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## Plasmapheresis

### Authors

Shane R. Sergent<sup>1</sup>; John V. Ashurst<sup>2</sup>.

### Affiliations

<sup>1</sup> Michigan State University College of OM

<sup>2</sup> Kingman Regional Medical Center

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## Continuing Education Activity

Plasmapheresis is a therapeutic intervention that involves extracorporeal removal, return, or exchange of blood plasma or components. The underlying mechanism of this procedure is accomplished by either centrifugation or filtration using semipermeable membranes. This activity reviews plasmapheresis as a therapeutic intervention that involves extracorporeal removal, return, or exchange of blood plasma or components. This intervention results in a filtered plasma product that can be used for the treatment of numerous diseases. It also highlights the interprofessional team strategies for improving care coordination and communication to advance plasmapheresis and improve outcomes.

### Objectives:

- Identify the indications and contraindications of plasmapheresis.
- Describe the equipment, personnel, preparation, and technique in regards to plasmapheresis.
- Review the potential complications and clinical significance of plasmapheresis.
- Outline interprofessional team strategies for improving care coordination and communication to advance plasmapheresis and improve outcomes.

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## Introduction

Plasmapheresis is a therapeutic intervention that involves extracorporeal removal, return, or exchange of blood plasma or components.[1][2] The underlying mechanism of this procedure is accomplished by either centrifugation or filtration using semipermeable membranes. While centrifugation is based on the principle of separation using different specific gravities of various blood components, membrane plasma separation filters blood components based on their particle size.[3][4]

The preferred method of plasmapheresis in most centers worldwide is by automated centrifuge-based technology.[5] However, in certain hospitals and patients on hemodialysis, plasmapheresis is done using membrane plasma separation.[3] In plasmapheresis using centrifugation, filtered plasma is discarded, and RBCs and replacement fluid (donor plasma or colloids) are returned. Membrane plasma separation allows selective removal of undesired macromolecules; hence, filtered, processed plasma is returned to the patient, eliminating the need for replacement fluids.

In this review, we will discuss the indications, contraindications, equipment, preparation, procedure, and complications of plasmapheresis.

## Indications

Therapeutic plasmapheresis is used for numerous diseases. The conditions involve the presence of a toxic substance in plasma (e.g., immunoglobulin), which can be filtered. The disorders where therapeutic plasmapheresis can be done are grouped into four categories by the Apheresis Applications Committee of the American Society for Apheresis (ASFA). Category 1 includes disorders where plasmapheresis can be done as a first-line treatment, category 2 includes disorders where plasmapheresis can be done as a second-line treatment in addition to the existing standard of care, category 3 includes disorders in which the evidence of the benefit of plasmapheresis is minimal, and therapy must be individualized, and category 4 includes disorders in which the evidence suggests that plasmapheresis is either ineffective or harmful, however, may be considered after approval from the institute ethics committee.[2]

The alphabetical list of various indications for plasmapheresis, along with their ASFA category, is as follows.

### Category 1

- Acute inflammatory demyelinating polyradiculoneuropathy/Guillain-Barre syndrome
- ANCA-associated rapidly progressive glomerulonephritis (dialysis-dependent or associated with diffuse alveolar hemorrhage)
- Anti-glomerular basement membrane disease-Goodpasture syndrome (dialysis independent or associated with diffuse alveolar hemorrhage)
- Chronic inflammatory demyelinating polyradiculoneuropathy
- Focal segmental glomerulosclerosis (recurrent in the transplanted kidney)
- Hyperviscosity in monoclonal gammopathies
- Liver transplantation: Desensitization
- Myasthenia gravis
- N-methyl D-aspartate receptor antibody encephalitis
- Paraproteinemic demyelinating neuropathies/chronic acquired demyelinating polyneuropathies (IgA/IgG/IgM mediated)
- Progressive multifocal leukoencephalopathy associated with natalizumab
- Renal transplantation: Desensitization and antibody-mediated rejection
- Thrombotic microangiopathy (Factor H autoantibodies and ticlopidine)
- Thrombotic thrombocytopenic purpura
- Wilson disease (fulminant)

