DONOR SELECTION, EVALUATION AND MANAGEMENT
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Approvals

ABMT Clinical Operations Director

Adult BMT Medical Director

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Duke University Medical Center  
Durham, NC
A. PURPOSE
To define the steps for donor selection, procurement, workup, evaluation and clearance for donation of various related and unrelated, allogeneic and autologous cellular products (stem and progenitor cells from mobilized peripheral blood or bone marrow, DLI, NK Cell, directed and unrelated donor umbilical cord blood, and directed donor granulocytes) to Adult and Pediatric patients in need of hematopoietic stem cell transplantation and supportive care.

B. INTRODUCTION
Donor Identification and Selection

Adult and Pediatric patients undergoing hematopoietic stem cell transplantation are affected with a variety of diagnoses which can be treated with a variety of types of transplantation therapy. While allogeneic transplants predominate in the pediatric population, autologous cells obtained from bone marrow (BM) or peripheral blood (PBPC) are used to facilitate marrow rescue after high dose chemotherapy in patients with certain high risk or recurrent solid tumors. Cell products from related donors are used as indicated by medical practice under 21 CFR 1271 and 361. More than minimally manipulated cells from unrelated donors including but not limited to DLI, ALDHbr, CD34, may be used under IND per FDA 21 CFR 1271, 361. Cells for transplantation are obtained from bone marrow, mobilized peripheral blood or umbilical cord blood. In addition, granulocytes, donor leukocytes (DLI), and NK Cells and others may be utilized in the peri-transplant period to enhance protection against opportunistic pathogens or graft versus tumor effects. The ultimate choice of treatment protocol and donor source is determined by the multidisciplinary BMT care team lead by the patient’s primary physician.

Both allogeneic and autologous donors must be cleared by medical personnel to undergo a bone marrow or PBPC harvest procedure. Bone marrow harvests are performed under general or spinal anesthesia in the appropriate, age specific operating room. Stem cell, granulocyte, donor leukocyte, and NK Cell donations are performed via leukapheresis which is conducted by teams consisting of a physician, Clinicians, RN staff, and, in the pediatric area, a medical technologist. Pediatric leukapheresis is performed in the Children’s Health Center Pediatric BMT Clinic treatment room while adult products are collected in the North Pavilion ABMT Clinic.

Pediatric allogeneic donors may be pretreated with therapeutic iron and/or vitamin K. For the Pediatric BMT program when possible, allogeneic donors donate an autologous unit of PRBCs in advance of bone marrow harvest procedures. If this is not possible, a directed donor, unit of RBCs is procured from an ABO compatible family member in advance of the procedure. Blood products are irradiated and leukocyte depleted before administration to the donor or recipient-patient. In rare selected situations, CMV negative products are used.

Pediatric donors of mobilized peripheral blood progenitor cells (PBPC) or granulocytes may have a central venous apheresis catheter placed prior to their donations. Adult donors require a central venous catheter only if peripheral access is unsuccessful. Donors may be mobilized with granulocyte-colony-stimulating factor (G-CSF) or, in the case of autologous stem cell donations, G-CSF +/- chemotherapy. Readiness for apheresis is determined by quantitation of CD34+ cells in the peripheral blood or other cytokines for PBPC donors, but this parameter is not used for granulocyte, DLI or NK cell donors. Quantitative cellular targets and endpoints based on
apheresis volume, total cells and CD34+ cells/kg of recipient body weight are defined for indicated procedures.

C. SCOPE
MD required. Nurse Coordinators/Clinician, RN Staff, Nurse Practitioner, Physician Assistant and Medical Technologist/Clinical Laboratory staff.

D. MATERIALS NA

E. EQUIPMENT NA

F. PROCEDURE
1. Donor Evaluation
   a. One or more clinic visits will be arranged for donor evaluation. The nurse clinician/transplant coordinator will arrange for a donor workup concomitant with the patient’s pre-transplant workup for stem cell donors and at the request of the attending physician for granulocyte, DLI or NK Cell donors.
   
   b. During these clinic visits, the donor will complete the Pediatric or Adult Donor History Questionnaire, undergo a physical examination, which includes assessment for signs of IV drug abuse, screening blood counts, chemistries, coagulation factors and blood type and screen. HLA-typing is obtained on allogeneic donors. Infectious disease screening is performed as outlined below. Pregnancy testing is performed in females of child bearing age. All evaluations are performed in a private clinic examination/consultation room where confidentiality can be maintained. Some donors will have chest xray and EKG performed.
   
