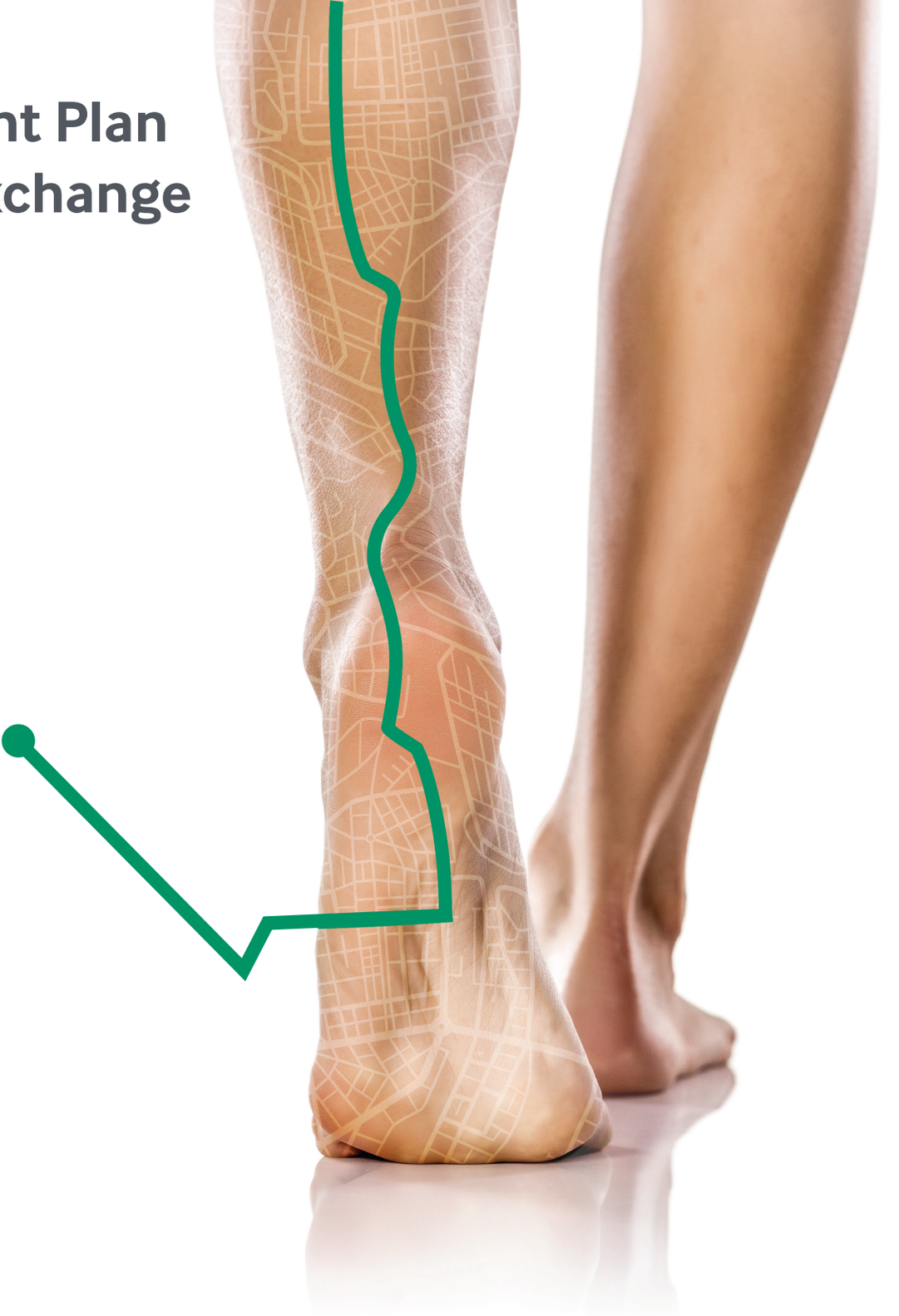
Map a Treatment Plan With Plasma Exchange

