



The Institute for
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Special Double Issue: Apheresis Update

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INTRODUCTION

Apheresis (Greek: "to take away") is a technology in which the blood of a donor or patient is removed from the circulation, passed through a machine that separates out and removes a particular blood component and returns the remainder to the circulation.

METHODS

Depending on the component being removed, different methods are employed in the performance of apheresis. They include: 1. Centrifugation: separates components based on [weight](#). 2. Membrane filtration techniques: remove plasma from cellular components based on pore size. 3. Selective removal of pathologic or harmful plasma-associated constituents without removing normal plasma components. This technique first requires separation of plasma either by centrifugation or filtration and subsequent removal/adsorption of the pathologic substance using specialized columns (e.g. LDL – apheresis).

TYPES OF APHERESIS

I. Based on indication:

1. **Therapeutic apheresis** - The purpose is to remove a component of the blood which contributes to a disease state.

2. **Donor apheresis** – The purpose is to obtain a specific blood component. The process of apheresis has become essential in providing blood components for therapy. During apheresis it is possible to process large volumes of blood and obtain a therapeutic dose of the desired component from one donor.

II. Based on the blood component removed:

1. [Plasmapheresis](#) – [blood plasma](#).
2. [Plateletpheresis](#) (thrombapheresis, thrombocytapheresis) – [blood platelets](#).
3. [Leukapheresis](#) – [leukocytes](#) (white blood cells).

4. [Stem cell harvesting](#) – circulating [hematopoietic progenitor cells](#) are harvested to use in [HPC \(Bone Marrow\) transplantation](#).

5. [Granulocyte collection](#) – white blood cells are collected for treatment of patients with severe leukopenia and infection.

6. [LDL apheresis](#) – removal of [low density lipoprotein](#) in patients with [familial hypercholesterolemia](#).

7. [Double red blood cell collection](#) – enhanced convenience for donors, especially useful for blood types on short supply (O Rh negative).

III. Other Techniques:

1. Photopheresis

INDICATIONS FOR APHERESIS

Therapeutic Apheresis

Indication Categories – American Society for Apheresis (ASFA), endorsed by AABB

- Category I: standard & acceptable, primary therapy or valuable, first-line adjunctive therapy.
- Category II: evidence suggests efficacy, acceptable as supportive or adjunctive therapy.
- Category III: insufficient evidence to establish benefit, trials show conflicting results - used in research protocol or an exceptional effort in pts for whom conventional therapies have failed.
- Category IV: lack of efficacy - research only.

Plasmapheresis or Therapeutic Plasma Exchange (TPE):

TPE has been found to be useful in treating a number of diseases in various categories, including:

autoimmune, hematologic, metabolic, neurological, renal, rheumatic and transplantation-related conditions.

Replacement fluids vary with the clinical indications for TPE. For most cases, the objective is removal of a disease-causing element associated with a patient's plasma and volume replacement with albumin or a combination of albumin and saline is standard. For certain indications (e.g. Thrombotic thrombocytopenic purpura or TTP) in which the disease pathogenesis may be related to the absence of a protective substance from a patient's plasma, replacement with normal donor plasma (containing the missing substance) is appropriate. Selection of proper replacement fluid(s) is best done by or in consultation with physicians experienced in plasmapheresis.

Typical volumes for TPE procedures are in the 1 to 1.5 plasma volume range. A one plasma volume exchange results in approximately 65% removal/replacement of the patient's plasma. Exchanging 1.5 times the patient's plasma volume increases that number to 75%. Increasing the volume exchanged beyond these levels results in progressively smaller increments, as the plasma removed/replaced is less and less that of the patient vs. the replacement fluid already given in the procedure.

In **autoimmune diseases**, a patient's plasma may contain antibodies, antigen-antibody complexes or other factors that may contribute to the deleterious effects of the disease. TPE helps to reduce the level of circulating antibodies and immune complexes. The only Category I indication in this group is cryoglobulinemia. Others (catastrophic antiphospholipid syndrome, pemphigus vulgaris and systemic lupus erythematosus) are Category III and IV indications.

Hematological diseases in which TPE may be indicated include:

Category I: Hyperviscosity due to monoclonal gammopathy (e.g. Waldenstrom's macroglobulinemia) and thrombotic thrombocytopenic purpura (TTP).

Category II: ABO-incompatible hematopoietic progenitor cell transplantation and RBC alloimmunization in pregnancy.

Categories III and IV: Aplastic anemia, Warm autoimmune hemolytic anemia, Cold agglutinin disease, Coagulation factor inhibitors, Immune thrombocytopenic purpura (ITP) and Post-transfusion purpura (PTP).

Some types of **metabolic diseases** may be treated with TPE, including:

Category II: Mushroom poisoning, and Refsum's disease.

Categories III and IV: Acute liver failure, Hypertriglyceridemic pancreatitis, Overdose/poisoning by other compounds, sepsis and thyrotoxicosis.

