DukeMedicine
Division of Cellular Therapy

ADULT AND PEDIATRIC BLOOD AND MARROW TRANSPLANT PROGRAM

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Detection & Management of Adverse Events

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APBMT-COMM-035
DETECTION & MANAGEMENT OF ADVERSE EVENTS

1 PURPOSE

1.1 To describe the detection and management of adverse events that may occur during apheresis, extracorporeal photopheresis (ECP), and bone marrow harvest (BM).

2 INTRODUCTION

2.1 Errors, accidents, and adverse reactions are types of adverse events (AEs). This procedure will allow staff to assess, detect and manage any AE that may occur while undergoing apheresis, ECP, or a BM harvest.

2.2 In the event an AE occurs, the appropriate staff member will document applicable findings on the APBMT-COMM-030 FRM1 *Adverse Event Form.*

2.3 APBMT-COMM-030 *Recording and Reporting of Adverse Events* outlines the steps for reporting adverse evets, if required.

3 SCOPE AND RESPONSIBILITIES

3.1 Physicians and nurse's responsible for the care of the blood and marrow transplant patients/donors.

3.2 Adult Blood and Marrow Transplant (ABMT) autologous and allogeneic donors are provided with printed educational materials describing select procedures, including after care instructions. Twenty-four (24) hour contact phone numbers are listed on these documents.

3.3 Pediatric Blood and Marrow Transplant (PBMT) autologous and allogeneic donors are provided with printed educational information describing select procedures, including after care instructions. Twenty-four (24) hour contact phone numbers are listed on these documents.

4 DEFINITIONS/ACRONYMS

4.1 Adverse Event (AE): Any unintended or unfavorable sign, symptom, abnormality, or condition temporarily associated with an intervention that may or may not have a causal relationship with the intervention, medical treatment, or procedure.

4.2 Adverse Reaction (AR): A type of adverse event that is a noxious unintended response suspected or demonstrated to be caused by the collection or administration of a cellular therapy product or by the product itself.

4.3 ABMT Adult Blood and Marrow Transplant

4.4 ACD Acid Citrate Dextrose

4.5 BLS Basic Life Support

4.6 CBC Complete Blood Count

4.7	CTCAE	Common Terminology Criteria for Adverse Events
4.8	DUH	Duke University Hospital
4.9	KVO	Keep Vein Open
4.10	IV	Intravenous
4.11	PALS	Pediatric Advance Life Support
4.12	PBMT	Pediatric Blood and Marrow Transplant
4.13	PQ	Performance Qualification
4.14	QA	Quality Assurance
4.15	SRS	Safety Reporting System
4.16	UVA	Ultra Violet A Light

5 MATERIALS

5.1 Associated medications as ordered by the physician

5.2 0.9% Normal Saline

6 EQUIPMENT

6.1 N/A

7 SAFETY

7.1 N/A

8 PROCEDURE

8.1 APBMT-COMM-030 FRM1 *Adverse Event Form*:

8.1.1 See APBMT-COMM-030 for instruction in completing the form.

8.1.2 The APBMT-COMM-030 FRM1 *Adverse Event Form* will be completed if there is a procedure related adverse event grade 3 or greater with the EXCEPTION of the following:

8.1.2.1 Fever, which will reported for grade 1

8.1.2.2 Rigors and or chills, which will be reported for grade 2

8.2 Types of Adverse Events listed in Common Terminology Criteria for Adverse Events (CTCAE):

NOTE: Adverse Events will be described below according to the APBMT-COMM-001 FRM1 *Adverse Event Form.*

8.2.1 Fever: When recognized early, appropriate treatments can be provided in a timely manner. Fever is defined as an elevation of the body's temperature above the upper limits of normal (> 38° Celsius or 100.4° Fahrenheit). Symptoms may include shivering, shaking, excess sweating, and skin flushing. Notify physician/designee and start

APBMT-COMM-030 FRM1 *Adverse Event Form.* Continuous monitoring may be needed for > 24 hours.

8.2.2 Chills: Patients may complain of feeling cold or develop chills during a procedure, primarily from lying still in a cold room. It is also common in apheresis and ECP with the reinfusion of blood, which is cooler than body temperature. Comfort measures such as a blanket and a warm drink can help alleviate chills. Blood warmers are regularly used in the ABMT apheresis area to help alleviate. If chills persist causing moderate tremors of the entire body, vital signs should be taken and the physician notified. Start the APBMT-COMM-030 FRM1 *Adverse Event Form.* An additional work-up may be needed (blood, urine culture, chest x-ray) to rule out other potential causes and narcotics may be indicated.