### Category 2

- Acute disseminated encephalomyelitis
- Cardiac transplantation: Desensitization
- Catastrophic antiphospholipid syndrome
- Cryoglobulinemia; symptomatic/severe
- Dilated cardiomyopathy, idiopathic (NYHA 2-4)

- Hashimoto encephalopathy: Corticosteroid responsive encephalopathy associated with autoimmune thyroiditis
- Hematopoietic stem cell transplantation, ABO-incompatible
- Lambert-Eaton myasthenic syndrome
- Multiple sclerosis
- Myeloma cast nephropathy
- Neuromyelitis Optica spectrum disorders
- Overdose, envenomation, and poisoning, such as mushroom
- Pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS)
- Phytanic acid storage disease (Refsum disease)
- Systemic lupus erythematosus (severe)

### Category 3

- Acute liver failure
- ANCA-associated rapidly progressive glomerulonephritis (dialysis independent)
- Anti-glomerular basement membrane disease, Goodpasture syndrome (dialysis-dependent, no DAH)
- Aplastic anemia, pure red cell aplasia
- Autoimmune hemolytic anemia
- Burn shock resuscitation
- Cardiac neonatal lupus
- Cardiac transplantation: Antibody-mediated rejection
- Chronic focal encephalitis (Rasmussen encephalitis)
- Complex regional pain syndrome; chronic
- Erythropoietic porphyria, liver disease
- Hemolysis liver enzymes low platelet (HELLP) syndrome (postpartum)
- Hematopoietic stem cell transplantation, HLA desensitization
- Hemophagocytic lymphohistiocytosis; hemophagocytic syndrome; macrophage activating syndrome
- Henoch-Schonlein purpura
- Heparin-induced thrombocytopenia and thrombosis
- Hypertriglyceridemic pancreatitis
- Immune thrombocytopenia; refractory
- IgA nephropathy; crescentic
- Lung transplantation: Desensitization and antibody-mediated rejection
- Paraneoplastic neurological syndromes

- Pemphigus Vulgaris; severe
- Pruritus due to hepatobiliary diseases
- Scleroderma (systemic sclerosis)
- Sepsis with multiorgan failure
- Stiff-person syndrome
- Thrombotic microangiopathy (complement factor gene mutations, MCP mutations, clopidogrel, and calcineurin inhibitors)
- Thyroid storm
- Toxic epidermal necrolysis (refractory)
- Vasculitis
- Voltage-gated potassium channel antibodies

#### Category 4

- Amyloidosis, systemic
- Dermatomyositis/polymyositis
- HELLP syndrome (ante partum)
- Lupus nephritis
- Thrombotic microangiopathy (gemcitabine and quinine)

### Contraindications

The contraindications for therapeutic plasmapheresis are as follows:[1]

- Non-availability of central line access or large bore peripheral lines
- Hemodynamic instability or septicemia
- Known allergy to fresh frozen plasma or replacement colloid/albumin
- Known allergy to heparin
- Hypocalcemia (restricts the use of citrate as an anticoagulant during the procedure); relative contraindication
- Angiotensin-converting enzyme (ACE) inhibitor used in last 24 hours; relative contraindication

### Equipment

Venous access for this procedure is either by a central venous catheter or large bore peripheral lines. There are multiple manufacturers of the centrifuge-based plasmapheresis machines.

Another technique of performing plasmapheresis is by using semipermeable membrane filters with a standard hemodialysis machine. However, for this technique, central venous access is mandatory due to the need for higher blood flow rates of 100 mL/min to 150 mL/min. There are two membrane-based technologies that are currently available; hollow fiber and parallel plate. Hollow fiber dialyzers are cylindrical shell-like structures, consisting of multiple polysulfone capillary fibers.

Parallel plate dialyzers consist of layered membranes, with ridges and grooves which facilitate filtration. Both these dialyzers allow plasma filtration based on particle size and pressure gradients. Hollow fiber dialyzers are more gentle as opposed to parallel plate dialyzers and are preferred for pediatric patients, whereas hollow fiber dialyzers use less blood volume, and hence require a reduced dose of citrate or heparin for anticoagulation.

