



## Clinical Protocol

CP.XX.xxx

The objective of this document is to be a resource, not a replacement for institutional specific protocols. It is intended as a template for your perfusion team to edit and adapt into a resource that fits your institutional specific needs. These Clinical Protocols may also be superseded by the judgment of the healthcare professional considering the facts and circumstances of the individual case.

**SUBJECT/TITLE:**                    **INTRAOPERATIVE THERAPEUTIC PLASMA EXCHANGE (TPE) DURING CARDIAC TRANSPLANT SURGERY**

**PURPOSE:**                            To provide a guideline and resource for treating highly sensitized anti-HLA (human leukocyte antigen) antibody donor recipients. TPE may decrease the risk of allograft failure via hyperacute or accelerated antibody-mediated rejection (AMR) after reperfusion of the transplanted heart.<sup>2</sup>

**TARGET POPULATION:** Highly sensitized patients with naturally occurring anti-ABO antibodies or acquired antibodies to HLA<sup>2</sup>:

- a. Those supported with cardiac assist devices
- b. Multiparous women
- c. Individuals with a previous allograft transplant
- d. Recipients of numerous homologous blood products

## DEFINITIONS:

1. **Apheresis:** A cell processing and cell collection platform utilizing continuous-flow centrifugation and optical detection technology.
2. **TPE during CPB:** A process where plasma is removed from the patient's circulating blood volume via centrifugal fractionation through an apheresis circuit in parallel with the CPB circuit. The remaining components, mostly red blood cells, are returned to the patient with either albumin, plasma or both.
3. **Circulating Blood Volume:** CBV (measured in mL)
4. **Heart Lung Machine:** HLM
5. **Panel Reactive Antibody:** PRA assay
6. **% Plasma Volume Calculation:**  $1 - \text{Hct} (\%) = \text{plasma volume} (\%)$
7. **Plasma Volume Exchange Calculation:**  $(\text{Plasma volume} (\%) \times \text{CBV (mL)}) + \text{HLM prime volume (mL)}$
8. **Calculated Total Blood Volume (TBV):**  $\text{TBV (mL)} = \text{patient CBV (mL)} + \text{HLM prime volume (mL)}$

## **POLICY:**

During any solid organ transplant necessitating full CPB in highly sensitized recipients, plasmapheresis may be necessary. The immediate concern with highly sensitized patients is the potential for hyperacute or accelerated AMR after reperfusion of the transplanted heart. The estimated incidence of patients listed for cardiac transplantation who have positive panel reactive antibody assay (PRA) titers is 11-15%.<sup>2</sup> AMR can be caused by naturally occurring anti-ABO antibodies or acquired antibodies to Human Leukocyte Antigens (HLA), as measured by PRA.<sup>3</sup> AMR occurs in up to 18% of heart transplant recipients.<sup>3</sup>

Anti-HLA antibodies are associated with an increased risk of allograft failure, morbidity and mortality.<sup>3</sup> Coupling plasmapheresis with CPB provides a means to remove cytotoxic antibodies in the PRA positive patient and provides for a high-flow exchange when it would not otherwise be possible in hemodynamically unstable patients.<sup>2</sup>

TPE is used within the perioperative setting to prevent AMR in pre-sensitized organ transplant recipients by centrifugal fractionation, removal of the patient's plasma, followed by volume replacement with equivalent homologous fresh frozen plasma (FFP).<sup>3</sup> Plasmapheresis can remove up to 90% of circulating antibodies.<sup>4</sup>

**PERFUSION PUMP CONSIDERATIONS:** See Procedure.

## **PROCEDURE:**

1. Heart Lung Machine Circuit Modifications:
  - a. **For apheresis circuitry 'INLET' connection from CPB circuit:**  
Insert size-appropriate straight connector with luer lock (LL) proximal to the inlet of the hard-shell venous reservoir (HSVR).  
Note: Place LL facing downward to prevent air entrainment from the venous line into the apheresis circuit. Place a stopcock on LL and turn off to the circuit.
  - b. **For apheresis circuitry 'OUTLET' connection to CPB circuit:**  
Place a stopcock to an available HSVR cardiotomy lured suction port and turn the stopcock off to the HSVR.
2. Notify the plasmapheresis team at least 30 minutes prior to procedure.
3. Prior to initiating bypass/plasmapheresis verify with apheresis clinician:
  - a. The total estimated plasmapheresis time. (Average time's can range from 60 minutes for neonates and infants, up to 120 minutes for adults)
  - b. The total calculated plasma volume to be removed during plasmapheresis.
4. Initiate CPB in the usual manner.
5. Plasmapheresis will begin at the Perfusionist's instruction at least 10 minutes after stable, full-flow CPB has been achieved and the post-dilutional Hct has stabilized with current value entered on the apheresis device. Once parameters are satisfied, initiate Plasmapheresis with the following sequence:
  - a. Open the 'INLET' stopcock on the venous HLM line to the apheresis circuit.
  - b. Open the 'OUTLET' stopcock on the HSVR lured port.