8.2.3 Nausea and Vomiting: At times, patient may feel a queasy sensation and/or the urge to vomit during a procedure, generally related to medications given during the procedure. Notify the physician to obtain an anti-emetic medication and continue to monitor patient throughout the procedure. If the patient vomits, provide medical intervention and possible intravenous (IV) hydration, if indicated.

8.2.4 Sinus Bradycardia: Sinus bradycardia is characterized by a dysrhythmia with a heart rate < 60 beats per minute that originates in the sinus node. During procedures, especially apheresis and ECP, bradycardia may be present due to imbalanced electrolytes in the blood, such as calcium.

8.2.5 Sinus Tachycardia: Sinus tachycardia is characterized by a dysrhythmia with a heart rate >100 beats per minute that originates in the sinus node. During procedures, tachycardia may be present due to anxiety related to the procedure, pain/discomfort, and/or medication given.

8.2.6 Hypotension: Hypotension during a procedure may occur due to many factors such as a vasovagal reaction, hypocalcemia, fluid shifts, and/or an allergy. Hypotension may occur during the beginning of apheresis and ECP if the patient's extracorporeal whole blood volume or red cell volume are close to the American Red Cross's recommended 15% limit. Prior to apheresis and/or ECP, extracorporeal volumes will be calculated and additional 0.9% Normal Saline can be given before the procedure if a patient's extracorporeal volumes are close to the allowed limits. If grade 3 or higher hypotension occurs during any procedure, the procedure should be temporarily stopped until the cause of the hypotension is determined. A bolus of 0.9% Normal Saline should be started, place patient in Trendelenburg position, the attending physician notified and the APBMT-COMM-001 FRM1 *Adverse Event Form* should be initiated. Inspect all tubing carefully for possible leakage. Notify the physician if any blood leaks are noted.

8.2.7 Hypertension: Hypertension during a procedure may occur due to many factors such as an increase in fluid balance, electrolyte changes, and/or medications. Hypertension prior to beginning of procedure should be

examined and procedure may be temporarily held until the cause is determined. If grade 3 or higher hypertension occurs during any procedure, the procedure should be stopped until the cause of the hypertension is determined. Notify the attending physician and initiate the APBMT-COMM-001 FRM1 *Adverse Event Form.*

8.2.8 Dyspnea: Dyspnea is characterized by an uncomfortable sensation of difficulty breathing. Dyspnea during a procedure may occur due to many factors such as a vasovagal reaction, increased fluid balance, anxiety, air embolism, and/or an allergy. Treatment consist of trying to find the cause of dyspnea, providing oxygen for relief, and patient reposition. Grade 3 dyspnea during a procedure, stop the procedure until the cause of the dyspnea is determined. Notify the attending physician and initiate the APBMT-COMM-001 FRM1 *Adverse Event Form.*

8.2.9 Hypoxia: Similarly to Dyspnea, hypoxia is characterized by a decrease in the level of oxygen in the body. Treatment consist of find root cause and providing supplemental oxygen. Grade 3 hypoxia (pulse oximeter < 88% at rest) during a procedure, stop the procedure until the cause of hypoxia is determined. Notify the attending physician and initiate the APBMT-COMM-001 FRM1 *Adverse Event Form.*

8.2.10 Hyperventilation: Hyperventilation due to anxiety can be accompanied by symptoms of lightheadedness, blurred vision, numbness and tingling. Symptoms can be alleviated by pausing the procedure and infusing saline at a KVO rate through the CVC/PIV. Reassuring and distracting the patient and having the patient breathe into a paper bag may be necessary if symptoms persist.

8.2.11 Vasovagal Reactions: When recognized in the early and mild stages, true psychogenic vasovagal reactions are easily treated. The hallmark of a vasovagal reaction is a slow bounding pulse. Symptoms may include pallor, lightheadedness, bradycardia, and hypotension. Treatment may include by putting the bed/chair in Trendelenburg and giving a bolus of 0.9% Normal Saline. If left untreated, a more severe vasovagal reaction can occur with symptoms of nausea, vomiting, diaphoresis, and loss of consciousness. Vasovagal reactions more often occur during venipuncture, at the beginning of procedure, and completion of the procedure. Prevention tactics may include distraction, explaining the procedure, placing patient in in Trendelenburg position, and covering the access line in apheresis or ECP.

