Therapeutic Plasma Exchange in Critical Care

Aim To provide evidence based guidance on the use of Therapeutic Plasma Exchange (TPE) in critically ill patients.
Scope Adult patients in Critical Care, using the PRISMAflex machine.

Therapeutic Plasma Exchange (TPE) Prescription

TPE is commenced at the discretion of the on-call DCCQ Consultant.

Check full biochemistry (including calcium), FBC and coagulation before treatment.

Some protein bound drugs must be given *after* TPE to avoid removal with plasma during treatment. Check Renal Drug Handbook or discuss with DCCQ Pharmacist.

Prescription

1. First calculate the patient's estimated plasma volume:

   Estimated Plasma Volume (litres) = 0.07 x Weight (kg) x (1- haematocrit)

2. Then calculate total plasma exchange volumes, replacement fluids and treatment days as follows:

Condition	Plasma Exchange Volume	Replacement Fluid	Number of Exchanges	Exchange Frequency
RPGN Vasculitis	1 - 1.5 times estimated plasma volume	Albumin (eg HAS 4.5%)	4 - 6	Daily
Anti-GBM Disease	1.5 times estimated plasma volume	Albumin - with FFP if pulmonary haemorrhage	7 - 10	Daily
HUS TTP	1 - 2 times estimated plasma volume	Fresh Frozen Plasma	Until platelets normal / no RBC fragments (typically 7-16)	Once or twice daily
Guillian-Barre Syndrome	2 times estimated plasma volume	Albumin (eg HAS 4.5%)	4	Alternate days

Version: 2.0 | Date: 06 Mar 15 | Revision Due: 06 Mar 17 | Authors: Dr S Blakeley, SSr L Hatch, Sr S Rivers

Therapeutic Plasma Exchange (TPE) Administration

Equipment Required

- PRISMAflex Machine
- TPE filter set, Effluent bags, 20ml syringe
- Sodium Chloride 0.9% 1000mls x 3 bags
- Heparin 5000units x1 ampoule for priming
- Replacement fluids e.g. Albumin, FFP
- Sodium Chloride 0.9% 500mls x 2 bags (for wash back and replacement line during priming)
- Anticoagulant as per DCCQ RRT Guideline

Priming PRISMAflex

- Prime TPE circuit according to manufacturer's instructions
- Add Heparin 5000units to 3rd Sodium Chloride 0.9% priming bag, or 2nd bag if coagulation abnormalities

Check Patient Prescription
(see calculations on Page 1)

PRISMAflex Settings

Haematocrit = percentage of blood cells in the whole blood volume (e.g 0.35 = 35%)

Total Replacement Input = total plasma exchange volume e.g. if total volume is 3 litres then 3000 ml should be entered.

Replacement Rate: set at 1000 ml/hr. May be increased if TMP below 50 mmHg

Blood Flow Rate: Initially set at 100 ml/min. May be increased to maximum of 150-180 ml/min.

Replacement Fluid Container Volume: If using 500ml Albumin bottle, enter 480ml. If using FFP set 10 ml less than volume shown on bag of FFP.

Plasma Loss Rate: must be set at zero ml/hr (otherwise plasma will be removed)

Anticoagulation Rates: check DCCQ Renal Replacement Therapy Guideline. TPE may require higher rates of anticoagulation than CRRT to prevent filter clotting.

Patient Monitoring

Monitor vital signs and coagulation times

Inform medical staff and prepare to stop TPE if any adverse signs:

- **Anaphylaxis**
- **Hypothermia**
- **Electrolyte Loss**
- **Haemolysis** (red or pink coloured effluent)

End of Treatment

Wash blood back to patient with Sodium Chloride 0.9% as per PRISMAflex guidance until blood lines clear.

Follow DCCQ Guideline for Dialysis Catheter Management.