   c. The donor’s physician/Extender will obtain a complete health history and perform a physical examination (when indicated) and record this information on the Duke Hospital Universal H&P Form or related document. Adult BMT Clinic Notes are located in browser. Pediatrics notes are located in the PBMT database. Current medications, blood transfusion history, vaccination history, and travel history will specifically be reviewed and recorded. High risk behavior will be reviewed. The completed form will be signed and filed in the donor section of the transplant recipient’s shadow chart and a copy will be sent to Duke Medical Records.
   
   d. The donor, or parent/legal guardian of-in the case of a child <18 years will be given the donor education materials “Important Information You Should Know About Stem Cell Donation”, and either the Pediatric “Donor Health History Questionnaire” (6CP.100 (FRM2)) or the Adult Donor History Questionnaire” (6CA.100 (FRM1)) to complete. The donor can complete this independently, and return it to the MD/Extender or Nurse Coordinator/Clinician. [Note: The sensitive questions about sexual activity have been removed from the Pediatric form. The Pediatric Nurse Coordinator will determine whether pediatric patients between 12-18 years of age should complete the pediatric or adult form.] Assistance in completing the Donor Health History Questionnaire will be provided if needed. The completed Donor Health History Questionnaire will be reviewed by the Nurse Coordinator/Nurse Clinician/MD Extender/Transplant Coordinator to identify any exceptions for
donation (e.g. questions that are answered “yes”). Unexpected responses or “yes” questions will be explained in the remarks section of the questionnaire. (e.g. travel outside the U.S., query where? etc.). After obtaining this additional information, any exceptions will be reviewed by the donor’s physician. If the physician deems that the donation should occur despite the exception, he/she will document this on the questionnaire (pediatrics only), in the donor’s medical record, and complete the Emergency/Exceptional Release section of the Summary of Donor Eligibility (6B.100, 6BA.100, 6BP.100, 6CA.100, 6CP.100 (FRM4)). If not, the donation will be cancelled and the donor will be informed of this decision.

e. The attending physician and transplant coordinator or nurse clinician will review the donor’s responses to the donor health history questionnaire and address any exceptions that may impact the donation of stem cells or other cellular products. If the donor answered a question indicating an increased risk of infectious disease transmission to the recipient, the physician will address the risks and benefits of the planned donation in the clinic note. The physician will make the final determination regarding the suitability of the donation in these situations.

f. Any exceptions to donation will be documented prior to the day of donation on the Adult or Pediatric Donor Health History Questionnaire and The Summary of Donor Eligibility; Section A: Infectious Disease Testing; Section B: Donor Eligibility Requirements; Section C: Emergency/Exceptional Release. These completed forms, signed by the physician, will be placed in the donor chart and available for review by the clinical staff as needed. The Emergency/Exceptional Release will cover the entire donation period of 30 days for PBSC, bone marrow and dedicated granulocyte donations, or 7 days for DLI and NK Cell donations, unless there is a change in donor status.

g. The Health History Questionnaire will be re-administered and updated every 30 days. The PBMT Nurse Coordinator will re-administer to the pediatric donors, and the apheresis care nurse or donor physician extender will re-administer in the adult population. The same procedure for reviewing and noting exceptions applies to each administration of the questionnaire. For donors undergoing multiple donation procedures, the Pediatric “Interim Questionnaire” (6B.100, 6BA.100, 6BP.100, 6CA.100, 6CP.100 (FRM3)) or the Adult “Interim Questionnaire” (6B.100, 6BA. 100, 6CA. 100, (FRM5)) will be administered by the care nurse before each apheresis procedure, reviewed and signed by the physician.

h. For donors undergoing multiple procedures, infectious diseases testing will be repeated every 30 days per FDA and FACT requirements for PBSC, bone marrow, and dedicated granulocyte donors, and every 7 days for DLI or NK Cell donations per FACT regulations. A Summary of Donor Eligibility will accompany each product collected to the stem cell lab.

i. Routine labs for the pediatric program including chemistries, blood count and coagulation factors will be tested within 72 hours of the first collection and 24 hours of all subsequent collections, or more often if indicated, and reviewed by the Nurse Clinician. Routine labs for the adult program include a daily CBC w/ manual diff, CMP, Mg, Phos, CD 34 (for PBSC donors). Adult labs are reviewed daily by the
clinic attending physician. All donors will have ABO Rh drawn the first day of
donation only. If any results are out of the normal range, they will be reviewed by the
Attending Physician and appropriate therapy will be prescribed. It is common for the
pediatric granulocyte donors to require calcium, Fe, and Vitamin K supplementation.

