Plasmapheresis

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- **Apheresis:**
- A general term for "taking away" a targeted cell type or substance from blood. Apheresis includes plasmapheresis (plasma) and cytapheresis (blood cells).

- **Plasmapheresis** –
- A general term used to denote selective removal of plasma. Plasma can be separated from blood using centrifugation or filtration. Plasmapheresis is mostly used to collect plasma from a healthy blood donor for transfusion (ie, plasma donation).

- **Therapeutic apheresis** –
- A general phrase that denotes replacement of plasma with another fluid such as colloid , crystalloid, or allogeneic plasma; or removal or replacement of abnormal or excessive cells for the purpose of achieving a clinical benefit.

- **Therapeutic plasma exchange (TPE)** – This phrase was historically used synonymously with "therapeutic apheresis“ because in the past only plasma was used as replacement fluid. However, TPE is now applied specifically to procedures that involve replacement solely with plasma.

- TPE is also referred to as plasma exchange or therapeutic plasmapheresis and involves removal of patient plasma and replacement with allogeneic or autologous plasma.

- Plasma removed during plasma exchange must not be used for transfusion to another individual, according to regulations from the US Food and Drug Administration (FDA).

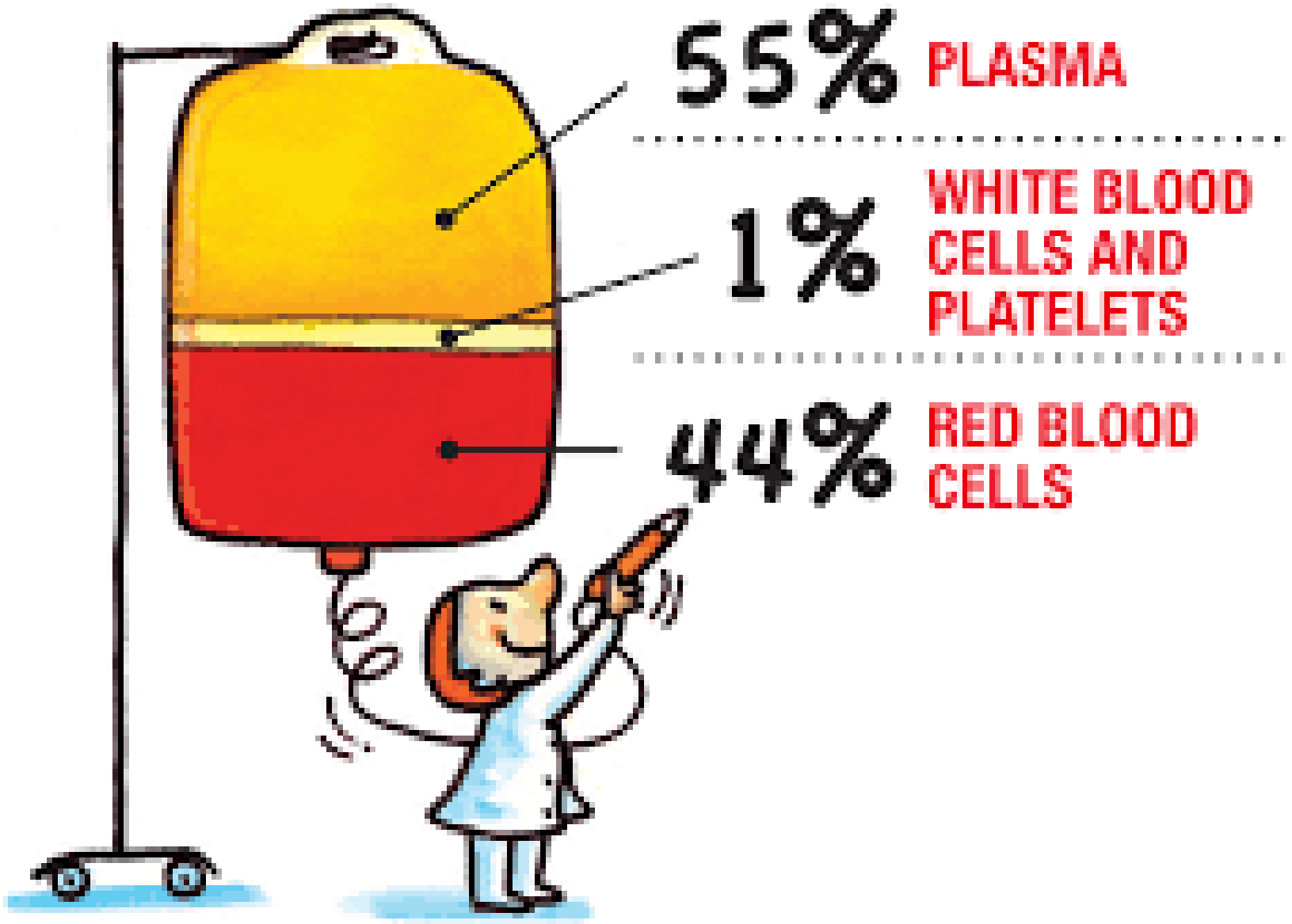
- **Therapeutic cytapheresis (hemapheresis**) – A term used to denote selective removal of abnormal blood cells (eg,sickled cells [erythrocytapheresis, red blood cell exchange]) or excessive numbers of cells (eg, platelets [thrombocytapheresis], white blood cells [leukocytapheresis]).

