



Therapeutic Plasma Exchange Series

Therapeutic Plasma Exchange: A Guide for Newbies

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About This Document

Therapeutic plasma exchange (TPE) is a procedure used to treat a variety of diseases and conditions where something circulating in the blood is causing or contributing to the disease process. TPE can be short-term, only requiring a limited series of TPE treatments to deal with an acute condition (for example, Guillain-Barre syndrome), or it can be required for a long-term or even life-long basis for some chronic conditions (for example, multiple sclerosis, myasthenia gravis, or systemic scleroderma).

Starting a new, unknown treatment like TPE can be scary and may lead to anxiety that can actually make it more difficult to perform TPE successfully. The goal of this document is to help to explain exactly what TPE is and how it is performed, how to prepare for a TPE treatment in order to make it as easy and successful as possible, what to expect during a TPE treatment, how you can make yourself as comfortable as possible while undergoing TPE, and what you can expect once a TPE treatment is completed.

What is Therapeutic Plasma Exchange?

Therapeutic plasma exchange, abbreviated TPE and sometimes called plasmapheresis, is a common procedure that is used to treat a wide variety of (mostly) autoimmune and neurological conditions. The basic idea behind TPE is actually very simple. If a disease is either caused by or made worse by something circulating in the blood stream, for example an autoantibody or some other abnormal protein, then if you can reduce the levels of this circulating substance, this should lead to a reduction in the symptoms. The way this is typically done is to: 1) withdraw blood from a vein in one arm, 2) separate the main blood components (red blood cells, white blood cells, platelets, and plasma – the liquid part of the blood) by a centrifugal separation process, 3) discard the plasma which contains the problematic substance, 4) replace it with a plasma substitute, typically either 4%-5% sterilized albumin or donor plasma, 5) combine the plasma substitute with the extracted red blood cells, white blood cells, and platelets, and 6) return the mixture to the patient through a vein in the other arm. Figure 1 below gives a representation of what the process looks like and Figure 2 shows some of the machines that are typically used to perform TPE.

Figure 1 - Therapeutic Plasma Exchange Circuit Diagram

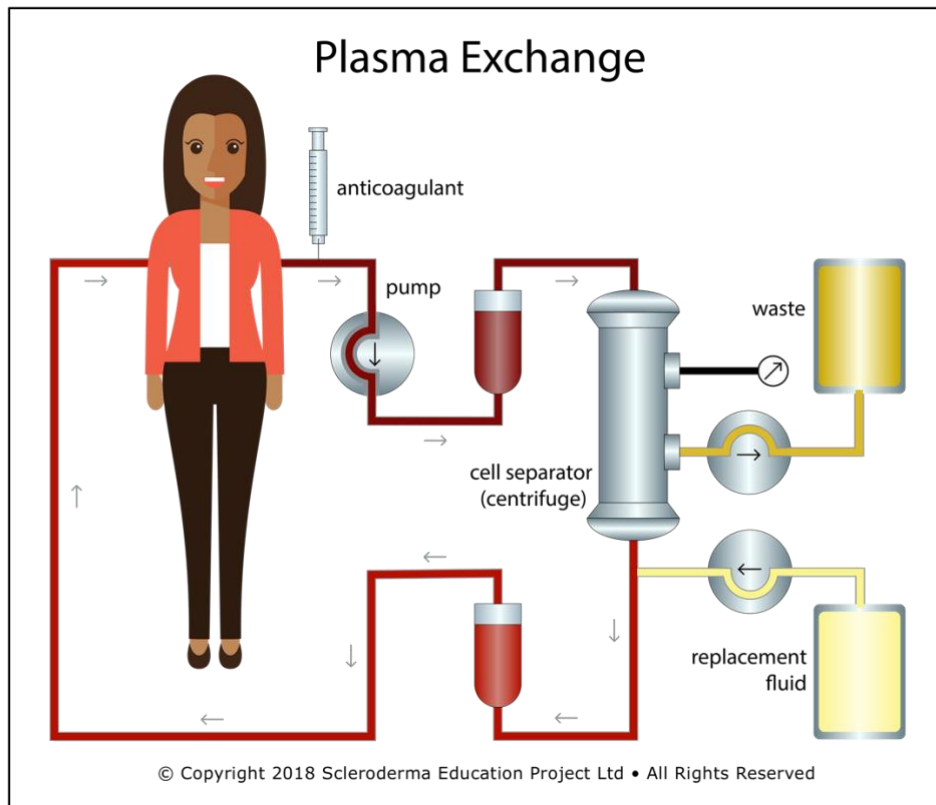


Figure 2 – Equipment Used to Perform TPE



How Long Does a Therapeutic Plasma Exchange Treatment Take?