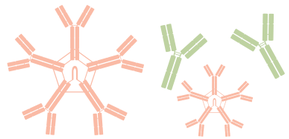


TERUMO BLOOD AND CELL TECHNOLOGIES

Take the fast road to results

Plasma exchange rapidly reduces disease mediators

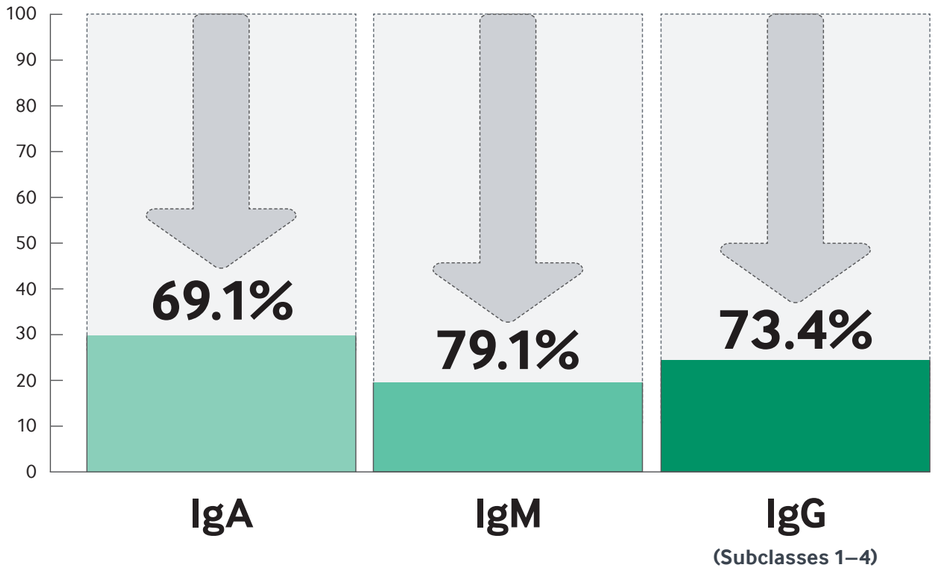
Plasma exchange is an established immunomodulatory therapy that rapidly reduces disease mediators and circulating immune complexes (CICs). Improvement following plasma exchange can occur within a few days.[1-2]



The results of reducing disease mediators

Physicians can quantify and measure known disease mediators before plasma exchange, as well as after, in order to inform the next phase of treatment, providing immediate objective results.[3]

In one study, for patients who received one course* of plasma exchange, the mean maximum reduction was as follows[3]:



*Patients underwent a median of 6 (range 5 to 27) plasma exchange procedures during the trial.

> Plasma exchange is a broadly used therapy across multiple therapeutic areas. In the most recent edition of the American Society for Apheresis (ASFA) guidelines, plasma exchange was recommended for more than 40 diseases (Category I or II).[2]

Plasma exchange as an immunomodulatory therapy

- Removes patient plasma and replaces it with appropriate fluids, while cellular components are returned to the patient[1-2]
- Removes both disease mediators (pathogenic substances) and CICs from patient plasma[2,4-5]
- May relieve symptoms of immune-related or antibody-mediated disorders[1,3,6-7]
- May benefit patients through both the removal of components of the plasma and the fluid given as plasma replacement[2,8]

Summary: Alteration in blood constituents by a 1-plasma-volume exchange[9]

Plasma exchange is an established immunomodulatory therapy that rapidly reduces disease mediators and CICs. Improvement following plasma exchange can occur within a few days.[1-2]

Constituent	% Decrease	% Recovery 48 Hours Post-Exchange
Clotting factors	25% to 50%	80% to 100%
Fibrinogen	63%	65%
Immunoglobulins (IgG, IgA)	63%	45%
Paraproteins	20% to 30%	Variable
Liver enzymes	55% to 60%	100%
Bilirubin	45%	100%
C3	63%	60% to 100%
Platelets	25% to 30%	75% to 100%

Adapted from: Weinstein R. Basic principles of therapeutic blood exchange. In: McLeod B, ed. *Apheresis: Principles and Practice.* 3rd ed. Bethesda, Maryland: AABB Press; 2010.