- **Dialysis** – A difuusion-based treatment best suited for the removal of fluid or small molecules (eg, uremic toxins,some drugs) from the blood using a filter. Fluid is removed by filtration (convection); solutes are removed by diffusion.

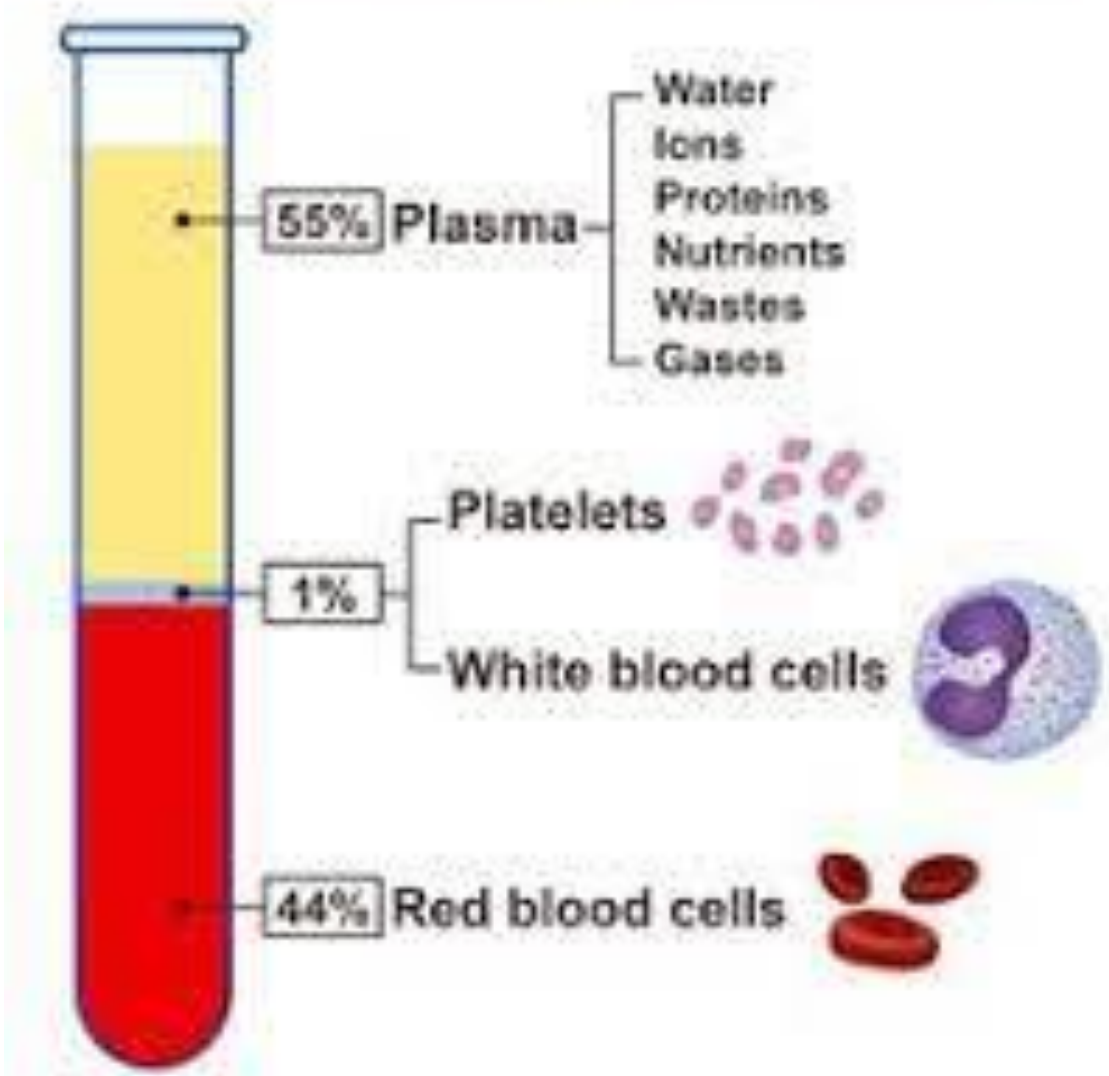
- **Plasmapheresis** is a term used to refer to a broad range of procedures in which extracorporeal separation of blood components results in a filtered plasma product

