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INFORMATION FOR THE USE OF HPC,CORD BLOOD PRODUCTS

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1 Notice to all users

This document is intended to provide general information to those who administer Human Progenitor Cell, Cord Blood (HPC,CB) products and serves as an extension and enhancement of the label found on HPC,CB units, as the space on those labels is limited. The acronym HPC,CB is used only as abbreviation and is not intended to be used on the product labels. HPC,CB units contain living human cells and are intended for use in patient treatment. The focus is restricted to minimally manipulated unrelated HPC,CB units. This document is intended to be used by facilities based in different countries, according to national and international applicable regulatory requirements. HPC,CB units must be used under medical prescription.

WARNING: Because HPC,CB products are derived from human blood, they may carry a risk of transmitting infectious agents including bacteria, viruses, fungi, protozoa, and prions. Donor screening and testing procedures are in place to minimize the risk of transmitting such infections, but cannot eliminate this risk. Transmission of malignant disease has been reported (1). Also, serious life-threatening septic and toxic reactions can result from administration of products containing bacterial toxins. In addition, HPC,CB products may contain certain immunizing substances other than those indicated on the label, such as red cells, mature white cells, platelets, and plasma proteins. Therefore, this document, in whole or in part, cannot be considered or interpreted as an expressed or implied warranty of the safety or fitness of the described products even when used for their intended purpose. Attention to the specific indications for HPC,CB products is needed to prevent inappropriate administration. *For detailed information see 'Circular of information for the use of cellular therapy products', AABB edition, curr. rev.*

2 General Information

HPC,CB preparations contain umbilical/placental cord blood collected by the delivery team in uncomplicated vaginal deliveries or elective caesarean sections. After thorough cleansing of the cord, the blood is collected by gravity drainage into standard blood collection bags containing citrate-phosphate-dextrose (CPD) anticoagulant. Informed consent is obtained from every mother and samples of the mother's blood are tested for Hepatitis B, Hepatitis C, HIV-1/2, HTLV-I/II, CMV, and syphilis, according to National Laws and International Regulatories. Maternal and familial medical history are obtained; newborn is evaluated for eligibility at birth and a six/twelve months follow-up of the baby is requested. Before to release a HPC,CB unit, familial and baby outcomes are updated.

3 Product description

HPC,CB products manufactured and issued by the Pescara Cord Blood Bank (PeCBB) are minimally manipulated cellular biologic products that contain stem/progenitor cells obtained from the cord/placental blood collected in CPD anticoagulant, after volume reduction and partial red cell and plasma depletion.

HPC,CB products are cryopreserved in a final volume of approximate 70 ml by using a cryosolution (vol/vol) containing a final concentration of 10% dimethyl sulfoxide (DMSO), 2% Dextran 40 and 1% Human Serum Albumin (HSA); approximate volumes of anticoagulant and additives included in the cryopreserved bag are showed in the following table:

Additives	Approximate Volumes (ml)
Residual CPD	3-7,5
DMSO	5,6-7
Dextran 40	1,12-1,4
HSA	0,56-0,7

To preserve the cell viability and potency and safety, products are cryopreserved in EVA bags with or without an overwrapping by a controlled rate program and permanently stored liquid phase/vapour phase of liquid nitrogen (-196°C); small aliquots are also frozen as pilot samples or attached segments and designed to be a source of reference material for identity and potency testing.

Minimal date showed on the label affixed on the cryobag are:

- the Name and Address of the CBB
- the Product Proper Name HPC-Cord Blood
- the Unique Product Identifier
- the overall volume of the cell content
- date of cryopreservation.

On the label for distribution the following data are shown

- Name and Address of the CBB,
- Product Proper Name HPC-Cord Blood
- Unique Product Identifier
- SEC
- Collection date
- Expiration date
- Overall volume
- Anticoagulant and additives
- Manipulation
- Temperature Storage
- Donor Blood type Group/Rh
- IDMS results
- Recipient's full name
- Recipient's ID
- Disclaimer “For Intended Recipient Only”
  “Rx only”
  “Properly Identify intended recipient and product
  “DO NOT Irradiate”
  “DO NOT use leukoreduction filters”

Products expiration is defined according to stability testing program carried out by the CBB on the banked products from the starting of the program to date.