A typical TPE treatment takes about 1 ½ to 2 hours and replaces 1 to 1 ½ blood volumes. Since the blood separation and separation process is a continuous process where plasma is replaced by a plasma substitute, it is not actually possible to completely remove the target substance completely in a single TPE session. The best estimate is that a single

TPE treatment removes about 60% to 70% of the target substance, which is why it is common for several TPE sessions to be done over a few days or weeks, depending on the condition.

How Safe is Therapeutic Plasma Exchange?

The overall safety profile for therapeutic plasma exchange is excellent. The most common side effects are very short term, e.g., swelling or pain at the sites where the IV needles are inserted, reduced blood pressure that can lead to feeling light-headed during or immediately following a TPE treatment, and fatigue for a few hours following a treatment.

However, in rare cases patients have allergic reactions or other issues with some of the agents used during TPE that can be more serious. Also, patients may have other conditions that make TPE an unsuitable treatment option. Because of this, we strongly recommended that TPE be performed in a facility that performs TPE on a regular and ongoing basis with experienced staff and facilities equipped to deal with the very rare but potentially serious complications that can arise during a TPE treatment.

Starting Therapeutic Plasma Exchange

TPE Part 0: Before You Start TPE Treatments

- Review your regular medications with your clinician. Some medications can affect TPE, for example, blood thinners, blood pressure medications, and any medications that affect the immune system (for example, steroids, anti-rejections drugs, or immunosuppressants used to treat inflammatory diseases). Other medications can be affected by TPE. TPE can significantly reduce blood levels of medications so you may need to change the timing of when you take certain medications when you are receiving TPE treatments. For example, if you take blood pressure medications, on days when you have a TPE treatment, you should delay taking these medications until after your treatment.
- Find out where your TPE treatments will be done, call them and make an appointment for a pre-TPE visit. They will show you the equipment, answer questions, take a look at your veins, tell you how to prepare for a TPE treatment, etc. Meeting the staff can definitely be helpful in reducing the natural anxiety that you might be feeling about starting TPE treatments.
- Ask the nursing staff at your pre-TPE visit about the option to pre-treat areas on your arms that are likely to be used for venous access using a topical anesthetic (numbing cream) such as Emla™. If you apply a small amount of a topical anesthetic to your skin about 30 minutes to an hour before starting your TPE treatment (covered by a Tegaderm™ patch or plastic wrap to prevent it from drying out), it can be a very effective way to reduce pain when the IV needle is inserted. You may be able to get the Emla cream (or equivalent) directly from the TPE clinic or if not, your clinician can give you a prescription for a numbing cream. Tegaderm is readily available at drugstores or even online through Amazon or other retailers.
- However, if you know from past experience that you are likely to feel a lot of anxiety about getting the procedure itself, or getting IV needles inserted into your veins, it may well be worthwhile to ask your clinician for a prescription for a short-acting anti-anxiety medicine such as alprazolam (Xanax) that you can take just before starting a TPE treatment. This will help you feel more relaxed and as a result, it will actually make venous access easier. If you are going to be doing TPE long-term, after a while you will feel much more comfortable with the entire TPE process and will probably no longer need to pre-medicate before starting each procedure.

