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

Therapeutic Apheresis Overview

Therapeutic apheresis encompasses:

- **TPE**
  - Centrifugal technique
  - Plasma filtration technique (plasmapheresis)
  - Double filtration technique

- **Photopheresis**

- **Cytapheresis**
  - Erythrocytapheresis
  - Leukocytapheresis
  - Thrombocytapheresis

Apheresis Technologies

Therapeutic apheresis can be performed using a variety of collection methods.
The two most common methods are:  

**Centrifugation:**
Centrifuge devices are more common worldwide (with the exception of Japan and Germany) and are the most widely used devices in the United States\(^2\)

**Membrane Filtration:**
Less common, but considered therapeutically equivalent to centrifugal apheresis\(^1\)

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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).

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.
## Comparing Apheresis Methods

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

Goals of Therapeutic Apheresis

• Removal of antibodies

• Removal of immune complexes

• Removal of plasma constituents

• Replacement of plasma deficiencies
The most comprehensive guidelines for therapeutic apheresis are published by the American Society for Apheresis (AFSA)

- 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 AFSA 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

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

<table>
<thead>
<tr>
<th>Substance</th>
<th>Molecular weight in Daltons (1 d. = 1/16(^{\text{th}}) H(^{+}) atom)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albumin</td>
<td>69,000</td>
</tr>
<tr>
<td>IgG</td>
<td>180,000</td>
</tr>
<tr>
<td>IgA</td>
<td>150,000</td>
</tr>
<tr>
<td>IgM</td>
<td>900,000</td>
</tr>
<tr>
<td>LDL-cholesterol (LDL apheresis)</td>
<td>1,300,000</td>
</tr>
</tbody>
</table>
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