2. Donor Test Requirements

   a. Testing for the following infectious disease is performed within 30 days of donation
   for PBSC, Bone Marrow, and Dedicated Granulocyte donation, and within 7 days for
   DLI, NK Cell donation, on blood samples drawn on stem cell or other cellular therapy
   donors (see procedure Sending of Samples to ARC NTL). Donors donating over a
   time period in excess of 30 days will have these tests repeated every 30 days (or 7
days if DLI or NK Cell).

   b. The testing panel for adult donors and pediatric donors > 6 months of age not on
   IVIG supplementation (within 6 months) of the donation is listed below.

   - Hepatitis B Surface Antigen (HBsAg)  
   - Hepatitis B Core (Anti-HBc)  
   - Hepatitis C Virus Antibody (Anti-HCV)  
   - HIV antibody (Anti-HIV 1/2)  
   - HIV NAT  
   - HCV NAT  
   - HBV NAT  
   - HTLV I/II Antibodies Serum  
   - CMV Immune Screen (Anti-CMV all antibodies)  
   - CMV NAT-(if CMV positive Peds Only)  
   - Syphilis-Treponema pallidum antibody for initial screen
   If the treponemal based screen is positive, but the confirmatory test is negative,
the unit may be used as long as it is labeled as an ineligible donation.

   - Syphilis screen is reactive a confirmatory test is performed using the RPR Card
   Test System
   - West Nile Virus NAT
   - Beta HCG – (pregnancy test) – will be drawn on females of child-bearing age
   - Trypanosoma Cruzi (Chagas)

Additional Testing for Pediatric Donors Only

- VZV – Varicella Zoster Virus IgG antibody
- EBV – Epstein Barr Virus (IgG, IgM, EBNA) antibodies
- HSV – Herpes Simplex Virus IgG antibody
- Toxoplasmosis antibody, IgG and IgM
  🌟 FDA Required testing.
  🔴FDA recommended. Obtain in all patients < 6 months of age or on IVIG or unable to make endogenous antibody.
  ★FDA Required for products containing high WBC content (i.e. Granulocytes, DLI, mobilized peripheral blood).

  c. For patients on IVIG or infants ≤ 6 months of age and/or on IVIG, the following panel is substituted:
     - Hepatitis B Surface Antigen 🌟
     - Nucleic Acid Test (NAT):
       HIV 🌟
       CMV 🌟
       HBV 🌟
       HCV 🌟
       WNV 🌟
       EBV
     🌟 FDA Required testing.
     🔴FDA recommended. Obtain in all patients < 6 months of age or on IVIG or unable to make endogenous antibody.
     ★FDA Required for products containing high WBC content (i.e. Granulocytes, DLI, mobilized peripheral blood).

3. **Donor Clearance**
   a. Bone Marrow donors must be cleared for the following:
      i. Infectious diseases testing negative or, if positive, cleared by patient/donor MD
      ii. Medically safe and cleared by the attending MD for general anesthesia and marrow donation
      iii. Evaluation of vaccination history
      iv. Evaluation of travel history
      v. Not currently pregnant
      vi. Not infected with HIV 1 or 2
   b. PBPC donors must be cleared for the following:
      i. Infectious disease screening and testing
      ii. Medically safe and cleared by the attending MD for apheresis procedure
      iii. Adequate venous access or CVL placement if indicated
      iv. Growth factor administration
v. Not currently pregnant
vi. Not infected with HIV 1 or 2
vii. For donors donating multiple times over > 1 week, additional parameters should be considered. These donors are more likely to become iron deficient, hypocalcemic, or hypoproteinemic over longer donation times. As such, they required more careful monitoring and follow-up. These donors must demonstrate that they can:

(a) Be compliant with medications prescribed by their MD

(b) Take care of their central lines, or report to care sites at Duke University Medical Center for this care

(c) Be compliant with appointments, generally 2x per week

(d) Be able to avoid contact sports or contact activities during work or other daily responsibilities

(e) Adult donors in pediatric program must have an adequate hemoglobin (>9 gms/dl) and platelet count >50,000/μL before each donation