- The filtering of plasma from whole blood can be accomplished via centrifugation or the use of semipermeable membranes.

- Therapeutic apheresis is an extracorporeal treatment that selectively removes abnormal cells or substances in the blood that are associated with or causative of certain disease states.

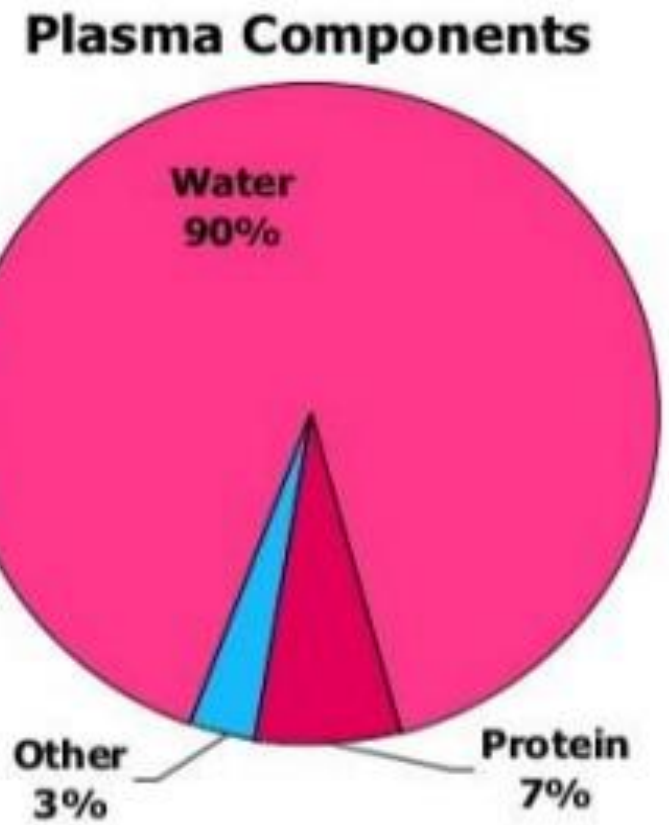

55% PLASMA
1% WHITE BLOOD CELLS AND PLATELETS
44% RED BLOOD CELLS

Components of Blood



Components of blood

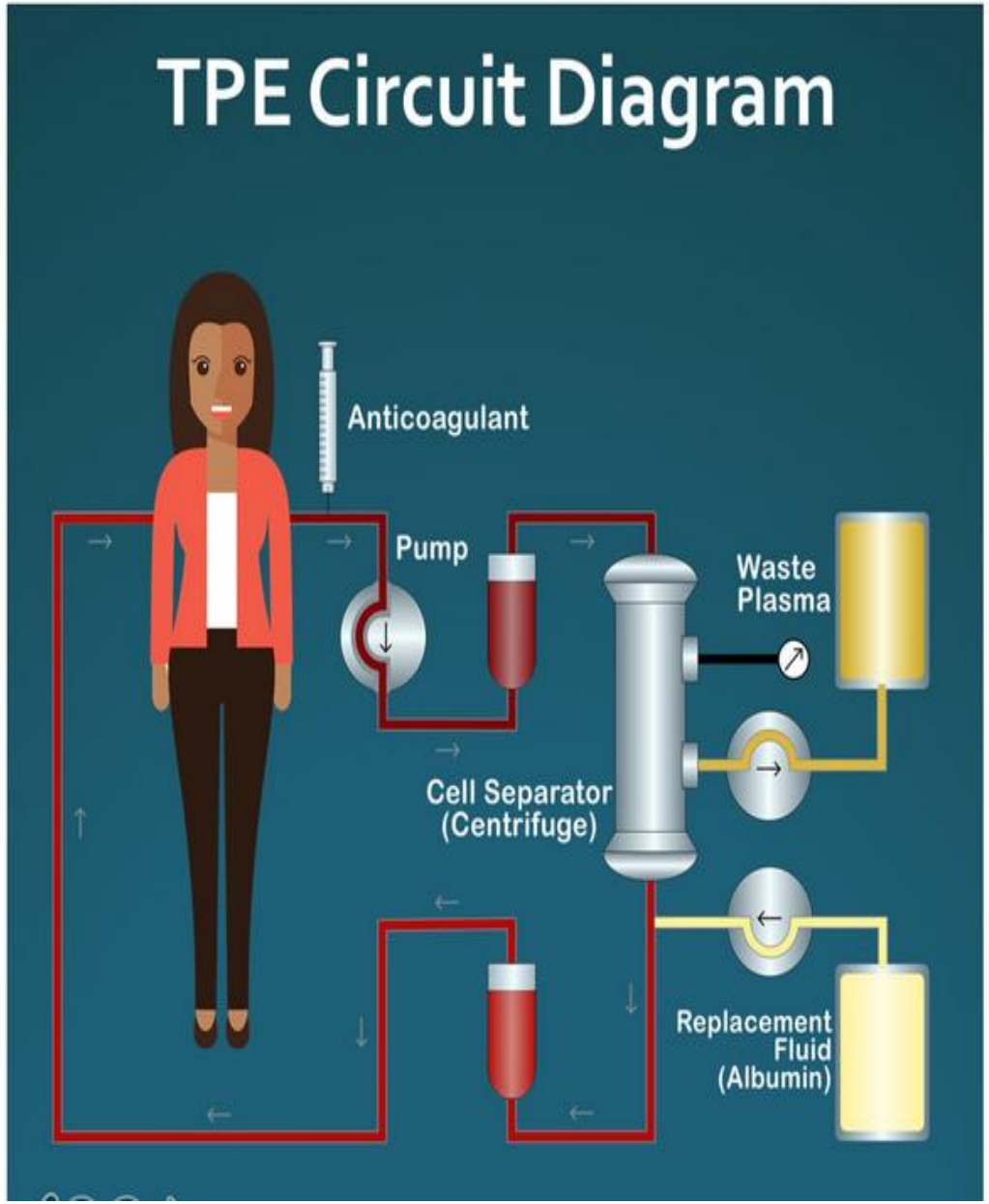
- Plasma
  - Transport mechanism
    - 90-92% water.
    - 6-7% proteins
    - 2-3%
      - Fats
      - Carbohydrates (glucose)
      - Electrolytes
      - Gases (O_2, CO_2)
      - Chemical messengers



- Centrifugation takes advantage of the different specific gravities inherent to various blood products, such as red blood cells (RBCs), white blood cells (WBCs), platelets, and plasma.

- Membrane plasma separation uses differences in particle size to filter plasma from the cellular components of blood

- in therapeutic plasma exchange, using an automated centrifuge, filtered plasma is discarded and RBCs along with replacement colloid (e.g., donor plasma or albumin) are returned to the patient.



Goal = removal of abnormal/excess cells or substances that:

