Therapeutic Plasma Exchange
Part II: Treatment Considerations

Tena Griffin, DNP, CRNP
Renal Clinical Educator
Baxter Healthcare

Overview

- TPE selection criteria, treatment goals, and plan
- Factors influencing TPE treatment dose and schedule
- Vascular access and blood flow rate
- TPE replacement fluids
- Anticoagulation
- Complications
- TPE and medications
- Influence of TMPa, blood flow rate, and patient hematocrit

TPE: Standard Medical Treatment

Treatment Goals

- Early treatment to halt inflammatory response
- Modulation of the abnormal immune response
- Remove the causative factor

Treatment Plan

- Immunosuppressant medications (i.e., steroids) to inhibit inflammatory response
- Chemotherapy/immunomodulators (i.e., Rituxan) to modulate immune function
- TPE to remove diseased components

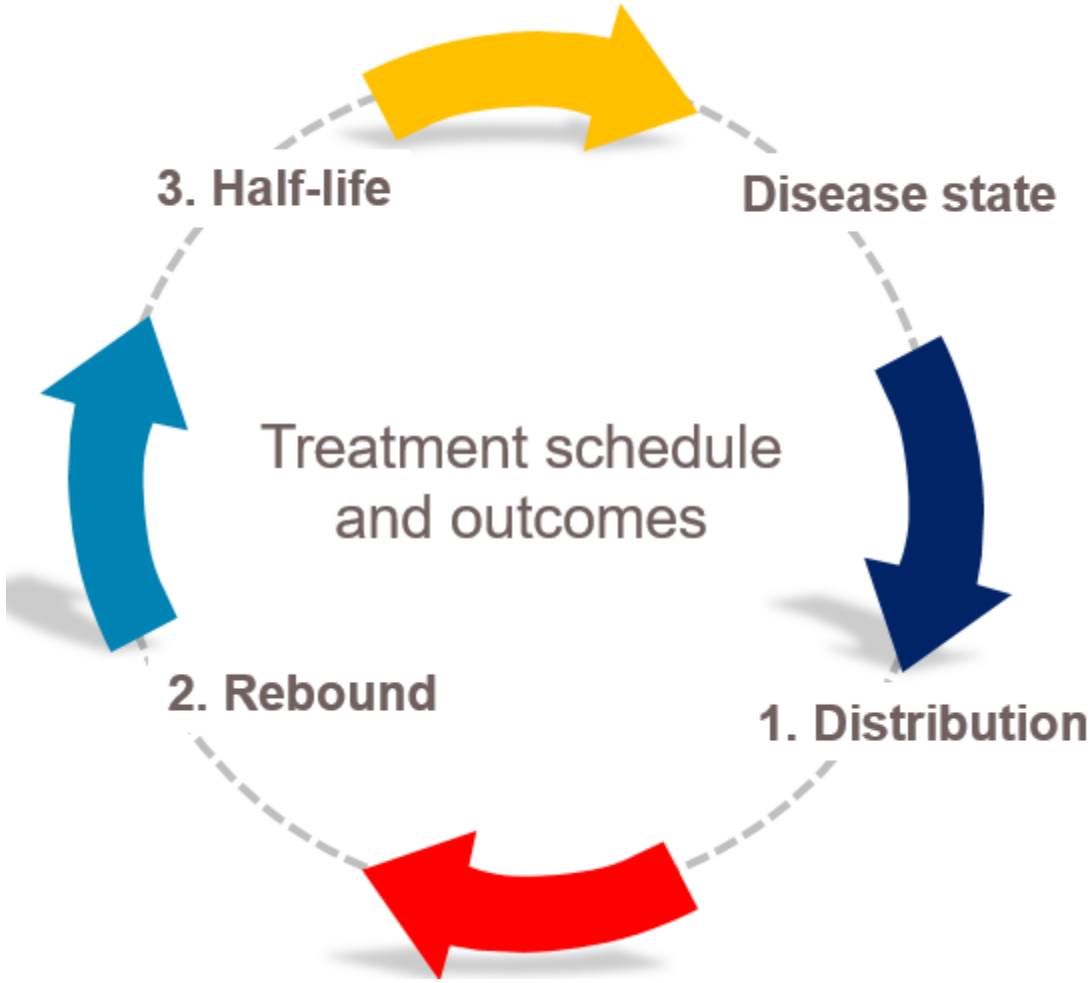
Kiprov DD, et al. in Daugirdas JT *et al. (Eds.)* Handbook of Dialysis 5th edition, 2015 (pp 323–348).