HPC,CB donations are screened to exclude potential donors with either a medical history of increased risk of infection or positive screening tests for anti-HCV (antibody to hepatitis C virus), HbsAg (hepatitis B surface antigen), Anti-HBc (antibody to hepatitis B core antibody), Syphilis (antibody to Syphilis), HIV-1/2 (antibody to HIV 1/2), HTLV-I/II (antibody to HTLV I/II), CMV

(IgG and IgM antibodies) Nucleic Acid Test (NAT) for HIV, HCV, HBV. Additional tests are performed according to Italian Laws in case of pandemia and/or increased local risks or on demand of the Transplant Center. CB units are also screened for hemoglobinopathies; at the request of the CB unit, testing are performed and CB unit is deferred in case of homozygous state. Acceptance criteria for HPC,Cord Blood banking and listing are showed in the following table:

Criteria		**Registration form**
Informed consent for unrelated umbilical cord blood donation and storage Informed consent on personal data	Signed by both expectant parents	Form CBB 6.5.1-01a Form PRY SCO 23a
Maternal medical history questionnaire	Donor eligibility in accordance with 'Att CBB 6.5.1-03Donor selection criteria' assessed and signed by CBB Medical Direct/delegate	Form CBB 6.5.1-07
Paternal medical history questionnaire	Donor eligibility in accordance with 'Att CBB 6.5.1-03 assessed and signed by CBB Medical Direct/delegate	Form CBB 6.5.1-08 Form CBB 6.5.1-07
Labor and delivery	Donor eligibility in accordance with 'Att CBB 6.5.1-03 assessed and signed by CBB Medical Direct/delegate	Form CBB 6.5.1-12 Form CBB 6.5.1-07
Newborn eligibility	Donor eligibility in accordance with 'Att CBB 6.5.1-03 assessed and signed by CBB Medical Direct/delegate	Form CBB 6.5.1-13 Form CBB 6.5.1-07
TNC	$\geq 8x10^8$ yy 2000-2008 $\geq 10x10^8$ yy 2008-2010 $\geq 12x10^8$ yy 2011-2015 ≥ 16x108 since y 2016 or ≥ TNC$12x10^8$ and CD34+≥2x106	Form CBB 02-03-01 CBUs processing worksheet Form CBB 02-04-01 CBUs cryopreservation worksheet
NC Viability	≥ 85%	Form CBB 02-03-01 CBUs processing worksheet Form CBB 02-04-01 CBUs cryopreservation worksheet
CD34+	$\geq 1x10^6$ CD34+ viable cells yy 2000-2015 ≥2x106 CD34+ viable cells since 2016	Form CBB 02-03-01 CBUs processing worksheet Form CBB 02-04-01 CBUs cryopreservation worksheet
CFU-C CFU-GM	CFU Growth CFU Intra-assay Variation ≤10% CFU plating efficiency: 25-60% *(on 120 CD34+ cells plate/seeded)*	Form CBB 02-03-01 CBUs processing worksheet Form CBB 02-04-01 CBUs cryopreservation worksheet
Check CBU long-term storage position	Match	Form CBB 02-04-01 CBUs cryopreservation worksheet
Check Maternal samples long-term storage position	Match	Form CBB 02-04-01 CBUs cryopreservation worksheet
Check Retention samples long-term storage position	Match	Form CBB 02-04-01 CBUs cryopreservation worksheet

IDMs test	Non reactive (except CMV IgG Ab)	Form CBB 02-06-01 CBU Qualification
Microbial colture	No grow	Form CBB 02-06-01 CBU Qualification
CBU AB0 blood group Rh type	Typed	Form CBB 02-06-01 CBU Qualification
Hemoglobinophaty testing	No Homozygous hemoglobinopathy	Form CBB 02-06-01 CBU Qualification
CBU HLA typing	Performed at banking Confirmatory HLA typing at release to search is required	Form CBB 02-06-01 CBU Qualification
Verification of maternal HLA typing	Match	Form CBB 02-06-01 CBU Qualification