The major advantage of membrane-based plasmapheresis over centrifuge-based technology is that the removed processed-plasma by ultrafiltration can be returned to the patient eliminating the need for replacement fluids or colloids.[1]

## Personnel

Plasmapheresis was traditionally performed in blood banks by centrifuge-based techniques. However, therapeutic plasmapheresis procedures are routinely performed by critical care specialists in the intensive care unit, nephrologists, and dialysis-technicians after specialized skill-based training.

## Preparation

No specific patient preparation is needed for this procedure. However, while inserting a central line, a local anesthetic may be needed. For this purpose, 2% lidocaine injection is used routinely. In pediatric patients, sedation with opioids and benzodiazepines may be considered for pain and anxiety control.

The patient is positioned supine for plasmapheresis; however, the position, especially of the neck, may be altered according to the location of central venous access to maintain adequate blood flow throughout the procedure.

A close watch on patient vitals is recommended throughout the procedure to assess for volume depletion, hypocalcemia, and complications of fresh frozen plasma transfusion.

## Technique or Treatment

The steps for performing plasmapheresis using centrifuge-based equipment are as follows:[6]

1. Initially, a waste of around 3-5 mL blood from the central venous catheter is discarded.
2. After drawing baseline samples for complete hemogram, calcium, and fibrinogen, it is flushed with 5-10 mL of heparinized saline.
3. The double lumen catheter is now connected to the machine tubing to start the priming procedure.
4. The machine calculates total body volume (TBV), and the effective plasma volume (which equals  $TBV \times (1 - \text{hematocrit})$ ) of the patient based on the operator entered height and weight.
5. The replacement product to be used and its desired volume (40 - 60 mL/kg) is decided by the clinician, and entered into the machine, based on which it calculates the centrifuge speed.
6. The separated plasma is discarded by the machine, and the RBCs are returned back to the patient along with the replacement fluid.
7. Finally, post-procedure, tubings are connected to heparinized saline, and reinfusion is initiated.
8. Post-plasmapheresis blood for fibrinogen and calcium is sent again, and lumens of central venous catheters are flushed.

## Complications

The common complications that can occur during or post-plasma exchange procedure are as follows:

- Hypocalcemia or hypomagnesemia as a result of the use of citrate anticoagulation. This is managed with the intravenous replacement of calcium and magnesium.[7]
- Hypothermia
- Transfusion reactions. They are managed symptomatically with pheniramine, hydrocortisone/dexamethasone, and/or epinephrine.
- Fluid and electrolyte imbalance.
- Bleeding diatheses due to hypofibrinogenemia and thrombocytopenia.
- Hypotension[8]
- Flushing
- Gastrointestinal symptoms like nausea and vomiting

## Clinical Significance

Plasmapheresis offers an effective therapy for many acute and chronic diseases. It can also be used as an adjunct to prepare for procedures, surgery, and even improve postoperative recovery or shorten ventilation periods. Generally, risks and side effects are mild, most common being transient hypotension and related symptoms.[9][10]

The American Society for Apheresis has done extensive research on plasmapheresis as a therapeutic strategy, and continue to update a comprehensive apheresis guideline using an evidence-based approach to aid physicians caring for these patients.[10] Using this evidence-based resource is the best way to standardize care and provide innovation.[9][10]

## Enhancing Healthcare Team Outcomes

Plasmapheresis is an intensive care procedure that needs appropriate decisions, specialized skill-based training, close monitoring, and follow-up for best clinical outcomes. It is recommended that a customized dedicated chart must be designed at all centers performing plasmapheresis procedures. This should include a brief history, with established/presumptive diagnosis.

The basis for the procedure, along with patient-specific concerns, must be listed. This chart should also indicate the total number of plasmapheresis sessions planned. The healthcare professionals must clearly discuss the clinical and/or laboratory parameters to monitor the effectiveness of the procedure and enlist criteria for completion/discontinuation. The urgency of the procedure (emergency, urgent, or routine) must be delineated while planning for plasmapheresis. These holistic goals can ensure the effectiveness and reduce complications of plasmapheresis in clinical settings.

## Review Questions

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