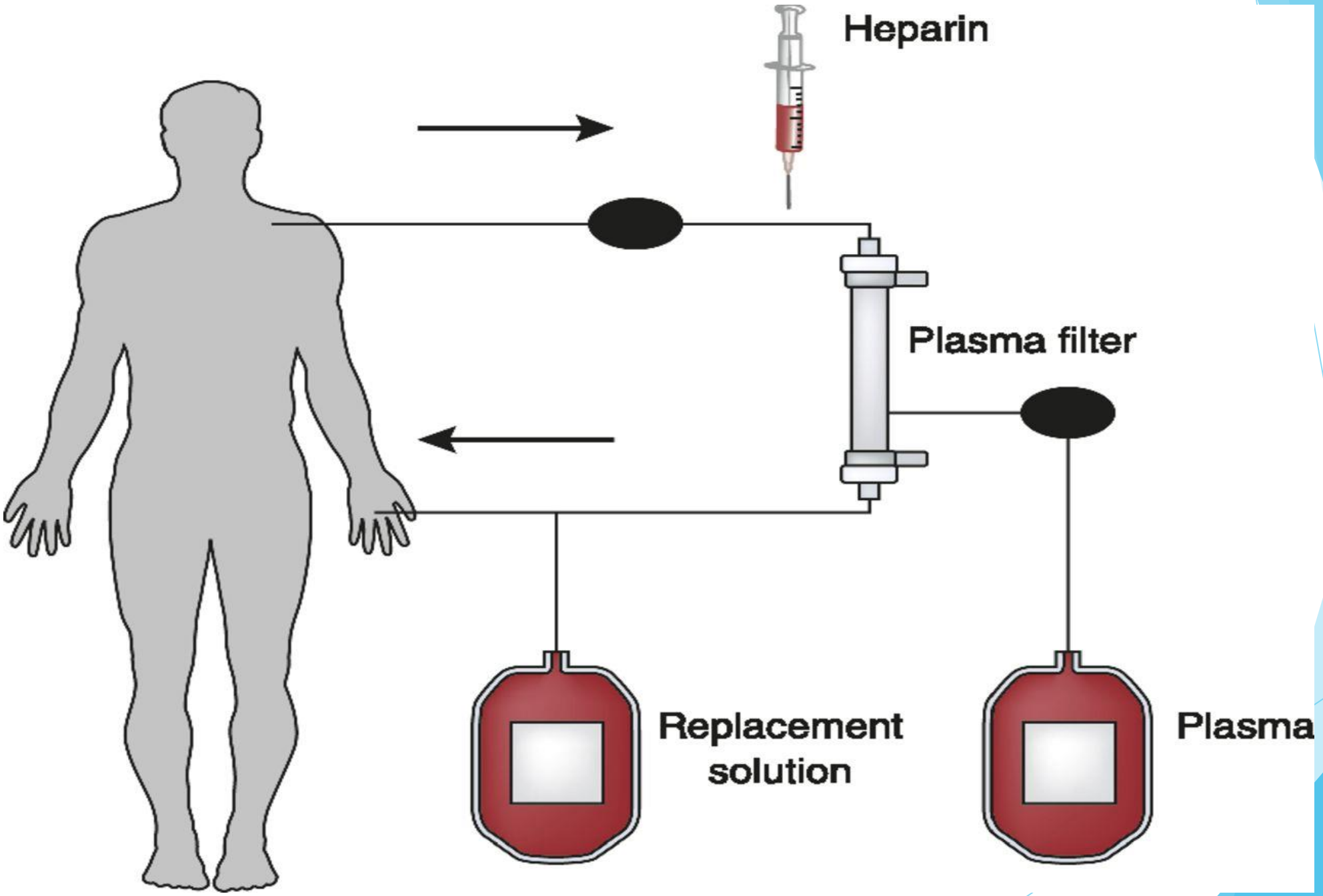
- Have a long half life
- Acutely toxic/resistant to conventional therapy
- Large enough to be removed by pheresis

Example:

- Autoantibody
- Immune complex
- Cryoglobulin
- Myeloma light chains
- Endotoxin
- Cholesterol-containing lipoprotein

* Safest treatment option for pregnancy (Ruffatti et al. Autoimm Rev. 2006)

- in membrane plasma filtration, secondary membrane plasma fractionation can selectively remove undesired macromolecules, which then allows return of the processed plasma to the patient instead of donor plasma or albumin.


Heparin
Plasma filter
Replacement solution
Plasma

- it is used when a substance in the plasma (eg, immunoglobulin) is acutely toxic and can be efficiently removed.

- Myriad conditions that fall into this category (including neurologic, hematologic, metabolic, dermatologic, rheumatologic, and renal diseases, as well as intoxications) can be treated with plasmapheresis.

Indication :

- The Apheresis Applications Committee of the American Society for Apheresis (ASFA) periodically evaluates potential indications for apheresis and categorizes them from I to IV in the basis of the available medical literature. **The following are some of the indications, and their categorization, from the society's guidelines:**

Plasma exchange: concepts, mechanisms, and an overview of the American Society for Apheresis guidelines

Jeffrey L. Winters[1]

Hematology 2012

Table 5. ASFA categories[2]

Category	Definition
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.
II	Disorders for which apheresis is accepted as second-line therapy, either as a stand-alone treatment or in conjunction with other modes of treatments.
III	Optimum role of apheresis therapy is not established; decision-making should be individualized.
IV	Disorders in which published evidence demonstrates or suggests apheresis to be ineffective or harmful. Institutional review board approval is desirable if apheresis is undertaken in these circumstances.