TPE Treatment Schedule

The TPE treatment schedule is prescribed by the physician based upon the patient-specific disease state

TPE treatment schedule and patient outcomes are influenced by the plasma protein kinetics of the targeted substance:

- Volume of distribution
- Rebound / resynthesis
- Half-life



Williams ME, Balogun RA. Clin J Am Soc Nephrol. 2014 Jan;9(1):181-90.

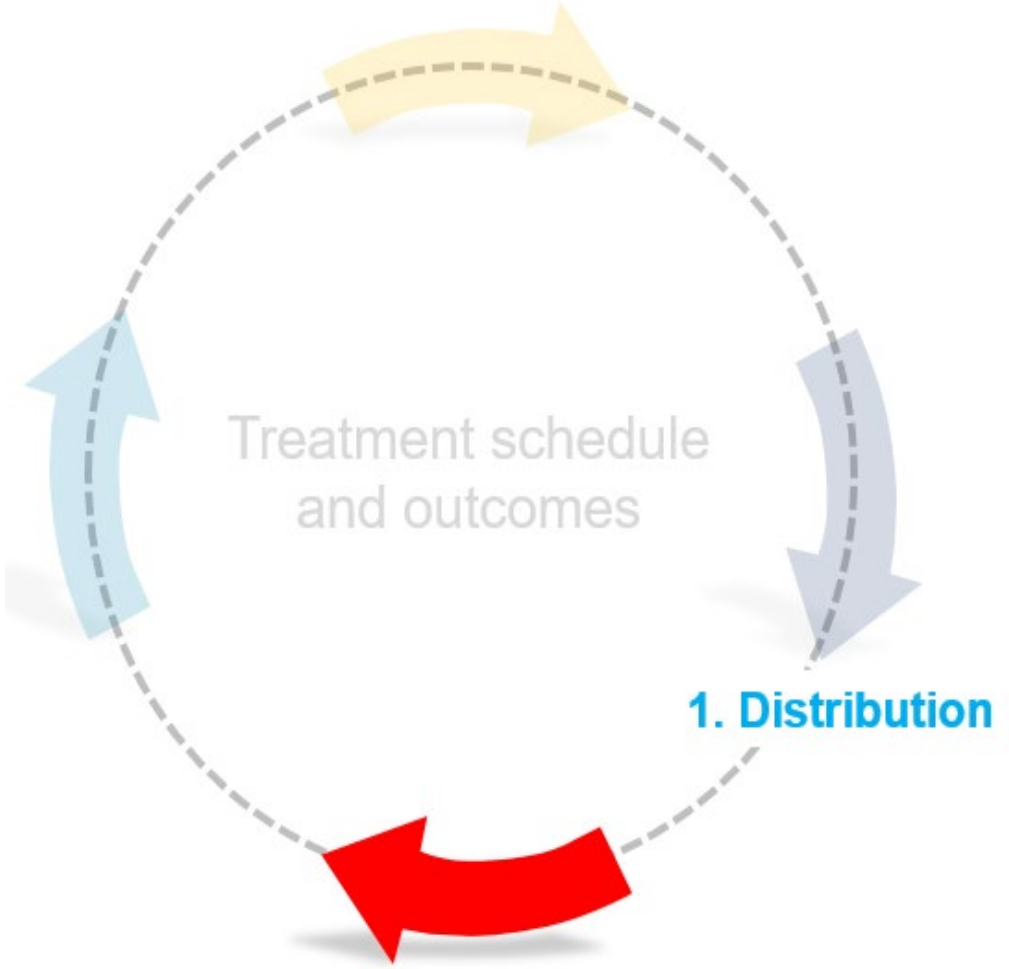
Volume of Distribution

Intravascular vs. extravascular

- Is the substance targeted to be removed primarily in the intravascular or extravascular space?

