MEMBRANE PLASMAPHERESIS
USING MEMBRANE SEPARATION IN A BIOLOGICAL APPLICATION

Plasma makes up over half of the whole blood in our bodies and contains the important components of blood that serve our bodies: proteins, glucose, hormones, electrolytes, and other vital compounds. Plasmapheresis greatly benefits people living with autoimmune diseases because the process allows for about 70% of plasma volume to be replaced in a treatment called plasma exchange therapy. The process effectively removes self-attacking antibodies from patients receiving the therapy by exchanging plasma.

Plasmapheresis is a separation process in which plasma is separated from blood, in either a treatment or donation, by using hollow-fiber membrane. The separated plasma is replaced with some type of substitution fluid (Figure 1). In therapeutic plasma treatments, patients have the “bad” plasma separated from their blood and replaced with “good” (fresh) plasma. In donations, donors have their “good” plasma separated from their whole blood and replaced with saline. In both scenarios, the blood cells are returned to the patient.

OVERVIEW
The process of plasmapheresis can be broken into three parts: collection, separation, and return. To understand the separation of plasma from blood, a circuit diagram can be constructed (Figure 2). Before the circuit is established, the patient is prepared for the process by a nurse or doctor to place a catheter in their arm to remove/return blood to the patient. Next, the plasma-blood mixture is sent through a pump to pressurize the feed. Then, the pressurized mixture is sent through a membrane to separate the plasma and blood; the blood flows over the membrane while the plasma flows through the membrane’s pores. After the actual separation, the blood cells are returned to the patient’s body.

![Figure 1. Plasma Substitution. (Source: Asahi Kasei. Asahi-kasei.co.jp)](image1)

![Figure 2. Circuit Diagram of Plasma Exchange. (Source: Asahi Kasei. Asahi-kasei.co.jp)](image2)
and the plasma is sent to its appropriate location (storage for donations, discard for treatments).

**COLLECTION: TAKING WHOLE BLOOD FROM THE BODY**

The patient or donor is prepared for the process in a very similar manner to that of blood donation; a needle or catheter is placed in a vein in the arm after extensive cleaning of the area. Once the line is established and good blood flow is achieved, the “circuit” can be started. The blood/plasma mixture exiting the body is mixed with an anticoagulant to prevent clotting of the blood during the separation process. Next, the stream of blood is pressurized to aid in the separation of plasma from blood through the membrane.

**SEPARATION: REMOVING PLASMA FROM BLOOD**

Typically, membranes are used to achieve the separation because it allows for a closed loop to be maintained. Having a closed loop reduces the risk of the devastating error of returning the wrong blood cells to the wrong patient or donor.

In order to separate plasma from whole blood using a membrane, the whole blood enters the membrane after being pressurized. The feed must be pressurized to drive the movement of plasma through the membrane. As seen in **Figure 3**, the plasma flows through the pores of the membrane because it is comprised of smaller molecules such as water, proteins, and electrolytes. The blood cells flow over the membrane because the cells are too large to pass through the membrane’s pores. The design of the membrane has been made carefully to ensure the most effective separation.

![Figure 3. Membrane Separation. (Source: Asahi Kasei. Asahi-kasei.co.jp)](image)

**TECHNICAL ASPECTS OF MEMBRANE DESIGN**

The membrane design is derived from other aspects of the plasmapheresis process. For example, the flowrate of blood through the closed circuit is determined by the volume of whole blood exchange needed in order to replace 70% of the original plasma. The volume exchanged works out to be about 3.6 liters, and most processes are timed to be approximately 2 hours. This means the volumetric flowrate can be determined to be about 30 milliliters of blood per minute. In addition, the mass transfer coefficient can be used to determine the necessary area of the membrane, which comes out to over 20 square meters. Since such a large membrane
area is needed, a *hollow-fiber membrane* will be the best to achieve the separation with sufficient surface area. The hollow fiber membrane induces a velocity profile similar to that of flow through a pipe, and this effect gives rise to other complications to consider.

The pressurization done during the collection step helps drive the separation through the membrane. Therefore, one would think that higher pressure would lead to better separation. However, increasing pressure increases flowrate (velocity) through the membrane, and increased flowrate through the membrane increases *shear stress* (Figure 4). Shear stress is a stress induced by flow, and can damage cells. Shearing effects caused at high flowrates can damage the blood cells by breaking the cells, known as *hemolysis*, which is extremely detrimental to the patient. Therefore, a balance must be found between keeping a reasonable flowrate through the hollow-fiber membrane and avoiding cell damage from shear stress.

![Figure 3](Source: Cardiovascular Research. Oxfordjournals.org)

**RETURN: PUTTING BLOOD BACK INTO THE BODY**

Once the plasma is separated from the blood cells, what is done with the plasma depends on whether the plasmapheresis was done as plasma exchange therapy or plasma donation. In plasma exchange therapy, the separated plasma is discarded as waste since the plasma contains self-attacking antibodies. In plasma donation, the separated plasma is frozen and stored until it is sent for further processing. The donated plasma typically goes into plasma therapy.

As seen in a Figure 1, a substitution fluid is needed after the membrane separation to replace the lost plasma. In donations, this is typically saline solution and is often given after the entire amount of plasma is collected from the donor. In therapies, the substitution fluid is fresh plasma which is typically from a donor. Since this process only takes plasma from donors, the body can replenish the lost plasma much faster than if whole blood was donated. Plasma donors can donate plasma up to twice a week. Plasma exchange therapies do not happen as frequently; instead patients wait about two or three weeks between each therapy.
CONCLUSION

Plasmapheresis provides an effective way to separate plasma from blood cells using a hollow-fiber membrane. This enables people with autoimmune diseases to receive plasma exchange therapy in which they receive donated plasma to replace their own plasma. The therapy serves as a treatment for many different autoimmune diseases. The process of plasmapheresis is accomplished using membrane filtration to separate plasma from blood cells. Having such an effective separation process in place allows for a simple and safe way for people both to donate plasma and to receive plasma treatments. Receiving plasma exchange therapies greatly increases the health, even temporarily, of the recipient of fresh plasma.