A number of **neurological diseases** are amenable to treatment with TPE. These include:

Category I: Guillain-Barré syndrome, Chronic inflammatory demyelinating polyneuropathy (CIDP), Myasthenia Gravis, Paraproteinemic polyneuropathies (IgG/IgA), Severe pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS) and Severe Sydenham's chorea.

Category II: Lambert-Eaton myasthenic syndrome, Acute CNS inflammatory demyelination in Multiple Sclerosis, Paraproteinemic polyneuropathy (IgM), and Rasmussen's encephalitis.

Categories III and IV: Acute disseminated encephalomyelitis, Devic's Syndrome, Chronic progressive Multiple Sclerosis, Paraneoplastic neurologic syndromes, Paraproteinemic polyneuropathy due to Multiple Myeloma, and Stiff-Person syndrome.

In **renal diseases**, TPE is used as a primary treatment modality (Category I) for Goodpasture's syndrome. Wegener's granulomatosis is a Category II indication. Other renal diseases (Focal segmental glomerulosclerosis, Hemolytic uremic syndrome, and rapidly progressive glomerulonephritis) are Category III indications.

For **rheumatic diseases** TPE is a Category III indication for treatment of scleroderma.

Finally, **transplant-related** indications for TPE include:

Category II: ABO incompatible solid organ kidney and heart (infants) transplantation.

Categories III and IV: Transplant-associated microangiopathy, ABO incompatible liver transplantation and heart transplant rejection.

Special Adaptation of Plasmapheresis

LDL APHERESIS: Selective removal of LDL by adsorption or filtration is indicated for treatment of homozygotic familial hypercholesterolemia (Category I) and heterozygotic familial hypercholesterolemia (Category II) unresponsive to conventional medical therapy. Medicare criteria: LDL-C \geq 200 mg/dl with documented CAD; unresponsive to medications. Treatment is performed every 2 weeks.

CYTAPHERESIS (Cell depletion)

- The purpose is to deplete a particular cellular component from the circulation (therapeutic) or to collect a component of the buffy coat (donor).
- Buffy coat: granulocytes, mononuclear cells (lymphocytes/monocytes) and platelets.
- Cells are separated based on their relative densities.
- HES (hydroxyethyl starch, a rouleaux-promoting agent) may be used to improve separation of RBCs from granulocytes.

Plateletpheresis: In myeloproliferative disorders, such as essential thrombocytosis, the platelet count can be very high. Removal of platelets can help to avoid complications of thrombosis and bleeding. Therapeutic plateletpheresis is indicated for patients with a platelet count above 1,000,000 or with high platelet counts and clinical signs of neurological (TIA, CVA, etc.) or cardiovascular complications (MI, thrombosis). It should be used as a bridge until pharmacologic therapy takes effect.

Leukapheresis: In some cases of leukemia with very high white blood cell counts, especially AML with blast crisis, removal of the excess leukocytes/blasts may help to prevent leukostasis, thrombosis, and resulting neurological and pulmonary complications.

Erythrocytapheresis (RBC Exchange)

For sickle cell disease: RBC exchange may be used prophylactically or therapeutically to prevent or treat complications of sickle cell disease such as: acute chest syndrome, sickle cell crisis, CVA, TIA, persistent priapism, preoperatively (in selected cases), for intractable pain crises resistant to standard therapy, and for prevention of iron overload due to repeated PRBC transfusions.

Other indications: Severe cases of malaria and babesiosis with parasitic hyperinfestation of the circulating RBCs can be treated by red cell exchange.

Special Adaptation of Cytapheresis

PHOTOPHERESIS: Also known as extracorporeal photochemotherapy (ECP), photopheresis is a form of apheresis therapy. It involves light-activated treatment of circulating blood cells outside the body. Indications and clinical applications of photopheresis will be the topic of an upcoming issue of Transfusion Medicine Update.

Donor Apheresis

PLATELETPHERESIS

Plateletpheresis: One unit of apheresis platelets equals approximately 5 units of random donor platelets. Donors can give platelets by apheresis more often than they can donate whole blood.

The primary indication for donor plateletpheresis is to supply HLA-matched platelets to patients who have become HLA alloimmunized and do not respond to transfusion of random donor platelets. Platelets from a single donor whose HLA type matches the patient's type are required for therapeutic efficacy.

Some transfusion centers use only apheresis platelets because they can also reduce the chance of bacterial contamination, decrease the risk of disease transmission associated with exposure to multiple donors, and reduce the chance of immune system reaction to transfusion compared to random donor platelets. This approach, however, is not always practical in transfusion centers with high transfusion volume requirements and is more expensive than using pooled random donor platelets.

PLASMAPHERESIS

Plasmapheresis: Donors can also give plasma via apheresis more often than they can donate whole blood.