The extent of removal of a substance during TPE depends on:[1,2]

- The volume of the patient's plasma removed in relation to total plasma volume
- The distribution of the substance between the intravascular and extravascular compartments
- How rapidly the substance re-equilibrates between compartments

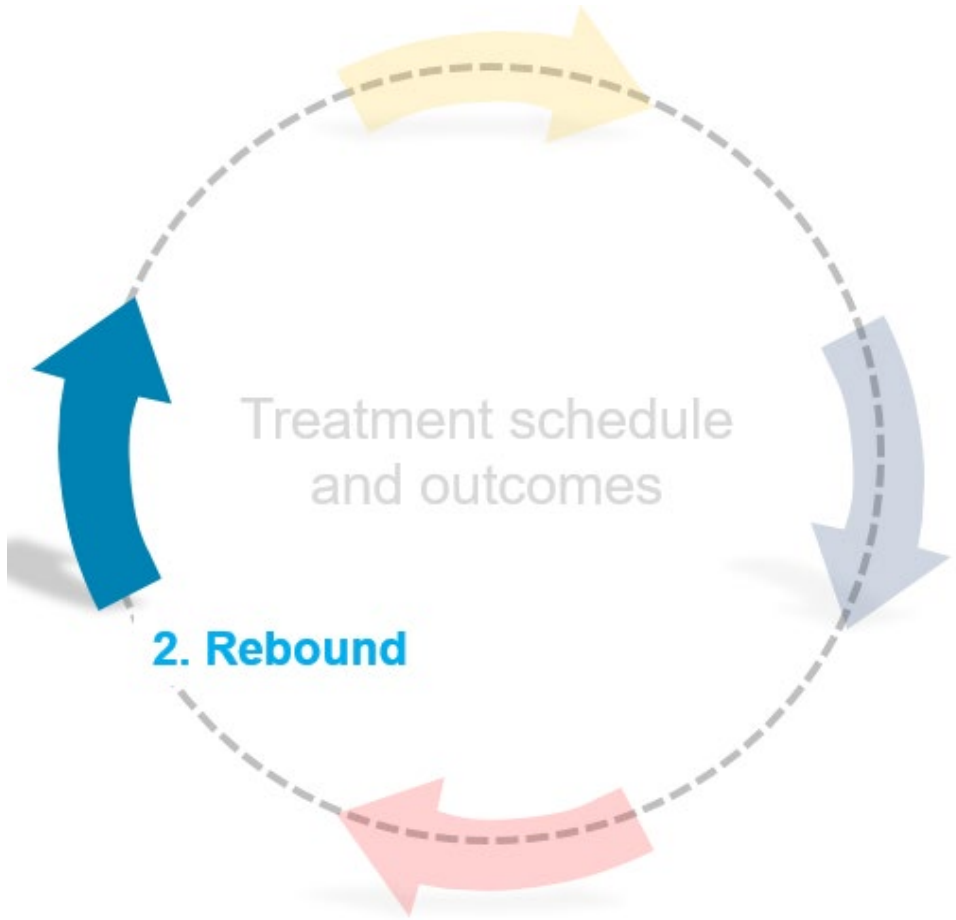


1. Williams ME, Balogun RA. Clin J Am Soc Nephrol. 2014 Jan;9(1):181-90.
2. Kiss JE. In Kellum J, *et al. (Eds.)* Continuous Renal Replacement Therapy 2nd edition. 2016; 49–173

Plasma Rebound

TPE is an intermittent therapy

- Intervals between treatments will be determined by the time it takes for plasma levels to rebound
- Plasma rebound is defined by the length of time it takes for the targeted substance to return to near pre-treatment value
- Plasma rebound is governed by two processes:
  - **Resynthesis:** as the substance is removed by TPE, the body continues to synthesize more
  - **Re-distribution:** the process by which a substance equalizes and moves from the intracellular to the extracellular then to the intravascular space.



