Anti-Xa Monitoring for Heparin Anticoagulation in Extracorporeal Membrane Oxygenation (ECMO)

Objective

- These guidelines concern the use of systemic intravenous unfractionated heparin (UFH) for anticoagulation in patients receiving **ECMO.**
- The aim is to provide a standardised approach using anti Xa monitoring ***in place*** of APTTr.

General Principals

- UFH provides rapid and titratable anticoagulation preventing clot formation hazardous to the circuit and patient whilst avoiding excessive bleeding.
- The benefits of instituting UFH have to outweigh the risks.
- ACT monitoring has no further role after initial UFH bolus dose at cannulation and should not be used to adjust UFH.
- Unless at high risk of bleeding, more intensive anticoagulation is required for VA ECMO than VV ECMO.
- Any patient with a true heparin allergy needs to be discussed with haematology prior to cannulation.

Pharmacology

- The half-life of an established UFH infusion varies but approximates between 1.5 and 6 hours to achieve a steady-state level.
- Heparin pharmacology varies between patients. Clinical evaluation of the individual patient is required to ensure appropriate anticoagulation. Regular evaluation and discussion with the ICU and Haematology Consultant may be required.

Medical patients

- During cannulation when guidewires are placed a bolus dose of UFH is usually given at 50 units/kg (eg 2500-5000 units). This will be decided by the cannulating consultant and is omitted in ECPR cases. An ACT target of 180-220 can be used at this point.
- UFH infusion is commenced *only* after discussion with the ICU consultant (consider the results of baseline FBC and coagulation screen, plus any CT brain to ensure intracerebral haemorrhage is excluded).
- Start UFH infusion at 10 units/kg/hr (use actual body weight up to max of 125kg) and monitor with anti-Xa level.
- **ACT monitoring has no further role and should not be used to adjust heparin.**
- In VA ECMO cases high risk for bleeding the lower anti Xa level 0.2-0.4 can be used (see below)

- Consider higher UFH starting rate (eg 18 units/kg/hr) if high risk of circuit or patient thrombosis (eg pulmonary embolism).

Surgical patients

- Post cardiotomy patients often bleed in the immediate peri-operative period thus UFH infusion initiation will likely be delayed for at least 12 hours.
- This approach is safe as long as extracorporeal blood flow is adequate (i.e. over 3L/min).
- When active surgical bleeding has ceased and there is agreement with the ICU and Cardiac Surgical Consultants, commence UFH infusion at 10 units/kg/hr. Monitor using anti Xa level at 6 hours.
- **ACT monitoring has no role and should not be used to adjust heparin.**
- If the patient remains high risk for bleeding in VA ECMO the lower anti Xa level 0.2-0.4 can be used before increasing to full protocol 0.3-0.7 (see below). This is at the discretion of the ICU Consultant.

Monitoring

- Measure anti-Xa level ("Unfractionated Heparin Assay All Sites" on Trak) after 6 hours from commencing UFH. Further monitoring is as described in the relevant chart
- Once three levels are in range without adjusting the rate monitoring can be changed to twice daily
- More intensive anticoagulation is required for VA ECMO than VV ECMO hence there are two separate infusion charts (see below) with distinct therapeutic ranges. The high risk for bleeding protocol uses the same target ranges as per VV ECMO.

Anti-Xa level for VV ECMO (or VA ECMO with high risk for bleeding): 0.2-0.4 U/ml

Anti Xa level for VA ECMO (or VV ECMO with thrombus): 0.3-0.7 U/ml

Title: Anti Xa monitoring for heparin infusion in ECMO	
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**FOR INTENSIVE CARE USE ONLY **

Adult Heparin Infusion Chart for VA ECMO

(or VV ECMO with thrombus)

Consultant		Name of Patient	
Hospital / Ward		CHI Number	
Weight (kg)		DOB	

Medicine (Approved Name)	Final Concentration	Total Dose	Volume	Route	Prescribed / Transcribed By Sign & print name
Heparin	1000 units/ml	40,000 units	40 mls	IV	

*Please note that in NHS Lothian heparin sodium solution for infusion is available in a ready concentration of 1000units/ml so further dilution is not required. If in doubt, contact pharmacy for advice.

Initiation of therapy

- Check baseline FBC, coagulation screen, urea, creatinine
- Prescribe continuous infusion on the patient main prescription chart. **No loading dose is given.**
- Start continuous infusion of heparin **10 units/kg/hour** (maximum 1250 units/hour). Use actual body weight capped at 125kg.
- For patients with a high risk of thrombosis (eg pulmonary embolism or circuit thrombosis) consider a higher starting rate.
- For patients with a high risk of bleeding use VV protocol initially.

Infusion Rate Instructions

	Date	Time	Rate ml/hr	Prescribed by	Adjusted by	UFH Anti-Xa level (units/ml)	Reason for Change/Comment
Initial Rate							
Change 1							
Change 2							
Change 3							
Change 4							
Change 5							
Change 6							

Dose Adjustment Instructions

TARGET UFH: **Anti-Xa LEVEL 0.3-0.7 units/ml (VA ECMO)**

Anti-Xa level	**INFUSION ADJUSTMENT:**	**REPEAT UFH Anti-Xa level:**
>1.2	Stop for 1 hour and decrease rate by 500 units (0.5ml)/hr	2 hours
0.9-1.2	Decrease infusion rate by 300 units (0.3ml)/hr	6 hours
0.71-0.9	Decrease infusion rate by 200 units (0.2ml)/hr	6 hours
0.3-0.7	No change in infusion rate	6 hours or after 3 consecutive levels 0.3-0.7, 12 hours
0.15-0.29	Increase infusion rate by 100 units (0.1ml)/hr	6 hours
0.06-0.14	Increase infusion rate by 200 units (0.2ml)/hr	6 hours
<0.06	Increase infusion rate by 400 units (0.4ml)/hr and administer bolus of 80 units /kg (maximum 10,000 units)	6 hours