Plasmapheresis is valuable in supplying rare AB plasma, found in only 4% of the population. People with AB blood type do not have circulating antibodies to A or B antigens and are, therefore, universal plasma donors. Their plasma is used in emergency cases when a patient's blood type is unknown.

Plasma can also be obtained by plasmapheresis for use in manufacturing plasma derivatives such as coagulation factor concentrates, IVIG, Rh immune globulin, and albumin.

Plasmapheresis may be used to collect IgA-deficient plasma from IgA-deficient donors for transfusion. IgA deficiency is the most common type of immunodeficiency in the Caucasian population. Some people with absolute IgA deficiency can develop anti-IgA antibodies, which may result in an anaphylactic-type reaction if plasma containing IgA is used for transfusion.

LEUKAPHERESIS

Harvesting of leukocytes from donors is utilized to supply granulocytes to help fight infection in patients (especially neonates) with very low granulocyte counts and for collection of peripheral blood stem cells for transplantation.

Granulocyte collection: Granulocyte transfusion may be indicated in patients with temporary bone marrow

suppression and granulocytopenia as a result of aggressive chemotherapy and/or radiation therapy who have documented infectious complications unresponsive to antibiotic therapy.

Granulocytes must be ABO-compatible because of the substantial red cell content of the product. HLA-matched granulocytes are desirable for patients that are alloimmunized to HLA antigens. Granulocytes should be collected and transfused as soon as possible within 24 hours, which is before viral testing can be completed. Therefore, careful donor selection is required with recently tested donors having priority.

Stem Cell Harvesting: Circulating bone marrow stem cells can be harvested to use in transplantation procedures.

- Allogenic or autologous (goal 2-5 x 10⁶ CD34 cells/kg per transplant).
- Used for bone marrow reconstitution after high-dose chemotherapy/myeloablative treatment (myeloma, lymphomas, leukemias and certain other malignancies).
- Progenitor cells can be mobilized into the bloodstream by “mobilizing chemotherapy” (in patients) and/or hematopoietic growth factor, G-CSF (in both donors and patients)
- 15-30 L of blood is processed over 4-6 hours.
- The procedure may cause platelet loss which may warrant platelet transfusion in patients who are already thrombocytopenic.

ERYTHROCYTAPHERESIS

Double red blood cell collection:

Erythrocytapheresis is employed to collect type O RBC's. People with the O blood type are universal red cell donors. Their RBCs are used in emergency cases when a patient's blood type is unknown.

Erythrocytapheresis can also be used to supply the Blood Bank's inventory of rare RBC phenotypes and blood that is negative for high frequency antigens. These RBC units can be used to prevent hemolytic transfusion reactions in patients with antibodies to RBC antigens, as a result of exposure to non-self RBC antigens from prior transfusion, pregnancy or organ transplantation.

ADVERSE REACTIONS/SIDE EFFECTS

1. Citrate toxicity: Citrate is used as an anticoagulant to prevent clotting in the apheresis machine. It acts by binding calcium and may produce transient hypocalcemia in patients or donors undergoing apheresis. Patients may experience some muscle

cramping and paraesthesias, including numbness or tingling of the nose, lips, or fingers, due to this effect. These symptoms are short-lived and easily treatable with oral or intravenous calcium supplements. In rare cases tetany and cardiac arrhythmias may occur.

These symptoms occur more commonly in plasma exchange with FFP replacement, as FFP contains citrate as the anticoagulant and increases the amount that the patient is exposed to during the procedure.

2. Allergic reactions: These occur mostly when plasma used as a replacement fluid. Symptoms: hives, wheezing, flushing, dyspnea, anaphylaxis. Treatment: antihistamines, steroids, H-2 blockers and epinephrine (for anaphylaxis).

3. Blood volume shifts: These can be seen when HES (hydroxyethyl starch) is used to increase the yield in granulocyte collection. HES is a volume expander and its use may result in hypertension or even acute heart failure in a susceptible donor.

4. Platelet reduction: This is associated primarily with stem cell collection procedures.

5. Hypovolemia: This can occur early in a procedure, when > 15% of the blood volume is in the extracorporeal system. Symptoms: decreased BP and increased HR (vs. vasovagal reactions with decreased HR and BP).

6. Transfusion-transmitted disease: This remains a possibility when FFP is used as a replacement fluid, but with the sensitivity of current screening tests is, fortunately, now rare.

7. Other possible complications include bleeding at the needle sites, thrombosis in blood vessels used for collection, and catheter-related issues in cases in which central venous catheters are used. Since the procedure involves penetrating the skin, and open access to blood vessels, infection is always a risk.

RESOURCES

1. Apheresis Principles and Practice. Bruce McLeod, 2nd edition.
2. Therapeutic Apheresis a Physician's Handbook. AABB, 1st edition.
3. Clinical Applications of Therapeutic Apheresis: An Evidence Based Approach. 4th Edition. J Clin Apher 2007; 22: Issue 3.

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