Williams ME, Balogun RA. Clin J Am Soc Nephrol. 2014 Jan;9(1):181-90.
Kiprov DD, et al. in Daugirdas JT *et al. (Eds.)* Handbook of Dialysis 5th edition, 2015 (pp 323–348).

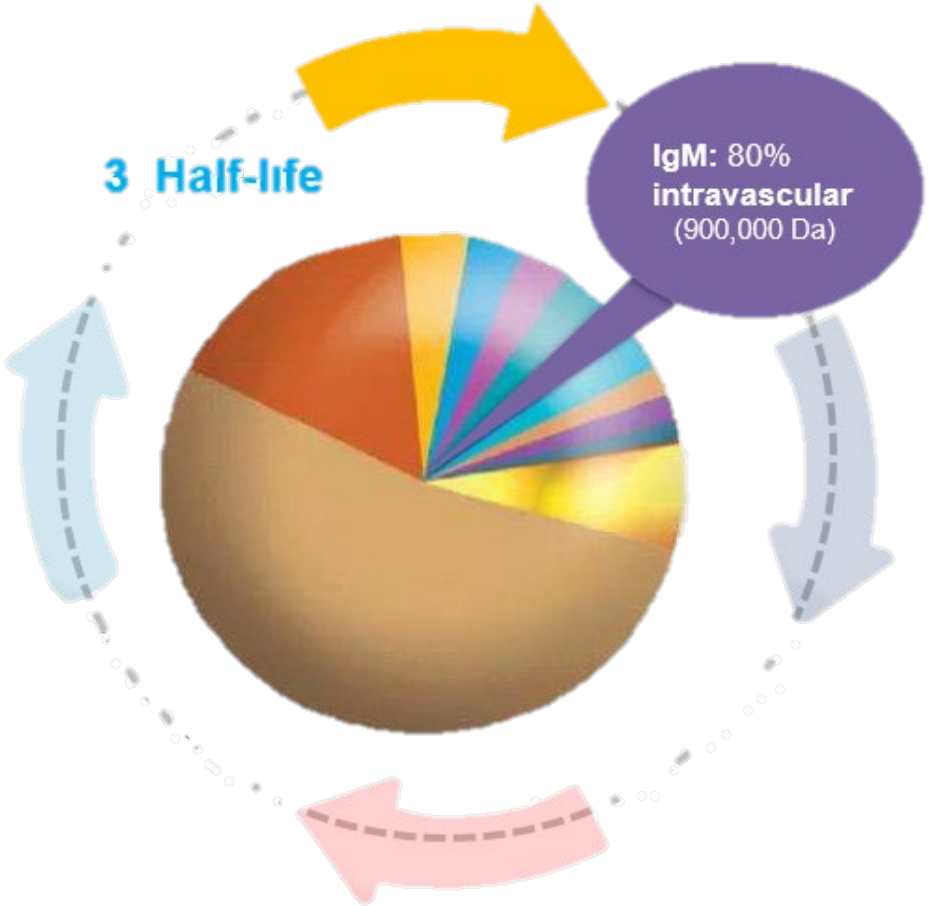
Plasma Half-Life

Half-life ($t_{½}$): the amount of time it takes for a substance to be reduced to half of its initial value

The half-life of a substance plays a role in TPE prescription because it predicts how long it takes for plasma rebound to occur