- **Category I indications** (disorders for which apheresis is accepted as first-line therapy, either as a primary standalone treatment or in conjunction with other modes of treatment) include the following:

- Guillain-Barre syndrome
- Myasthenia gravis (acute short-term treatment)
- Chronic inflammatory demyelinating polyneuropathy
- Hyperviscosity in hypergammaglobulinemia
- Thrombotic thrombocytopenic purpura
- Goodpasture syndrome (unless it is dialysis-dependent and there is no diffuse alveolar hemorrhage)
- Thrombotic microangiopathy, complement mediated (autoantibody to factor H)
- Wilson disease, fulminant

- **Category II indications** (disorders for which apheresis is accepted as second-line therapy, either as a standalone treatment or in conjunction with other modes of treatment) include the following:

- Lambert-Eaton myasthenic syndrome
- Multiple sclerosis (acute central nervous system demyelination disease unresponsive to steroids
- Thyroid storm
- Mushroom poisoning
- Acute disseminated encephalomyelitis
- Autoimmune hemolytic anemia (severe cold agglutinin disease)
- Systemic lupus erythematosus (severe)
- Myeloma cast nephropathy

- **Category III indications** (disorders for which the optimal role of apheresis therapy is not established; decision-making should be individualized) include the following:

- Posttransfusion purpura
- RBC alloimmunization in pregnancy
- Autoimmune hemolytic anemia (severe warm)
- Hypertriglyceridemic pancreatitis
- Thrombotic microangiopathy, complement mediated (complement factor mutations)
- Stiff person syndrome
- Drug overdose/poisoning
- Immune thrombocytopenia

- Category IV indications (disorders in which published evidence demonstrates or suggests apheresis to be ineffective or harmful; institutional review board [IRB] approval is desirable if apheresis treatment is undertaken in these circumstances) include the following

- HELLP syndrome (ante partum)
- Hemolytic uremic syndrome (typical diarrhea-associated)
- Multifocal motor neuropathy
- Idiopathic polyarteritis nodosa

Warning…

- patients who cannot tolerate central line placement
- Patients who are in an actively septic state or are hemodynamically unstable

- Although plasmapheresis can remove various mediators from the blood and so, in theory, would appear to be potentially useful in treating sepsis, patients in a septic state are often coagulopathic and hemodynamically unstable, which poses significant risks when catheters are inserted and connected to a mechanical circuit; there are some ongoing trials evaluating plasmapheresis in sepsis, but at present, there are no clear data to suggest that the clinical benefits of using plasmapheresis in this setting outweigh the risks associated with its use

- Patients who have allergies to fresh frozen plasma (FFP) or albumin, depending on the type of plasma exchange
- Patients with heparin allergies should not receive heparin as an anticoagulant during plasmapheresis
- Patients with hypocalcemia are at risk for worsening of their condition because citrate is commonly used to prevent clotting and can potentiate hypocalcemia
- Patients taking angiotensin-converting enzyme (ACE) inhibitors are advised to stop taking the medication for at least 24 hours before starting plasmapheresis

- As distinct from plasmapheresis, cytapheresis is the selective removal of RBCs, WBCs, or platelets and can be accomplished by using identical centrifuge-based equipment. Applications include the following:

- Erythrocytapheresis (selective removal of RBCs) is used in conditions such as sickle cell disease or malarial infection, in which RBCs are selectively removed and replaced with donor erythrocytes

- Leukapheresis (selective removal of WBCs) is used in conditions such as hyperleukocytosis, in which pathologically high number of white cells are present (as, for example, in leukemia); it can also be used to collect peripherally circulating stem cells that can then be infused in an autologous or allogeneic stem cell transplant

- Platelet apheresis (selective removal of platelets) can be used in conditions of thrombocytosis (eg, polycythemia vera)

- Venous access:
- Exchange volumes
- Replacement fluids
- Apheresis schedule

Exchange volumes

- For most conditions, it has become standard practice to perform 1 to 1.5 plasma volume exchanges per procedure.
- Exchange of the first 1 to 1.5 plasma volumes removes the largest concentration of the targeted substance, with diminishing amounts removed in each subsequent exchange during a procedure.
- A single plasma volume exchange in an average-sized adult uses approximately 3 liters of replacement fluid.
- In general, large molecular weight compounds equilibrate slowly between the vascular space and the interstitium.

