

## 1. Introduction

Plasma exchange is used for a number of indications related to kidney diseases (1). The evidence for its effectiveness is stronger for some indications (e.g. anti-GBM disease) than for others (e.g. desensitisation for transplantation). Plasma exchange is associated with significant risks and the potential benefits need to be weighed against these.

The aims of this guideline are to:-

- List renal indications for plasma exchange
- Highlight complications and how to avoid these

Clinical guidelines are 'guidelines' only. The interpretation and application of clinical guidelines will remain the responsibility of the individual practitioner. If in doubt consult a senior colleague or expert.

## 2. Scope

This guideline is to advise qualified staff working on the renal unit on prescribing and delivering plasma exchange treatment.

## 3. Recommendations, Standards and Procedural Statements

### 3.1 Indications

There is strong evidence that the following nephrological conditions benefit from plasma exchange

- antiGBM disease (but consider if risk/benefit if dialysis dependent and no pulmonary haemorrhage)
- Haemolytic uraemic syndrome/thrombotic thrombocytopenic purpura (HUS/TTP) particularly if diarrhoea negative
- Recurrent focal glomerulosclerosis in renal transplant

There is some evidence that the following conditions benefit from plasma exchange

- systemic vasculitis where patients is dialysis dependent, serum creatinine >500umol/l or rising despite oral immunosuppression (especially if oliguric)(2)
- Desensitisation of sensitised patient pre-transplantation especially for living donor transplantation
- HUS/TTP if diarrhoea positive or associated with malignancy
- Cryoglobulinaemia
- Waldenstrom's macroglobulinaemia/hyperviscosity syndrome

There is limited evidence that the following conditions benefit from plasma exchange

- Systemic lupus erythematosus unresponsive to other treatment

This guideline will NOT address Plasma exchange used for non-renal conditions e.g.

- Myasthenia gravis
- Guillain Barre syndrome
- Chronic inflammatory demyelinating polyneuropathy
- Limbic encephalitis

### 3.2 Vascular access

Access to the circulation is achieved by a double lumen central venous catheter or by an arteriovenous fistula if this is available. In some circumstances peripheral access can be used but is not ideal. The machine we currently use HF440 support plasma exchange using peripheral access. Decision on access type must be discussed with consultant and patient.

### 3.3 Patient consent

Discussion with the patient about indication for plasma exchange, alternatives and potential complications must be documented in the medical notes. Provide patient with an information leaflet available from ward 15A. Signed consent is not required for the Plasma exchange but is required for vascular access insertion.

### 3.4 Pre-treatment investigations

Patient should have FBC, Serum Calcium and clotting screen performed before each plasma exchange treatment. In addition Fibrinogen levels should be measured before the first treatment or if concerns about excess bleeding to guide the need for FFP. Patients with low fibrinogen levels should receive FFP/ Octaplas after each plasma exchange.

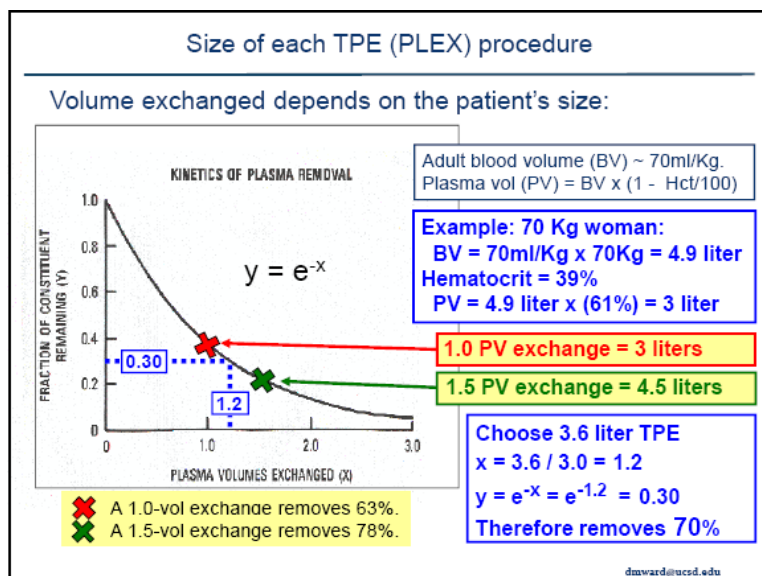
### 3.4 Prescription

3.4.1 The regimen should be determined by the target molecule and the underlying disease. The Guidelines on the Use of Therapeutic Apheresis in Clinical Practice—Evidence-Based Approach from the Writing Committee of the American Society for Apheresis: The Sixth Special Issue (Journal of Clinical Apheresis 28:145–284 (2013) or from ASFA website [www.apheresis.org](http://www.apheresis.org)) has a list of all conditions in which plasma exchange has been used and suggested regimens.