IgM as an example:

- **IgM $t_{½}$ = 5 days**
  - It takes 5 days to ↓ IgM levels by ½
- **IgM is accumulating** – although IgM is being exhausted by half over 5 days, it is also being resynthesized by the body
- **TPE treatment is planned to stay ahead of this production curve** and decrease total body burden



Williams ME, Balogun RA. Clin J Am Soc Nephrol. 2014 Jan;9(1):181-90.
Kiprov DD, et al. in Daugirdas JT *et al. (Eds.)* Handbook of Dialysis 5th edition, 2015 (pp 323–348).

TPE Prescription and Dose

After the patient- and disease-specific treatment schedule has been determined, the physician must make a few more prescription and TPE dose decisions:

- Vascular access and blood flow rate
- Estimated total blood volume (TBV) and plasma volume (PV)
- Plasma exchange volume (replacement fluid rate)
- Replacement fluid
- Anticoagulation
- Machine settings

Kiss JE. In Kellum J, *et al. (Eds.)* Continuous Renal Replacement Therapy 2nd edition. 2016; 49–173

Vascular Access & Blood Flow Rate

Vascular Access[1,2]

- Central Venous Catheter:
  - Internal Jugular
  - Femoral
  - Subclavian
- Arteriovenous fistula/graft

Blood Flow Rate

- Range: 100 – 250 ml/min[3]
- Minimum: 100 ml/min[3]
- *Lower rates can be delivered for low weight patients, if necessary; lower BFR may contribute to clotting and/or access issues*[2]

1. Gashti CN. Semin Dial. 2016 Sep;29(5):382-90.
2. Kiprov DD, et al. in Daugirdas JT *et al. (Eds.)* Handbook of Dialysis 5th edition, 2015 (pp 323–348).
3. Gambro. Prismaflex Operator's Manual (for use with software versions 7.xx). Order Number G5039110. 2005-2014

Volume Calculations: Total Blood, Plasma & Total Exchange

Several steps are involved in determining the volume of plasma to be exchanged per treatment

Necessary values and common formulas to determine TPE volume	
Patient's weight	In kg
Patient lab results	Pre-treatment HCT %
Estimated TBV	Weight (kg) x 70 mL/kg for adults = TBV
Estimated PV	TBV x (1.0 – HCT%) = PV
TPE prescription	Number of PV exchanges
Total exchange volume	PV x number of changes = exchange volume

Kiss JE. In Kellum J, *et al. (Eds.)* Continuous Renal Replacement Therapy 2nd edition. 2016; 49–173
Kiprov DD, et al. in Daugirdas JT *et al. (Eds.)* Handbook of Dialysis 5th edition, 2015 (pp 323–348).

Step 1:
Estimating Total Blood Volume (TBV)

Formulas:

Weight (kg) x 70 ml/kg for normal male adults = TBV

Weight (kg) x 65 ml/kg for normal female adults= TBV

Weight (kg) x 80/70 ml/kg for normal infant/child= TBV

Example: (normal adult male)

100 kg x 70 ml/kg = 7000 ml TBV

(Note: Some facilities may use alternative formulas to calculate TBV and Plasma Volume. Example: Nadler's Formula)

Kiss JE. In Kellum J, *et al. (Eds.)* Continuous Renal Replacement Therapy 2nd edition. 2016; 49–173
Kiprov DD, et al. in Daugirdas JT *et al. (Eds.)* Handbook of Dialysis 5th edition, 2015 (pp 323–348).

Step 2:
Estimating Plasma Volume (PV)

Formula:

TBV x (1.0 – Hct %) = PV

Example:

7000 ml x (1.0 - 0.42)

7000 ml x 0.58 = 4060 ml PV

(Note: Hct of 42% = 0.42)

Kiss JE. In Kellum J, *et al. (Eds.)* Continuous Renal Replacement Therapy 2nd edition. 2016; 49–173
Kiprov DD, et al. in Daugirdas JT *et al. (Eds.)* Handbook of Dialysis 5th edition, 2015 (pp 323–348).