TPE Part 1: Venous Access and Pre-Treatment Steps

- Most of the time, TPE is done using two arm veins. This provides good blood flow and is the least risky way to perform TPE. However, in about 25% of the cases, using normal venous access may not be possible. In these cases, there are several alternative ways to get the needed venous access for TPE. These include central line catheters, and for long-term venous access, surgically installed ports or fistulas. Venous access using these alternative techniques is discussed in a later section of this document.
- As we mentioned earlier, anxiety can make it harder to get good venous access as it can cause constriction of your blood vessels. Taking a short-acting anti-anxiety medicine can help to relax the blood vessels. If you are using anti-anxiety medications before starting your TPE treatment, the nursing staff can advise you about when you should take the medication.
- If you are dehydrated, this also can make venous access more difficult. You want to make sure that you have had plenty to drink before starting a TPE treatment. BUT, you also need to realize that when you are in the middle of a TPE treatment, it is really very challenging to get up and use the bathroom, and even dealing with bedpans or urinals can be a pain as well. This suggests that having a Starbucks Triple-Shot Latte just before starting your treatment may not be a great idea. 😊
- It is always a good idea to eat a full meal before a TPE treatment. Foods with a lot of calcium can be helpful to reduce some symptoms during your TPE treatment. Good examples, are cheese, yogurt, and milk.
- Inserting the IV needle can be painful but there are a number of ways to help reduce the pain. In addition to the use of a numbing cream as mentioned above, taking acetaminophen (Tylenol) can reduce pain levels a bit. You might want to take a standard dose of acetaminophen about 30 minutes before starting a TPE treatment. Do NOT take a pain killer like aspirin or a drug like Ibuprofen, Aleve, or other drug in this category, as these can reduce the ability of your blood to clot. If you are not sure which pain killers are safe to take, the nursing staff at the TPE clinic or your clinician can advise you on this.
- If you are fortunate enough to be getting your TPE treatments done at a larger clinic, they may have new equipment such as VeinViewer® or similar systems made by AccuVein that can help locate veins that will be good for the venous access needed to perform TPE. You can ask about this at your pre-TPE visit.
- Some clinics are now using a new technique called "ultrasound-guided peripheral venous access". This requires special equipment and takes longer but this technique significantly increases the likelihood of successful venous access, especially in patients where the veins are deeper so that normal access or even the use of viewing technology such as VeinViewer is not sufficient for successful venous access.
- One technique that is relatively new and can be VERY effective in reducing IV insertion pain is to inject the area where the IV needle will be inserted with a small amount of saline solution using a very tiny needle. There is almost no pain from the tiny needle used to inject the saline and it completely numbs the area for about a minute, so there is almost no pain when inserting the needle. This would also be a great topic to discuss with the TPE clinic staff during the pre-TPE visit. If this is not a procedure that the staff at the TPE clinic are familiar with, it is relatively easy to learn to do and we would suggest that you talk to the staff about learning this technique. Not only will it make it easier for you to have a positive experience with TPE, it will benefit many other people in the clinic as well.

- Sometimes if venous access is difficult, the nurses will use a heat pack to relax the blood vessels.
- You are going to be immobilized in a bed or reclining chair for at least an hour or two (sometimes longer) during your TPE treatment. **Make sure you use the bathroom just before you start TPE!**

TPE Part 2: During the Treatment

So what does it feel like to get a TPE treatment once the IV needles are in place? Also, what should you do to make this part of the TPE experience as successful and comfortable as possible?

- If you had some pain during the insertion of the IV needles, you may feel some mild discomfort at the insertion sites at first, but generally this will go away after a little while. This is entirely normal. However, if you suddenly start experiencing a *lot* of pain at an IV insertion site when the equipment is turned on, tell the staff immediately! This can often be an indication that the vein has "blown". While this is more likely to occur at the arm where blood is being returned, it could happen at either site. A "blown vein" is a term used to describe what happens to a vein when it ruptures or gets punctured causing blood to leak outside of the vein itself. This can become very painful very quickly, but as soon as the IV needle is withdrawn the pain subsides quickly. The bad news is that this means that your nursing staff will need to do another IV insertion in that arm.
- It is possible that you may feel a little dizzy or light-headed from the procedure. Also, some people report that the anticoagulant added to the blood or some of the replacement fluids used can cause tingling or a "pins-and-needles" sensations in the fingers and toes, around the mouth, or across the forehead. This type of reaction is more common in older equipment used for TPE such as the COBE Spectra®. Newer equipment such as the Spectra Optia® or the Fresenius COM.TEC® are less likely to have this reaction.

You can generally avoid this type of reaction by taking several TUMS® or other antacids containing calcium carbonate immediately before starting TPE. If you start feeling this type of sensation during the treatment, tell the nursing staff and they can usually easily deal with this discomfort by temporarily slowing down the procedure, giving you calcium supplements, or by adding calcium infusions during TPE. If you have this reaction during a treatment, it is definitely worth trying calcium supplements before future TPE treatments as this is likely to prevent similar problems in the future.

- **Don't Relax!** After telling you that it is important to try to be as relaxed as possible at the beginning of TPE in order to make venous access as possible, now we are going to tell you the opposite. You might think that the best thing to do during a TPE procedure is to listen to relaxing music, doze off, etc., now that the "anxiety" of getting the IV needles in is over and the TPE equipment is humming in the background. Paradoxically, that is actually not the best thing to do during a TPE treatment.