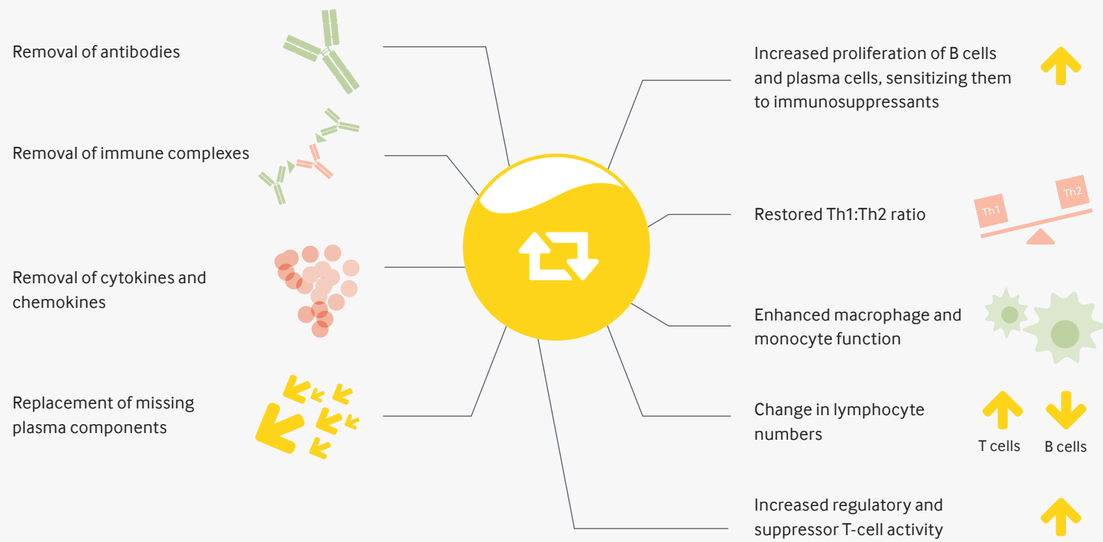
"In a number of diseases, the bulk removal of pathological substances does not explain all of the findings associated with the use of therapeutic plasma exchange (TPE) and therefore TPE appears to have additional therapeutic effects."[10]

Proposed mechanism of action

How TPE works to produce an effect in the body

Immunomodulatory effect

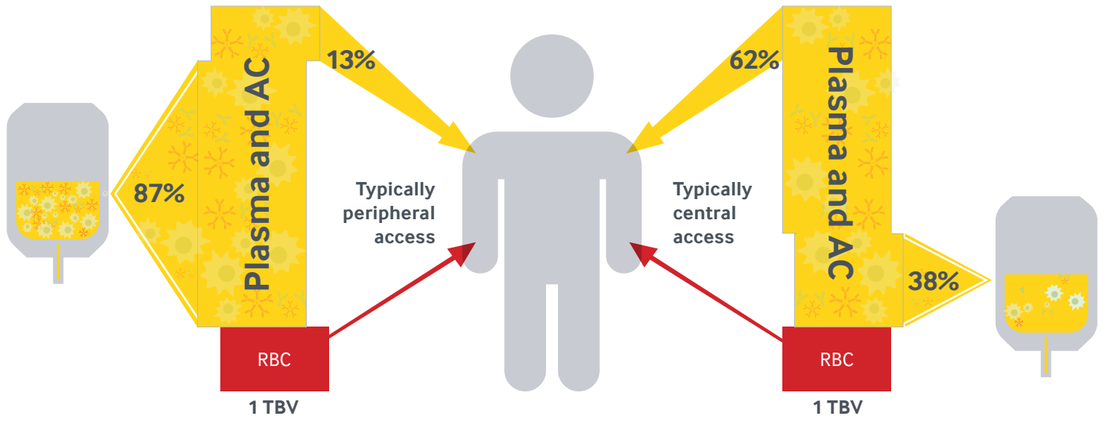
Effect of TPE enabling homeostasis of the immune system



Not all plasma exchange is the same

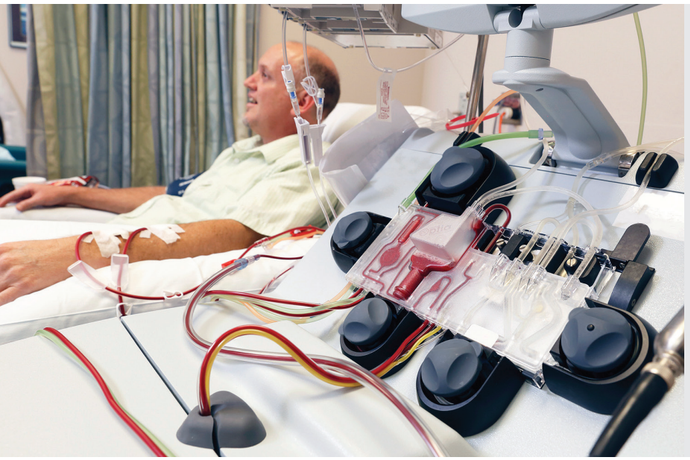
Because centrifugal therapeutic plasma exchange (cTPE) is more efficient than membrane therapeutic plasma exchange (mTPE), it removes 1.5 to 3 times more plasma per volume of whole blood processed. This can have an important impact on the patient experience, allowing shorter procedure times and lower flow rates to enable peripheral access.[5,11-12]

87% plasma removal with cTPE versus 38% with mTPE



AC: anticoagulant; TBV: total blood volume; RBC: red blood cells.