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1. INTRODUCTION

Therapeutic plasma exchange (TPE, plasmapheresis) is an extracorporeal blood purification technique designed for the removal of large molecular weight substances. Examples of these substances include pathogenic auto antibodies, immune complexes, cryoglobulins, myeloma light chains, endotoxins and cholesterol containing lipoproteins (1, 2). The aim of TPE therefore is that the removal of these substances will reduce further damage and may permit reversal of the pathological process.

The majority of TPE treatments are performed as part of an evidence-based treatment strategy for neurologic, renal, immunologic, or hematologic diseases (1, 3). The majority of treatments are usually undertaken in a renal unit setting, however if the patient requires critical care then these treatments may be commenced or continued in The Department of Critical Care (DCCQ).
In general an exchange equal to the patient's estimated plasma volume will lower plasma macromolecule levels by 60 percent and an exchange equal to 1.4 times the plasma volume will lower plasma levels by 75 percent.

The decision to commence TPE is at the discretion of the on-call DCCQ Consultant in collaboration with the patient's specialist Consultant e.g. Renal, Neurology, Haematology. The plasma exchange treatment should be determined according to the characteristics of the pathological substance that is being removed and by the desired endpoint (e.g. clinical improvement or a reduction in the level of a specific measurable pathogenic moiety).

This guideline should be read in conjunction with the following DCCQ clinical guidelines:

- Renal Replacement Therapy in Critical Care
- Dialysis Catheter Care in Critical Care

2. PURPOSE

To provide guidance on the use of Therapeutic Plasma Exchange (TPE) in critically ill patients according to best available evidence.

3. SCOPE

This guideline is for use on the Critical Care Unit using the PRISMAflex machine. Ability to comply with this guideline in full may be limited in times of excess demand on services, eg influenza pandemic. This guideline is subject to professional judgement and accountability.

4. DEFINITIONS

TPE – Therapeutic Plasma Exchange
RPGN – Rapidly progressive Glomerulonephritis
Anti-GBM Disease – Anti-Glomerular Basement Membrane Disease
HUS – Haemolytic Ureamic Syndrome
TTP – Thrombotic Thrombocytopenic Purpura
CRRT – Continuous Renal Replacement Therapy
FFP – Fresh Frozen Plasma

5. DUTIES AND RESPONSIBILITIES

- The decision to implement this guideline is at the discretion of the on-call critical care consultant
- Implementation of this guideline is the joint responsibility of appropriately trained critical care medical and nursing staff.
- This guideline is subject to professional judgment and accountability
- The author and the guidelines group will be responsible for this document
- This guideline can be found on the DCCQ website

6. PROCESS

ACTION	RATIONALE
Inclusion Criteria **Patients with:** • Anti-GBM Disease • RGPN • Guillain - Barre Syndrome • Myasthenia Gravis • TTP • HUS • Systemic Vasculitis • Acute Renal Failure due to myeloma	• Evidence based literature demonstrates that this group of patients have been shown to benefit from this treatment (1, 2, 3) • **Note this list is not exhaustive and the decision to start will be determined individually**

ACTION	RATIONALE
Prior to Treatment	
* The patient will require vascular access utilising a double lumen dialysis catheter	
* Check urea, electrolytes, Hb, coagulation, potassium and calcium prior to treatment	
* Avoid ACE inhibitors	* Risk of hypotension
* Administer protein bound drugs following treatment. (Refer to Renal Drug Handbook or DCCQ Pharmacist)	* Certain protein bound drugs will be removed during treatment (4)
Equipment Required PRISMAflex Machine TPE circuit Sodium Chloride 0.9% bags 1000mls x 3 Heparin 5000 units x1 ampoule Replacement fluid e.g. Albumin, FFP Sodium Chloride 0.9% bag 500mls x 2 Effluent bags 20ml syringe Anticoagulant according to DCCQ guideline	* As per PRISMAflex Machine guidance
Treatment is achieved using the PRISMAflex machine. A specialised TPE set using a highly permeable filter should be used. (Please refer to manufacturers guidance for priming TPE circuit)	* This therapy is undertaken using a highly permeable filter and renal replacement equipment e.g. PRISMAflex. (6)].
* 3 litres of Sodium Chloride 0.9% are used to prime the TPE circuit. Heparin 5000 units should be added to the 3rd bag. If the patient has coagulation problems this may be added to the 2nd bag instead	* To reduce the risk of heparin administration to patients at risk of bleeding (5)

