (peripherally) or 8.4% (centrally)
- Standardised furosemide stress test (FST) details from Crit Care. 2013 Sep 20;17(5):R207 and can be found at https://ccforum.biomedcentral.com/articles/10.1186/cc13015

SIZE OF KIDNEY AND TARGET BLOOD PUMP SPEED

- There are 2 sizes of kidney available HF 12 ($1.2m^2$) and HF19 ($1.9m^2$). The default option should be HF12 with a target blood pump speed of ≥250ml/min.
- If clearance targets are not achieved with an HF12 and / or the patient is very tall / muscular / catabolic then use an HF19 **BUT** the target blood pump speed should be ≥300ml/min.
- Failure to achieve the target blood pump speed results in blood stasis + haemoconcentration within the kidney and both treatment failure and circuit loss due to clot obstruction within the kidney.

MODES OF cRRT

- Haemofiltration (convection only - CVVH) - usual mode - BECAUSE, this permits predilution hence longer circuit life AND convection has greater efficiency than diffusion for larger molecules.
- Haemodiafiltration (convection and diffusion - CVVHDF) - when enhanced SMALL solute clearance is needed e.g. when CVVH fails to achieve target goals in 6-24 hours ***or*** some drug overdoses (e.g. salicylate) -
- Slow continuous ultra-filtration (SCUF) - if fluid removal is all that is required - USE CVVH, 10ml/kg/hr, split 90% predilution + 10% post replacement, NOT "SCUF" setting on machine in order to preserve circuit life.

NOTE - our current machines can switch mode of cRRT at **any time**.

PRESCRIBING cRRT

- For patients, in whom their metabolic derangement is felt to be contributing to their acute condition / instability, **START** at a DOSE of 20ml/kg/hour of "replacement fluid". This fluid principally contains sodium bicarbonate - Na 140mmol/l HENCE be very cautious if the patient's Na is <130 or >150mmol/l. A regime to dilute or enhance the sodium content of the replacement fluid can be found on the GICU website at http://www.gicu.sgul.ac.uk/resources-for-current-staff/renal-replacement-therapy/Mx%20of%20Na%20diorders%20during%20cRRT%20CC2010.pdf/view
  - **Actively titrate dose AND / OR mode to achieve predefinied goals of therapy**
  - **Suggested goals:**
    - **K^+ <6.0 mmol/l within 2 hours (using potassium free replacement fluid)**
    - pH rising by ≥0.5 within 6 hours
    - MINIMUM SOLUTE CLEARANCE should be 12mmol/l of urea every 24 hours
    - Fluid balance goals will depend upon the patient's ability to tolerate removal
- For all other scenarios start at 15ml/kg/hour of "replacement fluid".
- Our standard starting practice for CVVH is to apportion 1/3 of "replacement fluid" as "pre-dilution" and 2/3 as "post replacement".
- Our standard practice for CVVHDF is to apportion half of the "replacement fluid" as the counter current and half as "post replacement".
- Our standard practice is to set fluid removal at a MINIMUM of 50mls/hr. The rate of fluid removal can be increased up t o a maximum of 2000ml/hr
- Circuit anticoagulation:
  - Unless the patient is known or suspected to have a hypersensitivity to unfractionated heparin (including heparin induced thrombocytopaenia), circuits should be primed with a dilute heparin solution (10,000 units in 1000ml of 0.9% NaCl).
  - **PLEASE** ensure that there is **NO AIR** in the bubble trap as any air-blood interface is highly thrombogenic
  - The circuit should then be placed in "RECIRCULATION" mode for a minimum of 20 minutes before connection to a patient (UNLESS treatment is time critical).
  - Once connected, first line therapy is a BOLUS of 5000units followed by a continuous infusion of unfractionated heparin into the proximal end of the circuit. The starting dose is 1,000 units per hour. The target aPTTr is 1.5-2.0.
  - **If the patient is HYPERcoaguable** [DEFINED as a platelet count >450 $x10^9$/L &/or fibrinogen >4.8g/L &/or citrated kaolin (CK) TEG MA >69mm]
    - **CONSIDER** 5,000units unfractionated heparin INTRAVENOUS boluses every 6 hours, starting immediately before commencing cRRT
    - **IF 1 or more circuit losses every 24 hours due to clotting and NOT suboptimal vascular acces AND cRRT essential - CONSIDER switch to systemic argatroban (into the patient)**
  - HOWEVER, if the patient requires THERAPEUTIC anticoagulation - ensure the target is set and achieved.
  - In problematic circuits, minimising the procoagulant stimulus by maximising the blood pump speed and increasing the proportion (up to 90%) of replacement fluid that predilutes the patient's blood should also be considered.
- cRRT circuits have a maximum 80 hour lifespan. Unplanned, premature circuit loss, usually through problematic vascular access, is both very expensive and commonly results in 10-20g/l loss in the patient's [Hb], necessitating pRBC transfusion. Do **everything** possible to avoid this and seek specialist help early.
- Whenever a circuit does fail and / or reaches the end of its life, always consider a period **OFF** cRRT to assess the patient's renal recovery.

During the COVID-19 pandemic there may be demand for cRRT in excess of the number of machines we have available hence:

- PLEASE ENSURE all medical therapy and fluid management strategies have been optimised to avoid or delay the need for cRRT
- IF THE INDICATION IS **PRINCIPALLY METABOLIC** (K^+ / pH / uraemia) use a starting dose of 35ml/kg CVVH; check progress at 6 hours. If targets not achieved *AND* aPTTR >1.5, mode switch to CVVHDF *AND* increase the replacement fluid hourly rate by 50% (then split this 50:50 post-replacement : counter current).
  E.g. 70kg IBW starting @35ml/kg/hr CVVH = 800 pre & 1600 post; fails targets at 6 hours so mode switch + 50% increase = 2400 x 1.5 = 1800 post & 1800 counter.
  If aPTTR<1.5 *OR* high risk of clotting just increase replacement dose by 50%. Recheck goals every 6 hours
- IF THE INDICATION IS **PRINCIPALLY FLUID OVERLOAD** use a standard starting dose of 20ml/kg CVVH but start fluid removal at minus 250ml/hr; check progress at 4 hours and consider increasing the fluid removal rate up to (a soft maximum of) minus 500ml/hr for 2-4 hours. CONSIDER washing back at this stage.
- Aim to deliver 6-24hours of therapy every 72 hours. PLAN fluid / drug / metabolic issues around this timeline
- CONSIDER transfer to Champneys for iHD, especially if stable single organ (respiratory) failure *AND* has tolerated 1 or more cRRT therapy sessions. Please ensure Hep B / Hep C and HIV serology have been checked.

HOW TO TROUBLESHOOT cRRT

- There is troubleshooting guide on the ICU website - www.gicu.sgul.ac.uk/resources-for-current-staff