Step 3:
Calculating Plasma Exchange Volume

Formula:

PV x Number of exchanges prescribed = Total Exchange Volume

Example:

- *4060 ml x 1.5 (or 150%) = 6090 ml*
- Total plasma volume to exchange: 6090 ml

(Note: The total replacement volume ordered will reflect the total plasma volume to exchange.)

Kiss JE. In Kellum J, *et al. (Eds.)* Continuous Renal Replacement Therapy 2nd edition. 2016; 49–173
Kiprov DD, et al. in Daugirdas JT *et al. (Eds.)* Handbook of Dialysis 5th edition, 2015 (pp 323–348).

Number of PV Exchanges

The number of PV exchanges is prescribed by the physician based on treatment goals

- The relationship between plasma volume exchanged and concentration of substances is illustrated below:

Plasma Volume Exchanged	Volume Exchanged	Amount of Substances Removed (macromolecule reduction ratio)
0.5 or 50%	1,400	39%
1.0 or 100%	2,800	63% (24% increase)
1.5 or 150%	4,200	78% (15% increase)
2.0 or 200%	5,600	86% (8% increase)
2.5 or 250%	7,000	92% (6% increase)

Kiprov DD, et al. in Daugirdas JT *et al. (Eds.)* Handbook of Dialysis 5th edition, 2015 (pp 323–348).

TPE Calculation Practice

Patient characteristics	Results
Patient's weight	100 kg
Patient's lab result: Pre-treatment HCT %	34% or 0.34
TPE prescription: Number of exchanges	1.5
TBV: Weight (kg) x 70 mL/kg for adults = TBV	
PV: TBV x (1.0 – HCT %) = PV	
Total exchange volume: PV x number of exchanges = total exchange volume	

TPE Calculation Practice - Answers

Patient characteristics	Results
Patient's weight	100 kg
Patient's lab result: Pre-treatment HCT %	34% or 0.34
TPE prescription: Number of exchanges	1.5
TBV: Weight (kg) x 70 mL/kg for adults = TBV	**7000 mL**
PV: TBV x (1.0 – HCT %) = PV	**4620 mL**
Total exchange volume: PV x number of exchanges = total exchange volume	**6930 mL**

TPE Replacement Fluids

Purpose

- Restore vascular volume
- Restore oncotic pressure
- Supply coagulation factors

Most Common Types

- Colloid solution (albumin and/or fresh frozen plasma)
- Combination of crystalloid/colloid solution

Kiprov DD, et al. in Daugirdas JT *et al. (Eds.)* Handbook of Dialysis 5th edition, 2015 (pp 323–348).
Kaplan AA. J Clin Apher. 2013 Feb;28(1):3-10.

Albumin (5%)

Limitations

- Occasional hypotension
- Pulmonary edema following rapid increase in albumin
- Clotting factor depletion or Coagulopathy
- Immunoglobulin depletion

Benefits

- Most commonly used
- No viral transmission
- Less expensive than FFP
- Maintains stable blood volume
- Allergic reactions are rare

Clinical Note

A less commonly used mixture is 70:30 5% Albumin and 0.9% normal saline (with or without added electrolytes)

Kiprov DD, et al. in Daugirdas JT *et al. (Eds.)* Handbook of Dialysis 5th edition, 2015 (pp 323–348).
Kaplan AA. J Clin Apher. 2013 Feb;28(1):3-10.

Fresh Frozen Plasma (FFP)

Selection Criteria

- Fibrinogen level <125mg/dl
- Coagulation factors below normal value
- Reduced platelet count

Benefits

- Replaces plasma clotting factors
- No post-pheresis coagulopathy
- No immunoglobulin deficiencies

Limitations

- Anaphylactic reactions
- ABO matching
- Viral transmission (rare)
- Citrate load: Hypocalcemia
- Expensive

Kiprov DD, et al. in Daugirdas JT *et al. (Eds.)* Handbook of Dialysis 5th edition, 2015 (pp 323–348).
Kaplan AA. J Clin Apher. 2013 Feb;28(1):3-10.