ACTION	RATIONALE
TPE – Treatment Prescription *The decision to prescribe TPE is at the discretion of DCCQ on-call DCCQ Consultant in collaboration with the patient's specialist Consultant e.g. Renal, Neurology, Haematology *To prescribe TPE the patients Estimated Plasma Volume needs to be calculated using the following formula; **Estimated Plasma Volume (liters)** **= 0.07 x Weight (kgs) X (1-haematocrit)** ***** The plasma exchange volume, treatment days and replacement fluid are indicated in the table below	TPE treatments should be determined according to the characteristics of the pathological substance that is being removed (see table below) and in accordance with best evidence based practice (1, 2). The amount of plasma to be exchanged during TPE must be determined in relation to the patient's estimated plasma volume (1) * Typically 30-40mls/kg of plasma (1-1.5 plasma volumes) are removed and replaced with albumin or FFP during each treatment (1, 2). *A single plasma volume exchange will lower plasma macromolecule levels by 60 percent and an exchange equal to 1.4 times the plasma volume will lower plasma levels by 75 percent [5, 7]. * Most patient will require several consecutive treatments to effectively remove a substantial percentage of the unwanted substances e.g. auto antibodies, endotoxins, immune complexes (1) *The plasma removed during TPE must be replaced to maintain the patient's fluid balance (1) *FFP is the fluid replacement of choice in patient's with haematological disorders e.g. TTP (1)

Condition	Plasma exchange volume	Replacement Fluid	Number of Exchanges	Exchange Frequency
RPGN Vasculitis	1 to 1.5 x Estimated Plasma Volume	Albumin (e.g. HAS 4.5%)	4 – 6	Daily
Anti-GBM Disease	1.5	Albumin with FFP if pulmonary Haemorrhage	7 – 10	Daily
HUS TTP	1 to 2	All FFP	Until platelets normal / no RBC fragments (7-16)	Once or twice daily
Guillain - Barre	2	Albumin	4	Alternate days

ACTION	RATIONALE
TPE – during treatment **Flow rates on PRISMAflex** *** Pre-treatment haematocrit** = the percentage of blood cells in the whole blood volume – e.g. 0.35 = 35%) *** Total Replacement Input** = total plasma exchange volume e.g. if total volume is 3 litres then 3000mls should be entered *** Replacement Rate** – set at 1000mls/hr, may be increased if TMPa below 50mmhg to 2000mls/hr *** Blood Flow Rate** – initially set at 100mls/min and can be increased to maximum of 150-180mls/min *** Replacement Fluid Container Volume** - 480mls if using 500ml Albumin bottle - If using FFP set 10mls less than total volume *** Plasma Loss rate** – should be set at zero ml/hr (if not plasma will be removed) *** Anticoagulation rates** – refer to DCCQ RRT Guideline. TPE may require higher rates of anticoagulation than CRRT to prevent filter clotting. **Patient Observations** * Record frequent vital signs at least 1hrly during treatment * Observe for any signs of haemolysis (pink tinge in effluent fluid). If haemolysis suspected discontinue treatment but do not wash back blood * Inform medical staff of any complications	* To establish TPE according to Hospal PRISMAflex recommendations (5) * To prevent clotting of the TPE filter (5) * **In certain conditions such as TTP/HUS (where the platelet count is low) or conditions with pulmonary haemorrhage (e.g. Anti GBM disease or Wegener's Granulomatosis) then no anticoagulation may be considered if the patient is at risk of bleeding. This should be discussed with the duty Consultant** *To observe for any signs of complications e.g. anaphylaxis hypotension hypothermia hypocalcaemia