(f) Adult donors in the adult program must have an adequate hemoglobin (>9 gms/dl) and platelet count >50,000/μL before each donation

(g) Pediatric donors must be cleared by their treating physician. In general they must be cleared for the following:

(i) Infectious diseases testing negative or, if positive, cleared by patient/donor MD

(ii) Medically safe and cleared by the attending MD for general anesthesia and marrow donation

(iii) Evaluation of vaccination history

(iv) Evaluation of travel history

(v) Not currently pregnant

(vi) Not infected with HIV 1 or 2

(vii) Adequate hemoglobin (>9.0 gms) and platelet count (>50,000/μL)

c. Summary of Donor Eligibility

i. Prior to the first day of collection, The Summary of Donor Eligibility form (6B.100, 6BA. 100, 6BP.100, 6CA.100, 6CP.100 (FRM4) must be completed.

(a) If donor does not meet the criteria for donation and the donor is classified as an "URGENT MEDICAL NEED", the physician must advise the recipient of these findings.

(b) Summary of Donor Eligibility, Section C: Emergency/Exceptional Release must be completed and signed by the physician. The Quality Manager/designee signature is also required.

(c) Follow procedure 5C.100 (1C.120) Emergency and Exceptional Release for acceptance and release of product. This form will be effective for 30 days.(for
PBSC, Bone Marrow, Granulocytes) or 7 days (for DLI, NK Cells) if there are no new exceptions.

ii. The completed form must accompany the product to the Stem Cell Laboratory each day of collection.

4. Donor Consent

a. Donors are consented a single time for their entire course of donations.

b. Before signing the written consent, the donors undergo an educational session with the nurse/transplant coordination to review the details of the procedure, line placement (if applicable), growth factor administration (if applicable), expected complications, and the potential risks and benefits.

c. Written informed consent is obtained by treating MD.

d. The original copy of the consent is filed in the donor’s shadow/clinic chart. A copy of the consent is filed in the medical record at Duke University Medical Center. For directed allogeneic donations, a copy of the consent is also filed in donor section of the recipient’s shadow/clinic chart.

5. Donor Management

a. Bone Marrow Donors:

i. Bone marrow is collected by a Physician, Physician Assistant and Nurse Practitioner trained in marrow collection in the Duke Hospital Operating Room under sterile conditions.

ii. Bone marrow donors undergo a pre-operative assessment by the anesthesiologist to determine their candidacy for anesthesia per the Duke Hospital Clinical Practice Guidelines.

iii. Bone Marrow is harvested into a closed filtration system, filtered and transported (hand carried) at room temperature in a validated container to the Stem Cell Laboratory after the procedure is completed by the MD or NP who performed the procedure.

iv. Procedures for biological, chemical and radiation safety are in place per Duke Hospital.

v. Marrow collections are handled and discarded with precautions that recognize the potential for transmission of infectious agents.

b. Central Line Placement:

i. Central venous catheters are placed by a licensed physician qualified to perform the procedure. In pediatric patients this is generally a Pediatric Surgeon. In adult patients and larger pediatric patients, this is performed either by a general surgeon or a vascular radiologist.

ii. Correct placement of the central venous catheter is documented by a chest X-ray performed after the catheter is placed. The report of this x-ray is located on the Duke e-Browser and in the patient/donor’s medical record.
iii. Anesthesia is administered by a board certified adult or pediatric Anesthesiologist per Duke Hospital Guidelines. Conscious sedation may be used for adult donors whose catheters are placed in Vascular Radiology. In that case, the physicians administering the conscious sedation are approved by the Duke Hospital Certification Program for Administration of Conscious Sedation.

c. Growth Factor Administration:

i. Hematopoietic Growth Factors (cytokines) are administered under the supervision of a licensed physician experienced in the management of persons receiving these agents.

ii. Specific orders for each patient/donor are generated by the physician or Nurse Practitioner and filled by the Duke Inpatient/Outpatient Pharmacy, license pharmacy or Home Health Pharmacy depending on the patient’s arrangement with their third party payor.

iii. Growth factors are generally administered by the subcutaneous route a minimum of one hour or a maximum 12-16 hours before the next planned procedure.

d. Assessment of the Patient/Donor before each apheresis procedure:

i. Pediatric BMT: The patient/donor will have a complete blood count, differential, platelet count, chemistries, coagulation tests and ABO, Rh performed (bone marrow harvest or apheresis).

ii. Autologous Adult BMT: The patient/donor will have a complete blood count, differential, platelet count and routine chemistries drawn before each apheresis procedure. Donors will have an ABO,Rh on day 1 of collection.

e. Apheresis procedure:

i. Cellular therapy products from donors are collected on a cell separator.