Anticoagulation

- Recommended for use in TPE if no contraindication exists
- Heparin (systemic): preferred method for membrane filtration
- Citrate (regional): preferred method for centrifugal devices (but can be used for membrane devices)
- Follow hospital standard protocol

Kiprov DD, et al. in Daugirdas JT *et al. (Eds.)* Handbook of Dialysis 5th edition, 2015 (pp 323–348).
Kaplan AA. J Clin Apher. 2013 Feb;28(1):3-10.

Potential Complications

Adverse effects of TPE may include:

- Anaphalactoid reactions (with FFP)
- Fluid imbalance: hypovolemia or overload
- Hypothermia
- Convective electrolyte loss
- Hemolysis*
- Clotting*

* Risk of clotting and hemolysis can be minimized by closely monitoring TMPs and filtration fraction levels during therapy

Kiprov DD, et al. in Daugirdas JT *et al. (Eds.)* Handbook of Dialysis 5th edition, 2015 (pp 323–348).
Kaplan AA. Am J Kidney Dis. 2008 Dec;52(6):1180-96.

Medications and TPE

ACE inhibitors[1]

Risk

- Anaphylactic reactions if albumin is used for replacement solution during TPE
- Bradykinin release resulting in vasodilation and hypotension

Prevention

- Withhold ACE inhibitors for at least 24-48 hours prior to TPE procedure

Antibiotics, other medications[2,3]

Risk

- May be removed during TPE based on the volume of distribution of the drug in the body
- Drugs that are highly protein bound have a small volume of distribution and will easily be eliminated by TPE because the drug remains in the plasma component of the blood

Prevention

- Whenever possible, medications should be administered after the TPE procedure under physician guidance

1. Owen HG, Brecher ME. Transfusion. 1994 Oct;34(10):891-4.
2. Kiprov DD, et al. in Daugirdas JT *et al. (Eds.)* Handbook of Dialysis 5th edition, 2015 (pp 323–348).
3. Kaplan AA. Am J Kidney Dis. 2008 Dec;52(6):1180-96.