8.2.12 Allergic Reactions: Patients may experience allergic reactions to the ACD, given during apheresis and ECP. Exhibiting symptoms of an allergic reaction include urticaria, rash, nasal congestion, wheezing or headache. On rare occasions patients may be allergic to the ethylene oxide gas used to sterilize the apheresis/ECP tubing sets. If a patient/donor exhibits signs and symptoms of an allergic reaction, the procedure should be paused, and the line flushed followed by a KVO

rate. The attending physician responsible for the apheresis patient should be notified for orders of a hypersensitivity reaction. The procedure may be discontinued and deferred for a day. If an ethylene oxide reaction is suspected, the patient/donor should be pre-medicated prior to the next procedure and the tubing set used in apheresis/ECP should be primed twice to rinse out the ethylene oxide gas.

8.3 Other Potential Clinically Significant Adverse Events:

8.3.1 Hypocalcemia (Clinical Symptom Guidelines): Early education of clinical hypocalcemia with early intervention is an important aspect of prevention. Acid citrate dextrose (ACD) is the anticoagulant of choice for apheresis and ECP. ACD works by chelating free calcium in the body, which is a necessary component in clot formation and is metabolized by the liver in 5-7 minutes. If infused too quickly, clinical symptoms of hypocalcemia can occur, such as numbness or tingling in the face or lips, a feeling of vibration or buzzing, or ringing in the ears. Hypocalcemia related to ACD infusions can also progress to symptoms of nausea, vomiting, chest and abdominal cramping, hypotension, and involuntary contractions of the muscles. Patients should be instructed to tell their nurse if they are experiencing any symptoms. Treatment may include, decreasing the inlet collect blood flow on the collection machine, give IV calcium gluconate, and/or giving two TUMS. If symptoms do not subside or progress, the procedure should be paused and 0.9 % Normal Saline should be infused at a KVO rate until the symptoms decrease. In ABMT apheresis collections, if symptoms persist despite calcium gluconate IV infusion, the ABMT-COLL-014 *Heparin Protocol* can be used if the patient's platelet count is > 50,000/microliter.

8.3.2 Vascular Access Problems: In most cases, large bore will be used for vascular access in apheresis. An implanted port used specifically for ECP may be used for all ECP procedures. If adequate blood flow is not obtained during the procedure, the CVC may become clotted to some degree. If fluid can be infused easily but blood cannot be withdrawn despite efforts to flush the CVC and reposition the patient, an order should be obtained for a de-clotting medication. If a minimum blood flow cannot be obtained from a catheter, the placement of a peripheral IV should be considered.

8.3.2.1 If a peripheral vein is used for vascular access, a patient may experience pain, stinging, swelling and hematoma if the needle infiltrates. If infiltration occurs, the needle should be removed, a pressure bandage and ice applied to the site, and the arm elevated. Infection and phlebitis are also potential problems following peripheral IV insertion.

8.3.3 Clotting in the Extracorporeal Circuit: The ratio of ACD-A to whole blood used for apheresis and ECP generally is adequate to prevent clotting in the blood cell separator. On occasion, clots can be observed in the access line and/or the cell separated. Platelet clumping can be

seen in the collect line in patients/donors with high counts. Since coagulation is progressive and regenerative, the problem should be addressed immediately. In apheresis and ECP procedures, lowering the INLET/AC ratio (to deliver more ACD to the system) may be needed. If large clots are present, stop the procedure and notify the physician. The tubing set may be replaced and the collection restarted with a lower INLET/AC ratio, if physician deem appropriate.

8.3.4 Hemolysis: If pink plasma is present at any time during apheresis/ECP and cellular contamination is ruled out, hemolysis should be suspected. The procedure should be paused until the cause of the hemolysis is determined. The physician should be notified and the procedure ended without reinfusion if a large amount of hemolysis has occurred. Hemolysis can be prevented by carefully setting up the tubing sets and checking all lines for kinks, which can cause red cell damage.

8.3.5 Fluid Overload: Following apheresis and ECP patients will have a positive fluid balance as a result of the administration of prime and flush saline, anticoagulant and any electrolyte supplementation or transfusion. Patients presenting with a history of cardiovascular compromise may be predisposed to fluid overload. The signs and symptoms of fluid overload include dyspnea, cough, hypoxia, tachycardia, peripheral edema, hyper/hypotension, bounding pulse, and crackles. The attending physician caring for the patient will be notified of any side effects and orders for treatment such as diuretics will be obtained. The apheresis/ECP may be terminated early if patient signs and symptoms worsen.

8.3.6 Infection: The risk of infection always exists when an invasive procedure is performed. Special care should be taken to maintain strict aseptic technique when making all tubing connections, patient accesses, and when connecting the patient to the system.