   (a) If a pediatrics patient’s weight is < 40 kg, the cell separator is primed with a unit of irradiated, leukodepleted, ABO compatible PRBC prior to initiation of the apheresis procedure.

ii. After clearance is obtained, informed consent is obtained, catheter is placed (if indicated), and growth factor is administered, the donor will be given an appointment for the apheresis procedure. After the patient arrives for their appointment and checks into the clinic, the nurse will take vital signs and administer the “Interim Health Questionnaire”. If the donor is healthy and well, with no new issues, the nurse or medical technologist will proceed with the apheresis procedure. If the donor has any medical issues, the nurse or med tech will notify the physician for evaluation.

f. Management of Blood Loss

i. 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. The PBMT/ABMT physician or designee will be notified. A hematocrit may be drawn and transfusion arranged if necessary. Extracorporeal volumes can be recalculated based on the new hematocrit. A donor who has lost the equivalent
volume of a whole blood donation will be advised that he/she is deferred from
donation for 8 weeks. The donor may donate in less then eight weeks as long as
the donor meets the criterion for hemoglobin naturally or via transfusion and is
approved for donation by the medical director.

g. Management of Thrombocytopenia:
   i. Apheresis donors may develop thrombocytopenia, especially after repeated,
      frequent donations.

   ii. For Autologous donors, the clinical treatment protocol specifies the management
       of thrombocytopenia in this setting.

   iii. For Allogeneic donors in the Pediatric program, the apheresis procedure should be
        cancelled if the donor’s platelet count is <50 LuL.

   iv. For Allogeneic donors in the Adult program, the apheresis procedure should be
        cancelled if the donor’s platelet count is <50 LuL.

h. Management of Hypocalcemia:
   i. Many patient/donors develop hypocalcemia during the apheresis procedure. In
      anticipation of this potential complication:
     
     (a) All pediatric patients <6 years of age are placed on a calcium drip during the
         apheresis procedure.

     (b) All older patients (>6 years of age) may be given TUMS EX q 15-30 minutes
         during the procedure as ordered by their treating MD.

     (c) Patients unable to tolerate TUMS or experiencing clinical signs of
         hypocalcemia (e.g. tingling, numbness, posturing, twitching) are placed on a
         calcium infusion regardless of age.

     (d) Adult patient’s/donors are placed on a calcium drip during apheresis if they
         experience citrate toxicity symptoms. The heparin protocol can also be
         instituted to control citrate toxicity.

i. Management of Coagulopathy:
   i. Repeating apheresis donors may experience prolongation of their coagulation
      factors. These patients may be treated with age appropriate maintenance Vitamin
      K therapy.

j. Management of Anemia:
   i. Donors undergoing multiple apheresis procedures may develop iron deficiency
      anemia. These donors may be treated with therapeutic iron replacement as per
      their treating MD. Specific parameters for the lower limit of hemoglobin values
      prior to apheresis will be specified in the patient’s/donor’s orders. In general,
      healthy donors will be required to maintain a hemoglobin > 9 gm/dl to continue
      donations.

k. All adverse events must be documented on 4C.600 (FRM 1) Pheresis Adverse Event
   Form per procedure 4C.6001 Errors, Accidents, and Adverse Reactions.
G. RELATED FORMS

- 4C.600 (FRM 1) Pheresis Adverse Event Form
- 6B.100, 6BA.100, 6BP.100, 6CA.100, 6CP.100 (FRM1) Adult Donor History Questionnaire
- 6B.100, 6BP.100, 6CP.100 (FRM2) Pediatric Donor History Questionnaire
- 6B.100, 6BA.100, 6BP.100, 6CA.100, 6CP.100 (FRM5) Adult Interim Donor History Questionnaire
- 6B.100, 6BP.100, 6CP.100 (FRM3) Pediatric Interim Donor History Questionnaire
- 6B.100, 6BA.100, 6BP.100, 6CA.100, 6CP.100 (FRM4) Summary of Donor Eligibility

H. REFERENCES

- Food and Drug Administration. 21 CFR 1271, Human Cellular and Tissue-Based Products.