Other Instructions

- UFH stands for unfractionated heparin (iv heparin)
- UFH-anti-Xa levels are taken in a green citrated tube; fill tube to the level, send to haematology
- To order on TRAK: go to “search for order”, click on “order item” then enter “heparin”, then click on “Unfractionated Heparin assay All sites”: call RIE laboratory to inform sample is coming; WGH and SJH sites must courier samples to RIE lab.(ext 26093, OOH page 6550)
- Check UFH Anti-Xa level 6 hours after initiation, then adjust rate to achieve therapeutic range of **0.3-0.7 units/ml** using the **dose adjustment table** above. Measure the UFH-anti-Xa level 6 hours after each dose change
- Monitor FBC daily and be vigilant for heparin-induced thrombocytopenia
- If therapeutic range for UFH-anti-Xa level is not reached within 24 hours, seek advice from haematology
- Do not stop the heparin infusion to check the UFH-anti-Xa sample
- Do not take the UFH-anti-Xa sample from the limb with the infusion (or the same line in the case of central lines)

Medicine	Heparin	**Infusion Device Type**		**Name of Patient**	
Concentration	1000 units/ml	**Device Service Number**		**Patient Number**	Or affix patient label
Expected Completion Time				**DOB**	

Preparation Details	**Batch Number**	**Quantity**	**Prepared By**	**Checked By**
Heparin				
			Date:	Time:

Check infusion device 15 mins after set up and then every hour thereafter. **Sign box when the device has been checked.**

A	B	C	D	E	F	G	H	I	J
Date	Time	Site check	Rate (ml/hr)	Volume (ml) remaining in syringe – visual check	Volume (ml) infused since last check – calculated from E	Total volume (ml) infused – calculated from E	Total volume (ml) infused – device reading	Initials (two to set up / change rate)	Comments

Use a new page with every new syringe prepared, or if the infusion device is changed.
Syringe pumps must have the line purged and the volume recorded in column E. Start-up time may affect volume actually given to the patient.

**FOR INTENSIVE CARE USE ONLY **

Adult Heparin Infusion Chart for VV ECMO

(or VA ECMO with high risk of bleeding)

Consultant		Name of Patient	
Hospital / Ward		CHI Number	
Weight (kg)		DOB	

Medicine (Approved Name)	Final Concentration	Total Dose	Volume	Route	Prescribed / Transcribed By Sign & print name
Heparin	1000 units/ml	40,000 units	40 mls	IV	

*Please note that in NHS Lothian heparin sodium solution for infusion is available in a ready concentration of 1000units/ml so further dilution is not required. If in doubt, contact pharmacy for advice.

Initiation of therapy

- Check baseline FBC, coagulation screen, urea, creatinine
- Prescribe continuous infusion on the patient main prescription chart. **No loading dose is given.**
- Start continuous infusion of heparin **10 units /kg/hour** (maximum 1250 units/hour). Use actual body weight capped at 125kg.
- For patients with a high risk of thrombosis (eg circuit thrombosis) consider a higher starting rate.
- ***If Pulmonary Embolism then use VA protocol***

Infusion Rate Instructions

	Date	Time	Rate ml/hr	Prescribed by	Adjusted by	UFH Anti-Xa level (units/ml)	Reason for Change/Comment
Initial Rate							
Change 1							
Change 2							
Change 3							
Change 4							
Change 5							
Change 6							

Dose Adjustment Instructions

TARGET UFH: **Anti-Xa LEVEL 0.2-0.4 units/ml (VV ECMO)**

Anti-Xa level	**INFUSION ADJUSTMENT:**	**REPEAT UFH Anti-Xa level:**
>1.2	Stop for 1 hour and decrease rate by 500 units (0.5ml)/hr	2 hours
0.81-1.2	Stop for 1 hour and decrease rate by 300 units (0.3ml)/hr	2 hours
0.61-0.8	Decrease infusion rate by 200 units (0.2ml)/hr	6 hours
0.41-0.6	Decrease infusion rate by 100 units (0.1ml)/hr	6 hours
0.2-0.4	No change in infusion rate	6 hours or after 3 consecutive levels 0.2-0.4, 12 hours
0.1-0.19	Increase infusion rate by 100 units (0.1ml)/hr	6 hours
0.06-0.09	Increase infusion rate by 200 units (0.2ml)/hr	6 hours
<0.06	Increase infusion rate by 300 units (0.3ml)/hr	6 hours

Other Instructions

- UFH stands for unfractionated heparin (iv heparin)
- UFH-anti-Xa levels are taken in a green citrated tube; fill tube to the level, send to haematology
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- Check UFH Anti-Xa level 6 hours after initiation, then adjust rate to achieve therapeutic range of **0.2-0.4 units/ml** using the **dose adjustment table** above. Measure the UFH-anti-Xa level 6 hours after each dose change
- Monitor FBC daily and be vigilant for heparin-induced thrombocytopenia
- If therapeutic range for UFH-anti-Xa level is not reached within 24 hours, seek advice from haematology
- Do not stop the heparin infusion to check the UFH-anti-Xa sample
- Do not take the UFH-anti-Xa sample from the limb with the infusion (or the same line in the case of central lines)

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