3.4.2 Only 45% of IgG is intravascular, and within 48 hours of a procedure, the plasma IgG returns to 40% of the pre-exchange level. IgG production is also characterized by a "rebound" phenomenon, and may lead to increased levels of IgG when PE is stopped especially if the patient is not on immunosuppressive therapy. As a result, a more rigorous regimen involving frequent exchanges is required - five separate exchanges over 7 to 10 days is required to remove 90% of the total initial body immunoglobulin burden. Additional treatments may be required if new antibody production occurs. In most cases, PE is supplemented with chemotherapy or immunosuppressive therapy.

3.4.3 When prescribing plasma exchange, detail in the notes the volume of exchanges, frequency, planned monitoring and planned review date.

Usual volume is for 40-50ml/kg per exchange = roughly 1-1.5x plasma volume. The frequency varies with clinical indication – see section 3.4.5. Maximum suggested volume is 4.5 litres per exchange. Calculation is based on weight and haematocrit as explained on this slide from 'Practical Aspects of Therapeutic Plasma Exchange (PLEX / TPE) for Neurologists', David M. Ward, MD, FRCP, Professor, Division of Nephrology, University of California San Diego, Medical Director, Therapeutic Apheresis Program.



### 3.4.4 Intravenous Calcium

Hypocalcaemia is common post PLEX particularly when fresh frozen plasma is used. Always prescribe PRN IV Calcium Gluconate 10ml 10% and inform the nurses if this should be given before and after the PLEX treatment. Most patients will require pre and post PLEX calcium gluconate.

### 3.4.5 Frequency of plasma exchange

Diagnosis	Initial Regimen	Treatment Goal	Comments
<b>Anti GBM disease</b>	Daily for 14days	Reduce antiGBM titre to normal. Review after 14 days	Few patients come off dialysis
<b>Vasculitis</b>	7 exchanges within 14 days	Assess disease activity(clinical, C-RP, renal function etc)	
<b>TTP/HUS</b>	Daily	Platelet >100 on 2 consecutive days or markers of clinical improvement	
<b>Recurrent FSGS post transplant</b>	Three times per week	Until proteinuria remits	Review if no response after 1/12
<b>Densitisation for renal transplantation</b>	Individualised	Remove or lower HLA antibodies	

## 3.5 Replacement fluid

3.5.1 For TTP/HUS, replacement fluid is with fresh frozen plasma (Octaplas®). For TTP/HUS, prescription should be made in conjunction with the haematology team.

3.5.2 Albumin solution (human albumin solution – HAS 4.5%) is mainly used for other indications because it is heat treated to inactivate any blood borne viruses and has minimal risk of anaphylactic reactions. HAS can be used alone. Fresh frozen plasma (FFP) does not need to be given routinely. FFP (300- 600ml) at the end of each treatment as part of overall plasma replacement should be used in:-

- patients with pulmonary haemorrhage (consider using FFP as the only replacement fluid for the entire treatment if pulmonary haemorrhage is severe e.g. high oxygen requirement)
- If patient has had or due to have a renal biopsy.
- at risk of bleeding e.g. recent surgical procedure, coagulopathy (including low fibrinogen, abnormal INR or APTT ratio)
- For patients receiving daily plasma exchange give FFP every 3<sup>rd</sup> exchange.
- Patients with hypogammaglobulinaemia or active infection.

Complications are more common with FFP than with albumin due to citrate-induced hypocalcaemia and occasionally anaphylactoid reactions. To prevent hypocalcaemia, routinely give 10ml of 10% calcium gluconate intravenously at end of procedure if FFP has been used.

### 3.6 Anticoagulation

Heparin (unfractionated) is used as the standard anticoagulant. Larger doses are required compared to haemodialysis as some is removed by plasma exchange. Heparin free Plasma Exchange should be attempted in patients at high risk of bleeding.

Citrate can be used for anticoagulation with the HF440. This is not currently routine practice and a protocol is being developed for use on the renal unit. If in the interim a patient may benefit from citrate anticoagulation as heparin free treatment is unsuccessful please discuss with Dr. Dr Ricky Bell.

### 3.7 Complications and their prevention

Adverse reactions are more common with FFP than with albumin replacement (1). Serious complications, such as severe anaphylactoid reactions, typically follow the administration of FFP and other plasma-containing replacement fluid. The reported case fatality rate is 0.03-0.05%.

