

Baxter

**Therapeutic Plasma Exchange
Part I: Methods, Goals & Guidelines**



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Overview

- Therapeutic apheresis overview
- Comparing apheresis methods
- Goals of therapeutic apheresis
- Indications/guidelines/disease categories

Definition of Apheresis

Apheresis:

Derived from the Greek word “*aphaeresis*,” meaning “to separate,” “to take away by force,” or “to remove”

Apheresis is the process where plasma or cellular components are separated from the circulating whole blood and the remainder is returned to the patient/donor



Apheresis Categories

Apheresis is performed in two capacities:

- **Donor:**

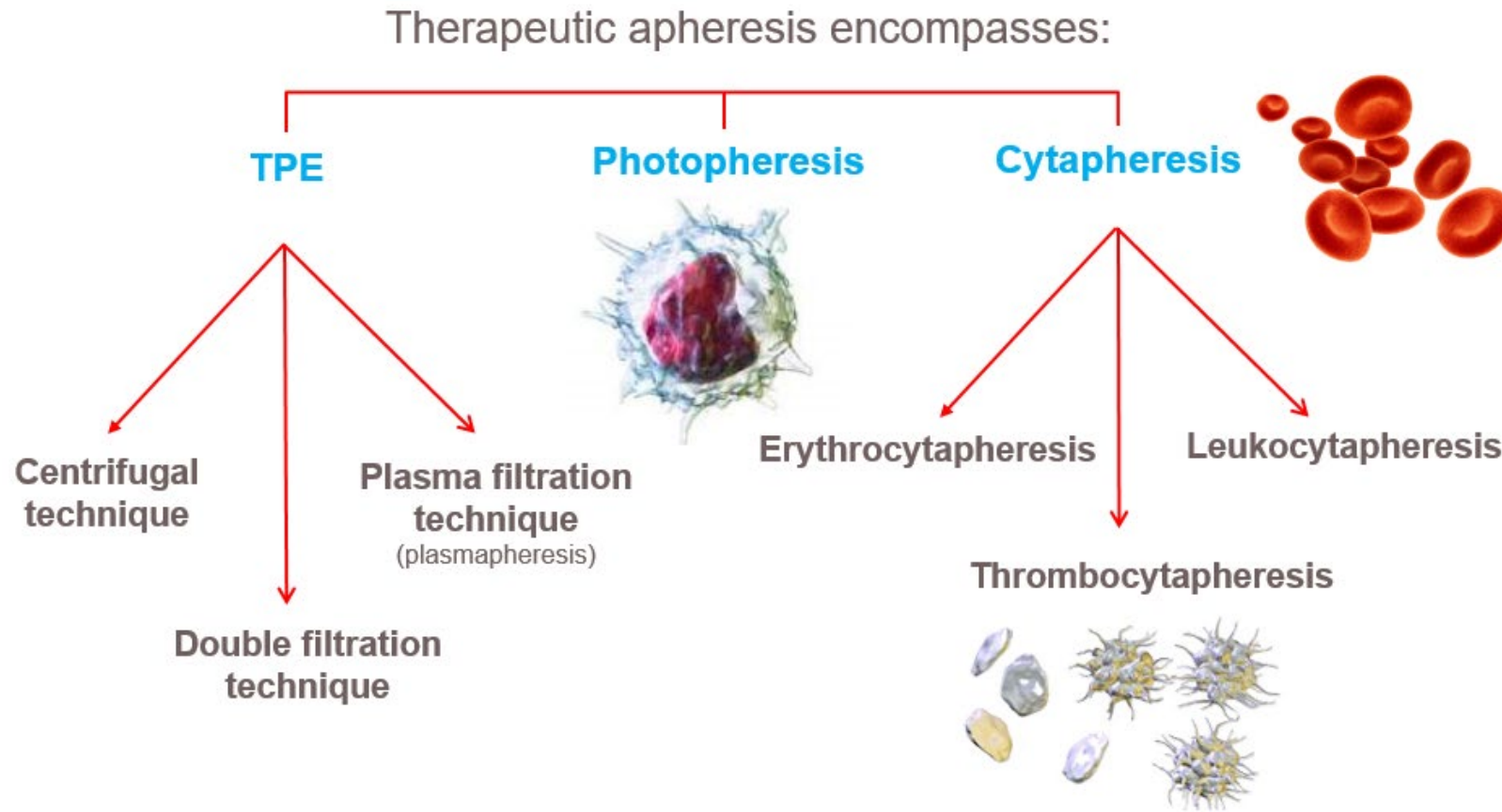
Extracorporeal removal of whole blood from a donor who is supplying one or more blood components