6. One of the primary concerns and side effects of plasmapheresis during CPB is removal of several drug therapies; including, heparin, anesthetics, steroids, and ionized calcium. Therefore, frequent activated clotting times (ACT's), heparin protamine titration (HPT) and arterial blood gasses (ABG's) are run during the entire plasmapheresis period to verify:
  - a. Maintenance of adequate systemic heparinization (determined by heparin concentration and/or ACT) according to institutional protocol. Additional heparin boluses may be required during rewarming or ultrafiltration.
    - i. **See Appendix for additional guidelines for Heparin Dosing**
  - b. Adequate ionized calcium levels (maintain > 0.80 mmol/L during bypass)
    - i. **See Appendix for additional guidelines for Calcium Dosing**
  - c. Hematocrit (Hct) values for the apheresis clinician to program into the apheresis device:
    - i. Note: Accurate Hct values are very important to establish an 'INTERFACE' for how the plasmapheresis device separates the plasma from the blood. If the Hct becomes inaccurate during plasmapheresis, RBC's will spill over into the waste, which would be visible to the technician.
1. For example, a Hct value of 30% is programmed into the apheresis device during the initial setup procedure. This value needs to be changed to the actual post-dilutional Hct of the patient after full CPB is achieved. Hct values should be rechecked within 2 minutes after any PRBC transfusion to program into the apheresis device.
7. While the PRA assay cannot be done on a stat basis to verify an appropriate decrease in circulating cytotoxic antibodies prior to cross clamp removal, the goal is to completely plasmapheresis the patient prior to removal of the cross clamp and reperfusion of the transplanted heart.
8. At the end of the intraoperative plasmapheresis period, request the following from the apheresis clinician:
  - a. Return any unused units of FFP to the primary perfusionist for transfusion to the HLM PRN.
  - b. Flush the apheresis circuit volume into the HLM before disconnecting from the HLM circuit.
  - c. Verify the total apheresis circuit volume (mL) to be flushed into the HLM circuit for adequate Input/Output (I/O) documentation on the perfusion record.

#### **CLINICAL ASSESSMENT/SCREENING:**

A. Contraindications: None.

#### **RELATED DOCUMENTS:**

A. None.

#### **REFERENCES:**

1. American Society of ExtraCorporeal Technology Standards and Guidelines for Perfusion Practice (May 23, 2017).
2. Larson DF, Copeland JG, et al. Plasmapheresis during cardiopulmonary bypass: A proposed treatment for presensitized cardiac transplantation patients. JECT. 1999 Dec;

- 31(4): 177-183.
3. Kazi S, Carberry D, Lagarde E, Wu DW. Simultaneous therapeutic plasma exchange in parallel with cardiopulmonary bypass for prevention of HLA-antibody mediated rejection in a pediatric double transplant patient. *North Amer Jour of Med and Science*. 2012 Oct; 5(4): 228-232.
  4. Robinson JA, Radvany RM, Mullen MG, et al. Plasmapheresis followed by intravenous immunoglobulin in pre-sensitized patients awaiting thoracic organ transplantation. *Therap Apheresis*. 1997;1:147-51.
  5. Despotis GJ, Summerfield AL, Joist JH, Goodnough LT, Santoro SA, Spitznagel E, Cox JL, Lappas DG. Comparison of activated coagulation time and whole blood heparin measurements with laboratory plasma anti-Xa heparin concentration in patients having cardiac operations. *J Thorac Cardiovasc Surg*. 1994 Dec; 108(6): 1076-82.
  6. Shore-Lesserson L, Baker R, Ferraris V, Greilich PE, Fitzgerald D, Roman P, Hammon J. STS/SCA/AmSECT Clinical Practice Guidelines: Anticoagulation during Cardiopulmonary Bypass. *J. Extra Corpor Technol*. 2018;50: 5-18.

### **IMPORTANT INFORMATION ABOUT THESE PROTOCOLS:**

If this protocol/process is adopted as is, the AmSECT logo must be removed and replaced with an institution specific logo.

This protocol/process encourages high quality patient care but observing it cannot guarantee any specific patient outcome.

This protocol/process should be reviewed or revised as warranted by institutional specific protocol, taking into account the evolution of technology and practice.

Review period: Review as changes occur or per institutional protocol.

Original hard copies and/or computer copies of this protocol are stored under the supervision of the Chief Perfusionist, Department of Cardiovascular Perfusion.

**APPROVED BY:** *(signature of CMO and CNE only required)*

**Source:** *(originating department/committee)*

**Effective Date:** *(can use 'created date' for this)*

**Version Number:** *(should match # of revisions, use 1.0 if new document)*

**Date Revised:** *MM/YYYY; all dates any content changes were made*

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Date:

*<Insert Name, Chief Nursing Executive>*