- A single plasma volume exchange will lower plasma macromolecule levels by 60 percent, and an exchange equal to 1.4 times the plasma volume will lower plasma levels by 75 percent

- Estimated plasma volume (in liters) = 0.07 x weight (kg) x (1 - hematocrit)

Plasma volume

- Plasma volume =

$$(0.07 \times \text{Body Weight}) \times (1 - \text{Hct})$$

$$(0.07 \times 70) \times (1 - .4)$$

$$= 2.9 \text{ L}$$

- Exchanging more than 1 to 1.5 plasma volumes in a single treatment increases procedure time, challenges patient tolerance, and increases cost.

- As an example, cell separators can perform one complete volume exchange in 1.5 to 2 hours; two to three plasma exchanges will double or triple the time required to perform the procedure.

Replacement fluids

- The patient's fluid volume removed by apheresis must be replaced to prevent marked volume depletion.
- Five percent albumin, saline, or a combination of albumin and saline are the replacement fluids of choice for most conditions

- We prefer 5 percent albumin or a crystalloid-colloid (ie, albumin-saline) combination as the replacement fluid, rather than saline alone.

Replacement fluid….

- Deciding which replacement product to use is based on the underlying condition and the risks and benefits associated with each replacement product.

- In general, albumin is the most common replacement product because of its low side-effect profile and broad availability.

Fresh Frozen Plasma (FFP)

- **Fresh Frozen Plasma** refers to the fluid portion of donor blood, separated and frozen at −18 °C (0 °F) within eight hours of collection[4].
- **Pros:**
  - Iso-oncotic
  - Replaces clotting factors, immunogloblins and other plasma proteins
- **Cons:**
  - High risk of reaction or infection
  - Provides citrate which may result in hypocalcemia
  - Needs to be blood type compatible

Albumin 5%

- Albumin (Human) 5% is a sterile, liquid preparation of albumin derived from large pools of human plasma, typically provided by approved blood transfusion services[5].

- **Pros:**
  - Colloid which is iso-oncotic so therefore will remain in intravascular space
  - Very low infection and allergenic risk

- **Cons:**
  - Doesn’t replace clotting factors
  - There have been periodic shortages

- RBCs are also separated by the centrifuge, then returned to the patient along with the previously selected colloid of either albumin or fresh frozen plasma (FFP)
- After the desired amount of plasma is removed, the machine is disconnected from the patient, and heparin is instilled into each catheter lumen to prevent clotting until the lumen is accessed again
- A post–plasma exchange fibrinogen level is checked if albumin was used as the replacement product (albumin does not contain fibrinogen, as opposed to FFP) to assess whether the patient has become severely hypofibrinogenemic

Apheresis schedule

- The therapeutic apheresis schedule should be based on the nature of the targeted pathologic substance and by the desired endpoint (as an example, clinical improvement or reduction in the level of the pathologic entity).

- In immunologically mediated, paraproteinemic, or hyperviscosity conditions, immunoglobulin compartmental shifts, especially of IgG and IgM, must be considered
- In many of these cases, therapeutic apheresis only serves an adjunctive role as the patients are receiving concomitant chemotherapy or immunosuppressive therapy.

- **IgM** – Approximately 75 percent of IgM is intravascular. As a result, only one or two procedures are usually required to rapidly reduce IgM levels.

- **IgG** – Only 45 percent of IgG is intravascular, and within 48 hours, plasma IgG returns to approximately 60 percent of the pre-apheresis level.

- IgG production is also characterized by a "rebound" phenomenon, and cessation of TPE after several procedures can result in pretreatment or even higher levels of IgG, especially if the patient is not on immunosuppressive therapy.

- Consequently, a more rigorous regimen involving several TA procedures and the institution of immunosuppressive therapy are important to significantly reduce IgG levels

- In acquired thrombotic thrombocytopenic purpura (TTP), TPE is usually performed daily

- Treatment for Goodpasture's syndrome (anti-GBM mediated disease) is generally also performed on a daily or everyother- day basis.

Laboratory evaluation

- Laboratory assessment is based upon the desired endpoint of therapy, the number of planned procedures, and the type of replacement fluid.
- For therapeutic apheresis performed without plasma, a baseline complete blood count (CBC), immunoglobulin levels, and coagulation and electrolyte studies should be obtained.
- If serial or several closely spaced procedures are planned, more frequent subsequent laboratory evaluation may be needed


Thank You!