- **Therapeutic:**

Extracorporeal removal of plasma or cellular components from a patient to remove or treat abnormal/diseased components

1. 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).

Therapeutic Apheresis Overview



Gambro. Introduction to Therapeutic Plasma Exchange. Renal Intensive Care – Self-learning Module (Version 2). 2004.

Apheresis Technologies

Therapeutic apheresis can be performed using a variety of collection methods

The two most common methods are:^{1,2}

Centrifugation:

Centrifuge devices are more common worldwide (with the exception of Japan and Germany) and are the most widely used devices in the United States²

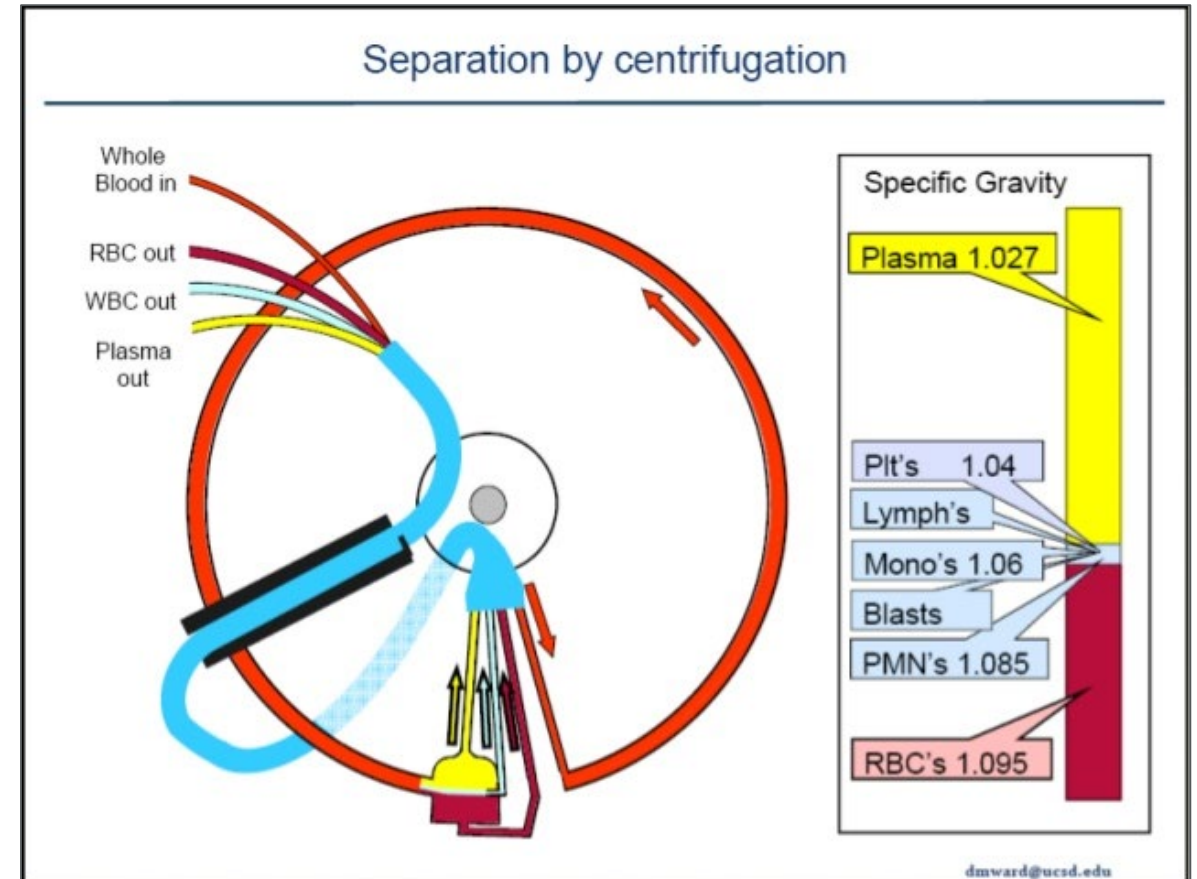
Membrane Filtration:

Less common, but considered therapeutically equivalent to centrifugal apheresis¹

1. Williams ME, Balogun RA. Clin J Am Soc Nephrol. 2014 Jan;9(1):181-90.
2. Gashti CN. Semin Dial. 2016 Sep;29(5):382-90.

Centrifugation

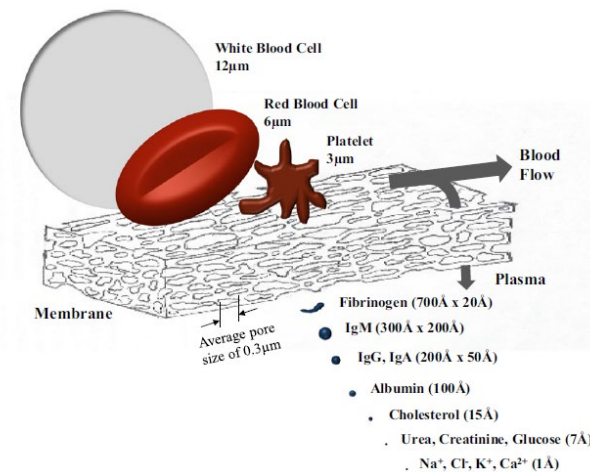
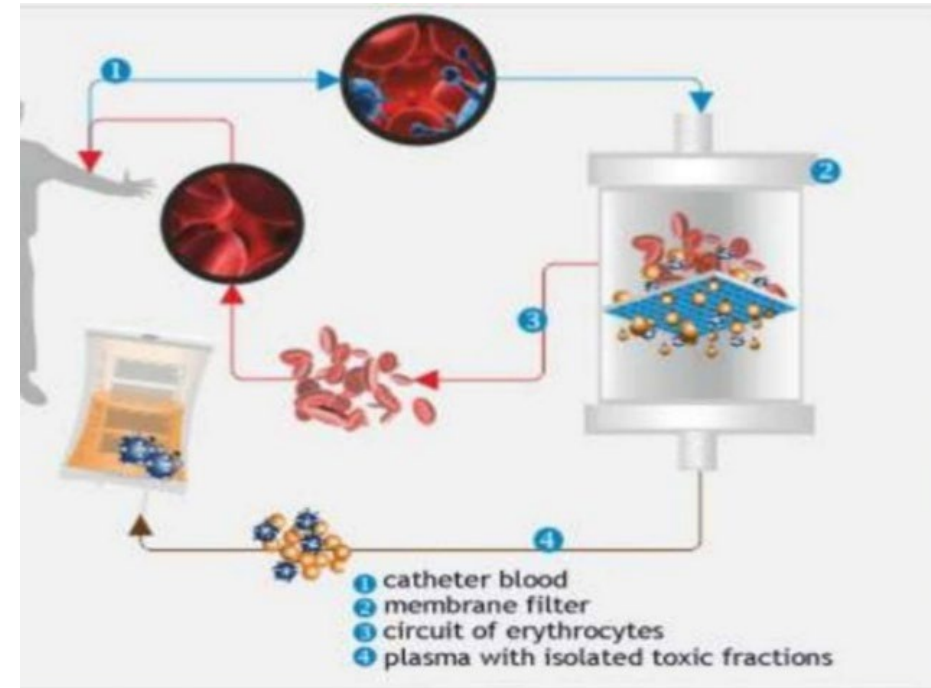
- A system draws whole blood from a donor patient, adds anticoagulant, separates the blood components, collects or removes specific components, and returns uncollected components back to the donor patient
- Separates blood components based on specific gravity (density) rather than molecular size
- Can remove all blood components (cellular components and plasma)