8.3.7 Thrombocytopenia: As a result of repeated apheresis, a lowering of the platelet count is seen and expected. During a 6 hour apheresis, the pre-platelet count can be reduced 50%.

8.3.7.1 An CBC is drawn prior to every apheresis procedure, day one of ECP, and 24 hours prior to BM.

8.3.7.2 ABMT patients and donors who require follow-up blood counts will be given an appointment to return to ABMT Clinic or other lab facility for lab tests. Test will be reviewed and arrangements made for any abnormalities.

8.3.8 Air Embolism: Although a very rare occurrence, air can enter the apheresis system if a tubing connection becomes loose of there is a leak in the tubing set. The blood call separators are equipped with safety features, which will detect and trap air in the system and automatically clamp the return line and stop the pumps to prevent air from being returned to the patient. A leak below the return air trap would not be detected necessitating the close monitoring of this line throughout the

procedure. Symptoms include chest pain, shortness of breath, pallor, diaphoresis, mental confusion, syncope, and shock. If air embolism occurs, have the patient turn onto their left side, put the bed in Trendelenburg, and terminate the procedure without reinfusion. The physician should be notified immediately and oxygen should be administered until the patient can be transported to the DUH emergency room. A peripheral IV should also be started and vital signs monitored closely. Careful set-up and priming of all tubing (especially the return line and blood warmer tubing in apheresis) will reduce the risk of air embolus.

8.3.9 Photosensitivity: Patient receiving ECP should be told emphatically to wear ultra violet A (UVA) absorbing, wrap-around sunglasses for twenty-four (24) hour after ECP. They should avoid all exposure to direct or indirect sunlight, whether they are outdoors or exposed through a window.

8.3.10 Blood Loss: If for any reason the blood contained in the extracorporeal circuit cannot be returned to the patient, the volume of blood lost will be recorded on the RUN sheet. A CBC may be drawn and transfusion arranged if necessary. The attending physician will be notified. Fluid balance is calculated following each apheresis. A donor who has lost the equivalent volume of a whole blood donation will be advised that he/she is deferred from whole blood donation for 8 weeks.

8.3.11 Cardiac and/or Respiratory Arrest:

8.3.11.1 ABMT Clinic: The Clinic is equipped with a "code" cart, AED, oxygen and suction. All nursing staff are Basic Life Support (BLS) certified. In the event of an emergency, the staff member will call 911 for paramedic support. The clinic attending physician/extender will manage the emergency situation. Whenever possible, the patient's blood should be reinfused immediately and IV access should be maintained.

8.3.11.2 PBMT Clinic: The clinic is equipped with a "code" cart, oxygen, and suction. A defibrillator is located in the building. All nursing staff are BLS and Pediatric Advance Life Support (PALS) certified. In the event of an emergency, the staff member will call for 115 to initiate a code response. The clinic attending physician/extender will manage the code response until the code team arrives and then care will be coordinated/transitioned as needed. IV access should be maintained.

8.4 Errors and Accidents

8.4.1 Report any procedural error, accident, or equipment/tubing malfunction during the collection to the apheresis coordinator and attending physician/designee. The apheresis coordinator will provide re-training, educational in-service, and review of the procedure, if applicable. If related to equipment, the apheresis coordinator/designee will place

equipment out of service until it can be repaired and approved for service by the Duke Clinical Engineering Department.

8.4.1.1 Performance Qualification (PQ) must be done on the equipment after repair by the apheresis coordinator or designee before placing back into use.

8.4.2 Errors or accidents, grade 3 or higher or cause patient potential harm, will be documented in the patient record and may be reported to the hospital online Safety Reporting System (SRS) depending on severity of error and/or accident. The SRS is available on the computer desktop screen pin station.

9 RELATED DOCUMENTS/FORMS

9.1 APBMT-COMM-030 FRM1 Adverse Event Form

9.2 APBMT-COMM-030 Recording and Reporting of Adverse Events

10 REFERENCES

10.1 AABB Technical Manual, Current Edition

10.2 Common Terminology Criteria for Adverse Events (CTCAE), Current Edition

10.3 McLeod, B, et.al.eds. Principles of Apheresis, AABB Press, 2003

11 REVISION HISTORY

Revision No.	Author	Description of Change(s)
08	M. Christen	-This heavily revised SOP has been updated to narrow the scope to potential toxicities associated with apheresis, bone marrow harvests, and photophoresis. Due to depth of revision, content should be read as a new document. -Details around the documenting and reporting of AEs has been removed and transferred to APBMT-COMM-030.

Signature Manifest

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