For reasons too technical to get into here, it is very common for your blood pressure to decrease somewhat during a TPE treatment, sometimes leading to a condition called hypotension (abnormally low blood pressure). This can lead to symptoms such as feeling dizzy or lightheaded, fatigue, nausea, etc. If you start feeling these symptoms, let your nursing staff know and they can do a variety of things to reduce these symptoms.

If you try the "listen to relaxing music and doze off" approach that we mention above, that will actually increase the likelihood that your blood pressure will drop

enough to cause some of the problems listed above. So here is actually a much better suggestion: if the infusion center where you are having your TPE treatment done is set up to allow you to watch a DVD during the procedure, bring in an exciting/or otherwise highly entertaining movie to watch during the procedure. Or, if you have a laptop computer or an iPad or similar tablet, download an exciting movie and watch it during the procedure. (It can actually help distract you when getting the initial IV insertion done as well, making that part of the procedure easier as well.) In fact, the more exciting the movie is the better as it is more likely to increase your adrenaline levels. This simple technique may actually completely counteract the normal blood pressure drop that typically occurs during TPE.

- If you start to gradually feel cold (or hot) during a procedure, this might be an issue with the blood warmer that is built in to the TPE equipment. As you know, your normal body temperature is considerably warmer than the temperature in the room. As a result, the TPE system includes a system that warms the plasma substitute when it is re-combined with your extracted blood cells before being reinfused into your body. For most patients, this works very well. However, sometimes patients end up feeling overheated (this is more common in heavier patients) and patients prefer to have the blood warmer turned off or the temperature reduced in order to feel more comfortable. If you start to feel cold, then mention this to the nursing staff because it is actually possible that they accidentally forgot to turn the blood warmer on.
- Sometimes during a TPE procedure, you may hear a warning alarm. Most of the time these are just informational warnings, e.g., time to change to a new bottle of plasma substitute, but sometimes the nurse will need to do some minor adjustments to change flow rates, slightly alter the position of one of the needles, etc. Very rarely will there be anything to be concerned about when you hear an alarm from the TPE system. (In 23 years of regular TPE treatments, I only had to deal with one slightly serious issue that occurred because of a leak in some of the tubing – Ed.)

TPE Part 3: After a TPE Treatment

- When the TPE treatment is done and the IV needles are done, the nurses will check your blood pressure and make sure that you are feeling OK before releasing you. As you will feel tired for a while and might even be a bit light-headed, it is always a good idea to have someone take you home. **We do not recommend driving for several hours following a TPE treatment.** You can generally expect that you will feel tired for up to 24 hours after a TPE treatment, so plan your activities accordingly. If you are having treatments done on a very frequent basis, e.g., daily or several times a week, the fatigue is likely to be greater and last longer, so you should plan your activities accordingly.
- Depending on how the IV insertion went, you may have some localized pain, swelling, or even bruising following a TPE treatment. This will usually subside fairly quickly. Heat applied directly to the IV sites during your treatment may feel very soothing during the procedure. However, to reduce the likelihood of bruising, cold packs should be applied after the needles have been removed. If there is any swelling from a dislodged needle, elevating the arm for several hours will help.
- TPE removes a significant amount of *everything* from your plasma, including substances that allow your blood to clot quickly if you are injured. While these "clotting factor" regenerate fairly quickly (about two days), your blood will not clot as quickly as usual until then so it is a good idea to avoid any activities with an increased risk of injuries (e.g., juggling knives 😊). Note that with more frequent TPE, it may take longer for your blood clotting factors to return to pre-TPE levels.

Your clinician and the staff at the TPE clinic can provide you with more specific information based on your specific TPE protocol.

- As was noted earlier, you sometimes need to change the timing of certain medications on the days you receive TPE. Your clinician can guide you on this.

TPE Part 4: Long-Term TPE Potential Issues

The only known side effect/risk of long-term TPE is that most people will develop mild iron deficiency anemia (IDA). This can typically be treated with over the counter iron supplements, but if you are unable to tolerate iron supplements, iron infusions can easily be done in conjunction with TPE treatments.