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

Membrane Filtration/Plasmafiltration

- Plasma is removed from the patient's blood by filtration across a plasma filter membrane and replaced with fresh plasma or a protein solution post-filter
- Blood components are separated based on molecular size using convection
- Limited to removal of plasma; no cellular components are removed



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

. Schematic of a membrane plasma separator with comparative sizes of blood cellular components and plasma constituents.

USMP/MG120/19-0022 09/19

Comparing Apheresis Methods

Characteristic	Centrifuge	Membrane
Mechanism	Centrifugal force	Capillary membrane filter
Blood flow, mL/min	10-150 (potential peripheral access)	100-250, 150 average (requires central access)
Plasma extraction, %	80	30
Plasma removal, mL/min	Variable	30
Anticoagulation	Citrate	Heparin
Separation	Specific gravity	Molecular size
Blood volume in circuit, mL	Approximately 180	Approximately 125
Molecular weight cutoff, D	N/A	3 million
Sterilization	γ -radiation or ethylene oxide	Ethylene oxide
Fluid replacement	Albumin, fresh frozen plasma	Albumin, fresh frozen plasma

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

Goals of Therapeutic Apheresis

- Removal of antibodies
- Removal of immune complexes
- Removal of plasma constituents
- Replacement of plasma deficiencies

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

Indications / ASFA Guidelines

The most comprehensive guidelines for therapeutic apheresis are published by the American Society for Apheresis (ASFA)

- TPE can be used to treat a variety of disease states, both acute and chronic, that are fully outlined in the ASFA guidelines
- Treatment is based on current guidelines and evidence grading
- The ASFA evidence-based approach assigns diseases to categories based on a systematic review of the literature

ASFA Categories

Category I

Disorders for which apheresis is accepted as first-line therapy, either as a primary stand-alone treatment or in conjunction with other modes of treatment

Category II

Disorders for which apheresis is accepted as second-line therapy, either as a stand-alone treatment or in conjunction with other modes of treatment

Category III

Disorders for which the optimum role of apheresis is not established; decision making should be individualized

Category IV

Disorders for which published evidence demonstrates or suggests apheresis to be ineffective or harmful; Institutional Review Board approval is desirable if apheresis treatment is undertaken in these circumstances

AFSA Category Examples

Category I

- Guillain-Barre syndrome
- Thrombotic thrombocytopenia purpura (TTP)
- Myasthenia gravis
- Goodpasture syndrome

Category II

- Cryoglobulinemia
- Multiple sclerosis (acute attack, relapse)
- ABO transplant incompatibility

Category III

- Heparin-induced thrombocytopenia and thrombosis
- Immunoglobulin A nephropathy

Category IV

- Schizophrenia
- Rheumatoid arthritis

Padmanabhan A, et al. J Clin Apher. 2019 Jun;34(3):171-354.

TPE Selection Criteria

One or more of the following conditions should be met:

- Targeted substance is >15,000 Da
- Targeted substance has a relatively long half-life, so that removal provides a therapeutically useful period of diminished serum concentration
- Targeted substance is acutely toxic and/or resistant to conventional therapy

TPE is designed for the removal of large-molecular-weight substances

Typical Solute Molecular Weights

Substance	Molecular weight in Daltons (1 d. = 1/16 th H ⁺ atom)
Albumin	69,000
IgG	180,000
IgA	150,000
IgM	900,000
LDL-cholesterol (LDL apheresis)	1,300,000

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

Knowledge Check



- Can you discuss basic TPE terms and principles?
- Can you differentiate between centrifuge and membrane TPE?
- Can you identify the common TPE therapeutic goals and associated disease states?

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
- Kiprof 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.