Factors Influencing Plasmafiltration

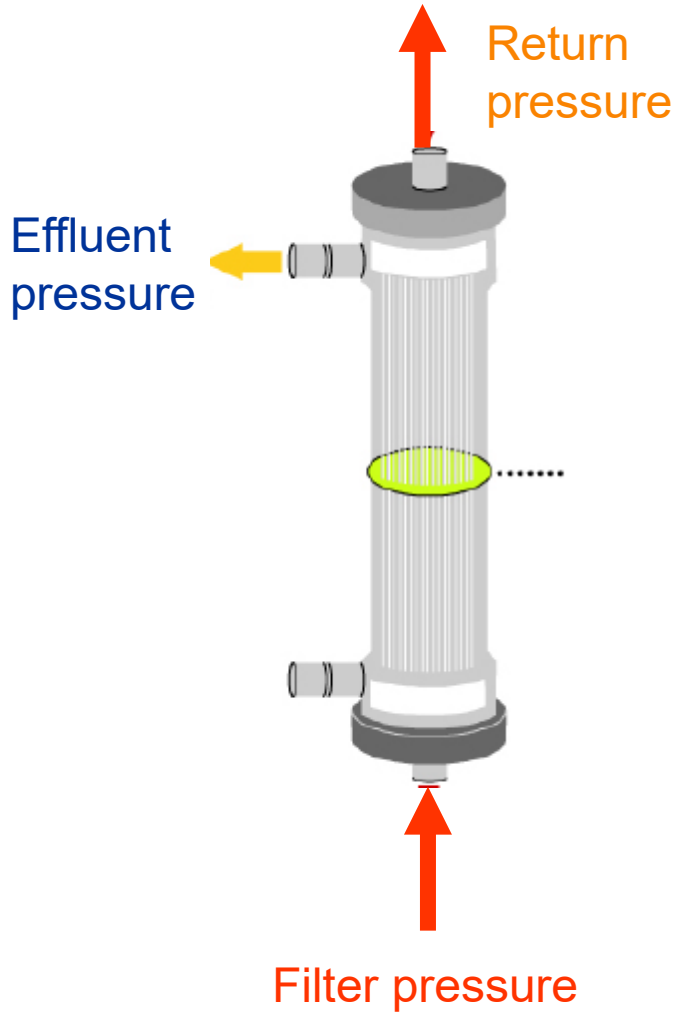
TMPa

- Access Transmembrane Pressure
- Machine calculated
- Alarm limit varies with BFR

Blood flow rate (BFR)

- Minimum of 100 ml/min
- Maximum of 250 ml/min

Patient's hematocrit (Hct)



To decrease the TMPa and filtration fraction:

- Decrease the replacement rate or patient plasma loss flow rate
- And/or increase the blood flow rate

Gambro. Prismaflex Operator's Manual (for use with software versions 7.xx). Order Number G5039110. 2005-2014

Knowledge Check

- Can you identify the common TPE therapeutic goals?
- Can you identify the basic TPE prescription components?
- Can you cite nursing considerations when administering TPE?

Please refer to your facility's protocols before performing this treatment.

References

References

- Gambro. Introduction to Therapeutic Plasma Exchange. Renal Intensive Care – Self-learning Moduler (Version 2). 2004.
- Gambro. Prismaflex Operator's Manual (for use with software versions 7.xx). Order Number G5039110. 2005-2014.
- Gashti CN. Membrane-based Therapeutic Plasma Exchange: A New Frontier for Nephrologists. Semin Dial. 2016 Sep;29(5):382-90.
- Kaplan AA. Therapeutic plasma exchange: a technical and operational review. J Clin Apher. 2013 Feb;28(1):3-10.
- Kaplan AA. Therapeutic plasma exchange: core curriculum 2008. Am J Kidney Dis. 2008 Dec;52(6):1180-96.
- Kiss JE. Chapter 22: Therapeutic Plasma Exchange in Critical Care Medicine. In Kellum J, *et al. (Eds.)* Continuous Renal Replacement Therapy 2nd edition. 2016; 49–173. Oxford University Press
- Kiprov DD, et al. Chapter 18: Therapeutic Apheresis. In Daugirdas JT *et al. (Eds.)* Handbook of Dialysis 5th edition, 2015 (pp 323–348). Wolters Kluwer Health.
- Owen HG, Brecher ME. Atypical reactions associated with use of angiotensin-converting enzyme inhibitors and apheresis. Transfusion. 1994 Oct;34(10):891-4.
- Padmanabhan A,et al. Guidelines on the Use of Therapeutic Apheresis in Clinical Practice - Evidence-Based Approach from the Writing Committee of the American Society for Apheresis: The Eighth Special Issue. J Clin Apher. 2019 Jun;34(3):171-354.
- Sarode R. Merck Manual Professional Version. Therapeutic Apheresis. 2016. https://www.merckmanuals.com/professional/hematology-and-oncology/transfusion-medicine/therapeutic-apheresis?query=apheresis (Accessed 26 July 2019).
- Williams ME, Balogun RA. Principles of separation: indications and therapeutic targets for plasma exchange. Clin J Am Soc Nephrol. 2014 Jan;9(1):181-90.
- Winters JL. Plasma exchange: concepts, mechanisms, and an overview of the American Society for Apheresis guidelines. Hematology Am Soc Hematol Educ Program. 2012;2012:7-12.