- **Hypotension** — often the result of volume depletion and responds to increased infusion rate. Other possibilities include vasovagal, anaphylactic reactions, sepsis – individual assessment required
- **Dyspnoea** — often due to pulmonary oedema due to fluid overload. Non-cardiogenic oedema can rarely occur and, if the blood components being re-infused are not adequately anticoagulated, massive pulmonary emboli can ensue. Allergic reactions associated with bronchospasm can be observed in patients receiving FFP.
- **Hypocalcaemia** — This occurs commonly when citrate is used as an anticoagulant and this binds to free calcium thereby lowering the free, but not the total, serum calcium concentration. FFP administered as a replacement fluid also contains citrate. Potential symptoms of hypocalcaemia include perioral and distal extremity paraesthesia. Intravenous calcium is given routinely to try to avoid this.
- **Coagulation abnormalities** — After a single plasma volume exchange, the prothrombin time increases by 30 percent and the partial thromboplastin time doubles; these changes tend to return towards normal within four hours. However, more severe and long-lasting changes can be induced when multiple exchanges are performed over a short period e.g. three or more treatments per week. This is the rationale for the use of routine FFP in patients who may be at high risk of bleeding.

- **Anaphylactic reactions to FFP** — This is the most common cause of serious complications and death associated with plasma exchange and has been reported in up to 21% of patients. It is characterised by fever, rigors, urticaria, wheezing, and hypotension; cardiopulmonary collapse is rare. The risk and severity of anaphylactoid reactions can be diminished by pre-treatment with hydrocortisone and chlorpheniramine. Adrenaline should be readily available at all times.
- **Infection** — Removal of immunoglobulins and complement can in theory lead to an immunodeficient state prone to infection particularly when combined with immunosuppressive drugs.
- **Other potential complications**
  - **Viral transmission with FFP**
  - **Hypokalaemia** — due to low potassium in HAS
  - **Drug removal** — Substantial drug removal by plasma exchange should be anticipated for those drugs which are highly protein bound
  - **ACE inhibitor reactions** — Flushing, hypotension, abdominal cramping, and other gastrointestinal symptoms have been reported during plasma exchange in patients receiving angiotensin converting enzyme inhibitors. These symptoms may reflect increased kinin generation which has been thought to account for the angioedema that can occur with ACE inhibitors.

#### 4. **Education and Training**

Medical staff from nephrology and transplant service and nursing staff (ward nurses, haemodialysis nurses and renal community team) should be familiar with guideline and access it for specific advice on dosing.

## 5. Monitoring and Audit Criteria

Key Performance Indicator	Method of Assessment	Frequency	Lead
Bi-annual audit of prescriptions of PLEX against this guideline.	Review prescriptions of PLEX	Annual to bi-annual	Chee Kay Cheung

## 6. Legal Liability Guideline Statement

Guidelines issued and approved by the Trust are considered to represent best practice. Staff may only exceptionally depart from any relevant Trust guidelines and always only providing that such departure is confined to the specific needs of individual circumstances. In healthcare delivery such departure shall only be undertaken where, in the judgement of the responsible healthcare professional' it is fully appropriate and justifiable - such decision to be fully recorded in the patient's notes

## 7. Supporting Documents and Key References

1. Mokrzycki MH, Kaplan AA. Therapeutic plasma exchange: complications and management. Am J Kid Dis 1994;23:817-827
2. Pusey CD, Rees AJ, Evans DJ, et al. Plasma exchange in focal necrotising glomerulonephritis with out anti-GBM antibodies. Kidney Int 1991;40:757-763
3. National Blood Service Clinical Guidelines for Therapeutic Apheresis. [www.blood.co.uk/HOSPITALS/library/bm/issue10/BM1203.htm](http://www.blood.co.uk/HOSPITALS/library/bm/issue10/BM1203.htm) (accessed 24June2006)

## 8. Keywords (up to six)

plasma exchange, plasmapheresis, membrane filtration

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REVIEW RECORD			
DATE	ISSUE NUMBER	REVIEWED BY	DESCRIPTION OF CHANGES (IF ANY)
1Jan2006	1	G Warwick	Initial guideline
3Jan2016	2	Reem Al-Jayyousi	Substantial rewrite; neurological indications and nursing aspects removed; updated to new guideline template
24 <sup>th</sup> February 2019	3	Reem Al-Jayyousi	Addition of patient consent section 3.3.

2 <sup>nd</sup> July 2019	4	Chee Kay Cheung	Minor changes
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