ACTION	RATIONALE
TPE - discontinuation of Treatment * Following completion of treatment wash back blood according to PRISMAflex instructions using 500ml bag Sodium Chloride 0.9%. Wash back with enough saline to ensure that the line is free of blood. * Post treatment – check FBC, coagulation profile and full biochemistry (including calcium) *Refer to Dialysis catheter care guideline and Taurolock guideline, for management of vascular access following treatment	

7. TRAINING REQUIREMENTS

This guideline should be read in conjunction with the ICU Renal handbook. Training will be disseminated through the teaching and renal teams.

8. MONITORING COMPLIANCE WITH, AND THE EFFECTIVENESS OF, PROCEDURAL DOCUMENTS

This guideline will be reviewed initially at 6 months and thereafter 2 yearly by the DCCQ Guidelines Group. Measurement of compliance will be achieved by unit-based audit. Results reviewed will be fed back to members of the senior medical /nursing team and the Critical Care Governance Group.

Minimum requirement to be monitored	Lead	Tool	Frequency of Report of Compliance	Reporting arrangements	Lead(s) for acting on Recommendations
Given the small numbers of patients we plasma exchange, data will be collected every 2 years providing patient demographics and outcome	Dr Sara Blakeley	Data collected from CIS	2 years	Policy audit report to: • Department of Critical Care Governance Group	Dr Sara Blakeley

The details of the monitoring to be considered include:

- The aspects of the procedural document to be monitored: identify standards or key performance indicators (KPIs);
- The lead for ensuring the audit is undertaken
- The tool to be used for monitoring e.g. spot checks, observation audit, data collection;
- Frequency of the monitoring e.g. quarterly, annually;
- The reporting arrangements i.e. the committee or group who will be responsible for receiving the results and taking action as required. In most circumstances this will be the committee which ratified the document. The template for the policy audit report can be found on the Trust Intranet Trust Intranet -> Policies -> Policy Documentation
- The lead(s) for acting on any recommendations necessary.

9. REFERENCES AND ASSOCIATED DOCUMENTATION

1. Kaplan A. (2008) Therapeutic Plasma Exchange Core Curriculum. American Journal of Kidney Diseases. Vol. 52(6) p.1180-1196

2. UK Blood Transfusion Handbook: (2007) www.transfusionguidelines.org.uk

3. Szczepiorkowski ZM, Winters JL, Bandarenko N, et al. Guidelines on the use of therapeutic apheresis in clinical practice--evidence-based approach from the Apheresis Applications Committee of the American Society for Apheresis. J Clin Apher 2010; 25:83.

4. Ashley C, Currie A (2009) The Renal Drug Handbook Third Edition. Radcliffe Publishing, Oxford. UK

5. PRISMAflex Operators Manual Software version 4.XX (2008). Gambro Lundia AB, Sweden

6. Gerhardt RE, Ntoso KA, Koethe JD, et al. Acute plasma separation with hemodialysis equipment. J Am Soc Nephrol 1992; 2:1455.

7. Kaplan AA. A simple and accurate method for prescribing plasma exchange. ASAIO Trans 1990; 36:M597.

Appendix A

Checklist for the Review and Ratification of Procedural Documents and Consultation and Proposed Implementation Plan

To be completed by the author of the document and attached when the document is submitted for ratification: a blank template can be found on the Trust Intranet. Home page -> Policies -> Templates