Important Note: clinicians often monitor for conditions such as IDA using a simple blood test called a ferritin test. However, in patients undergoing long-term TPE, ferritin levels may be in the normal range. An alternate test called a serum iron level is more likely to be abnormally low in IDA, according to recent research.

When Normal Venous Access Can't Be Done

As we mentioned above, most patients are able to have therapeutic plasma exchange using the veins in their arms. Unfortunately, for some patients, this is not an option. Sometimes veins are too small or too deep to support the type of needles used for TPE, and sometimes scar tissue develops after years of multiple blood draws and IV therapy. There are several alternative ways that TPE can be done when normal venous access is not an option.

Catheters

The first option is a type of access catheter. This catheter is placed in a vein in your chest, the tubing is outside the skin, and the apheresis nurse uses the tubing for both drawing the blood out of your body and returning it back as part of the TPE circuit. This type of catheter is similar to a catheter used for dialysis. It will have a dressing for protection. The nursing staff will change the dressing and perform any care the catheter requires during your appointments for TPE. The advantage of this catheter is easy access for TPE. The disadvantage is the constant presence of tubing and a dressing on your chest. This will also require you to only shower, and the catheter cannot go under water. Swimming with this type of catheter is not allowed. Also, there is a risk that an infection may develop at an incision site shortly after catheter placement. The risk is less if you carefully follow instructions about caring for the incisions as they heal.

Central Access Ports

While catheters are a very reasonable option for short-term TPE, for patients who are receiving long-term TPE, catheters are really not the best solution. A second option is to have a central access port, or access device, placed under the skin. This port will be placed on the upper part of your chest and the tubing will go into a vein in your chest. Some of these ports have two chambers so both the access and return IVs go into the implanted port. However, current two-chamber ports don't allow blood to flow as rapidly as can be done using regular arm veins. The leads to significantly longer TPE treatment times because of the reduced blood flow. A newer option is a high-speed, single chamber port that is used for access only. The return IV still goes into an arm vein, but since the return IV can use a smaller gauge needle, it is usually possible to find a suitable arm vein for the return. When the TPE procedure is finished for the day, the port will be flushed with Heparin and the needle(s) will be removed.

Installing a port is a minor surgical procedure, usually done on an outpatient basis. Once the access port is implanted, it usually takes a few weeks before the port can be used for

TPE (or any other infusions you might be receiving). Central access ports have major advantages over catheters, both from a safety perspective and also that you are not restricted from activities such as bathing and swimming.

Fistulas

A third option is a fistula placed in a vein in your arm. This is the same type of system commonly used by dialysis patients. A surgeon connects a vein and an artery in your arm in the operating room. This artificial connection allows the vein to become larger and for the walls of the vein to thicken, allowing very easy access for TPE or other procedures. Typically, it takes three to six months for a fistula to be ready to use for TPE, but in rare cases, it can take up to a year. Fistulas do not require any dressings or have any tubing that comes out from your skin. Some care must be used to never cut a fistula as severe bleeding may occur, but you may bathe or swim with a fistula with no restrictions.

Summary

Therapeutic plasma exchange can be a very effective treatment for a variety of diseases and in some cases, can be lifesaving. If you are going to be starting a strange new treatment like TPE, it is completely normal to feel anxious, especially before your first TPE treatment. Our hope is that by providing you with detailed information about the procedure itself, what to expect during and after a treatment, and how to be better prepared, your experience with TPE will be more successful, leading to a better outcome.

**About the Authors*

Ed "wrong side of the needle" Harris is a patient diagnosed with a rare autoimmune disorder called systemic scleroderma in early 1990 who began receiving regular therapeutic plasma exchange treatments in 1993. Ed has had more than 460 TPE treatments over 27 years to date. Since being diagnosed, Ed has become a patient educator, advocate, and is now a published author involved in medical research on new treatment approaches for his rare disease. Ed is the founder and CEO of the Scleroderma Education Project, a 501c3 non-profit organization focused on scleroderma education and research. He is also an Honorary Associate/Fellow (Rheumatology) in the Dept. of Medicine at the University of Wisconsin in Madison, WI.

Jacki Hershberger is a Registered Nurse with 20 years of experience caring for patients requiring apheresis therapy. She graduated from nursing school in 1981 and acquired her bachelor's degree in Nursing in 1998. She started working at UW Hospital in 1983 and learned pheresis nursing in 1996. Her areas of expertise include hematology, oncology, bone marrow and solid organ transplant, as well as infusion and apheresis nursing.