Plasma exchange on centrifugal apheresis devices



- Automatically monitors the fluids used in the procedure
- Can be performed on an inpatient or outpatient basis
- Has a median procedure time of 1 hour and 45 minutes[13]
- Accommodates smaller patients
- Offers multiple venous access options, including:
  - Single- or dual-needle peripheral venous access*
  - Other options, such as central venous catheter, arteriovenous (AV) fistula, or AV graft and implanted ports

*Single-needle access is not available in all world areas.

Many patients receive peripheral access treatment

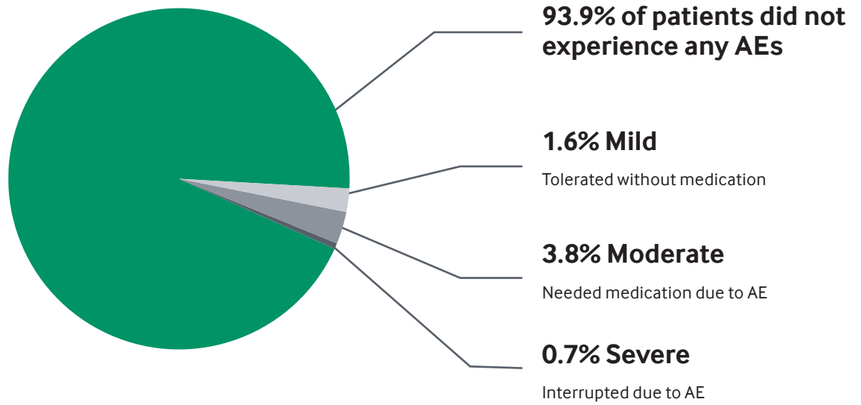
In one prospective plasma exchange study of 42 patients, 90% were treated as outpatients and 83% completed all TPE procedures using peripheral access.[4]

Patient safety

Plasma exchange is known to be safe and well-tolerated, with the majority of reactions being mild to moderate, easily treated and of limited duration.[14]

Adverse events (AEs) in recent literature[14-15]

The World Apheresis Association (WAA) registry data update of more than 15,000 cTPE procedures reported 93.9% of patients did not experience any AEs. Of the 6.1% of patients who did experience AEs, the type and severity of reactions are detailed below:



Safety information

Contraindications:

Leukocytapheresis is contraindicated in acute myeloid leukemia FAB M3 (acute promyelocytic leukemia) because of the accompanying disseminated intravascular coagulation.[16-17]

Other contraindications for the use of apheresis systems are limited to those associated with the infusion of solutions and replacement fluids as required by the apheresis procedure and those associated with all types of automated apheresis systems.

Adverse events of apheresis procedures can include:

Anxiety, headache, light-headedness, digital and/or facial paresthesia, fever, chills, hematoma, hyperventilation, nausea and vomiting, syncope (fainting), urticaria, hypotension, allergic reactions, infection, hemolysis, thrombosis in patient and device, hypocalcemia, hypokalemia, thrombocytopenia, hypoalbuminemia, anemia, coagulopathy, fatigue, hypomagnesemia, hypogammaglobulinemia, adverse tissue reaction, device failure/disposable set failure, air embolism, blood loss/anemia, electrical shock, fluid imbalance and inadequate separation of blood components.

Reactions to blood products transfused during procedures can include:

Hemolytic transfusion reaction, immune-mediated platelet destruction, fever, allergic reactions, anaphylaxis, transfusion-related acute lung injury (TRALI), alloimmunization, posttransfusion purpura (PTP), transfusion-associated graft-versus host disease (TA-GVHD), circulatory overload, hypothermia, metabolic complications and transmission of infectious diseases and bacteria.[18-20]

Restricted to prescription use only.

- Operators must be familiar with the system's operating instructions.
- Procedures must be performed by qualified medical personnel.

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