CHECKLIST FOR REVIEW AND RATIFICATION			
TITLE OF DOCUMENT BEING REVIEWED:		**YES/NO N/A**	**COMMENTS**
1	**Title**		
	Is the title clear and unambiguous?	Yes	
	Will it enable easy searching/access/retrieval??	Yes	
	Is it clear whether the document is a policy, guideline, procedure, protocol or ICP?	Yes	
2	**Introduction**		
	Are reasons for the development of the document clearly stated?	Yes	
3	**Content**		
	Is there a standard front cover?	Yes	
	Is the document in the correct format?	Yes	
	Is the purpose of the document clear?	Yes	
	Is the scope clearly stated?	Yes	
	Does the scope include the paragraph relating to ability to comply, in the event of a infection outbreak, flu pandemic or any major incident?	Yes	
	Are the definitions clearly explained?	Yes	
	Are the roles and responsibilities clearly explained?	Yes	
	Does it fulfill the requirements of the relevant Risk Management Standard? (see attached compliance statement)		
	Is it written in clear, unambiguous language?	Yes	
4	**Evidence Base**		
	Is the type of evidence to support the document explicitly identified?	Yes	
	Are key references cited?	Yes	
	Are the references cited in full?	Yes	
	Are associated documents referenced?	Yes	
5	**Approval Route**		
	Does the document identify which committee/group will approve it?	Yes	
6	**Process to Monitor Compliance and Effectiveness**		
	Are there measurable standards or KPIs to support the monitoring of compliance with the effectiveness of the document?	Yes	
7	**Review Date**		
	Is the review date identified?	Yes	
6	**Dissemination and Implementation**		
	Is a completed proposed implementation plan attached?	Yes	
7	**Equality and Diversity**		
	Is a completed Equality Impact Assessment attached?	Yes	

Appendix A
continued

CONSULTATION AND PROPOSED IMPLEMENTATION PLAN	
Date to ratification committee	06 Mar 15
Groups /committees / individuals involved in the development and consultation process	Critical Care Governance Group Multidisciplinary staff working in DCCQ
Is training required to support implementation?	Yes
If yes, outline plan to deliver training	Multidisciplinary teaching via unit based teaching teams, regular teaching sessions on Fridays and bedside teaching from experienced staff
Outline any additional activities to support implementation	Promotion of introduction of guideline via unit based webpage and verbally through presentation at teaching sessions

Individual Approval

If, as the author, you are happy that the document complies with Trust policy, please sign below and send the document, with this paper, the Equality Impact Assessment and NHSLA checklist (if required) to the chair of the committee/group where it will be ratified. To aid distribution all documentation should be sent electronically wherever possible.

Name	**Dr Sara Blakeley**	**Date**	02 Mar 2015
Signature	*signed electronically*		

Committee / Group Approval

If the committee/group is happy to ratify this document, would the chair please sign below and send the policy together with this document, the Equality Impact Assessment, and NHSLA checklist (if required) and the relevant section of the minutes to the Trust Policies Officer. To aid distribution all documentation should be sent electronically wherever possible.

Name	**Dr N Tarmey**	**Date**	06 Mar 2015
Signature	*signed electronically*		

If answers to any of the above questions is 'no', then please do not send it for ratification.

Appendix B

Equality Impact Assessment

To be completed by the author of the document and attached when the document is submitted for ratification: a blank template can be found on the Trust Intranet. Home page -> Policies -> Templates

Title of document for assessment	Therapeutic Plasma Exchange in Critical Care
Date of assessment	02/03/2015
Job title of person responsible for assessment	Dr N Tarmey
Division/Service	DCCQ / CHAT CSC

	Yes/No	Comments
Does the document affect one group less or more favorably than another on the basis of:		
Race	No	
Gender (including transgender)	No	
Religion or belief	No	
Sexual orientation, including lesbian, gay and bisexual people	No	
Age (for HR policies only)	No	
Disability – learning disabilities, physical disabilities, sensory impairment and mental health problems	No	
Does this document affect an individual's human rights?	No	
If you have identified potential discrimination, are the exceptions valid, legal and/or justified?		

If the answers to any of the above questions is 'yes' you will need to complete a full Equality Impact Assessment (available from the Equality and Diversity website) or amend the policy such that only an disadvantage than can be justified is included. If you require any general advice please contact staff in the Equality and Diversity Department on 02392 288511