When the CB units are selected for transplant, quality controls are carried out on pilot vial or attached segment to confirm post thaw safety, potency and identity, and HLA confirmatory etst is performed. Before patient conditioning begins, the HPC,CB unit is shipped to the Transplant Center in the cryopreserved state, in special shipping containers designed to maintain a controlled environment at ≤-150 degC. At the transplant center the HPC,CB must be stored in vapour phase until ready for thawing and administration. For patient administration HPC,CB unit must be thawed and can be directly infused to the patient or diluted by a reconstitution solution or washed before infusion, to remove the DMSO and free hemoglobin (2). In this case a solution of 10% Dextran and 5% Human Serum Albumin can be used.

4 Manufacturing and Distributing Facility

HPC,CB Units are manufactured and distributed by:

PESCARA CORD BLOOD BANK
TISSUES ESTABLISMENTS AND BIOBANKS
DEPARTMENT OF ONCOLOGY AND HEMATOLOGY
ASL PESCARA - Via Fonte Romana, 8 - 65124 Pescara

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Tel: +39 0854 252374 Fax +39 085 4252265; e-mail: pescaraCBB@ausl.pe.it
e-mail: tiziana.bonfini@ausl.pe.it
Any question/concern about the product released must be directed to: Pescara Cord Blood Bank at the address above indicate.

5 Indications and Usage

Allogeneic HPC,CB products are intended to provide hematopoietic reconstitution after myeloablative or nonmyeloablative preparative regimens for hematologic malignancy, bone marrow failure and thalassemia; Lysosomal storage and peroxismal enzyme deficiency disorders, Hurler Syndrome (MPS I), Krabbe Disease (Globoid Leukodystrophy), X-linked Adrenoleukodystrophy; primary immunodeficiency diseases. For patients with certain malignancies, the product is also intended to provide immune reconstitution and immunotherapy, known as graft-vs-tumor effect. The therapy is intended to treat the patient's underlying condition by replacing the diseased hematopoietic system with a healthy graft from the HPC,CB unit.

6 Dosage and Administration

A HPC,CB unit contains a minimum of 8.0×10^8 cells, 85% viability pre-cryopreservation. The nucleated cell count, $CD34^+$ cell count and CFU-GM content are listed in the CB unit Report sent with each individual unit; cell doses per kilogram of recipient weight are also calculated. Appropriateness of a CB unit for the patient to be transplanted must be determined by the transplant patient's physician. According to the literature, recommendations for cell dose, based on HLA match are the following:

1. CB units with 6/6 or 5/6 HLA match

Mimimum cell doses in malignant/non malignant disorders:

Nucleated cell dose at freezing: 2.5 to 3.0 $x10^7$/Kg

After thawing: 2.0 to 2.5 $x10^7$/Kg

2. CB units with 4/6 HLA match

Mimimum cell doses in malignant disorders:

Nucleated cell dose at freezing: 3.5 $x10^7$/Kg

After thawing: 3.0 $x10^7$/Kg

Mimimum cell doses in non malignant disorders:

Nucleated cell dose at freezing: 4 to 5 $x10^7$/Kg

After thawing: 3.5 $x10^7$/Kg

According to the literature, the minimum allowed dose of thawed nucleated cells should be at least $1x10^7$/Kg (3) recipient weight. Administration of any CB unit should begin only after identification of the product(s) and the intended recipient, according to institutional policies. HPC,CB infusion should be infused at a rate of ≈5cc/Kg/hour. Sufficient observation should be undertaken by nursing and medical staff to detect symptoms and/or signs suggestive of acute immunologic or infectious complications. Specifically, vital signs (pulse and respirations, blood pressure and oximetry) should be measured at baseline, during, and for 2-4 hours post infusion. The administration time will be determined by the total volume relative to the patient weight to be infused. If the thawed products have not been washed to remove DMSO, care should be taken not to exceed 1 gr. (1 ml) of DMSO per kilogram of recipient weight per day administration [70 mL of a 10% solution contains 7 mL (≈7 gr) of DMSO]. HPC,CB units must be inspected for container integrity and unusual appearance immediately before administration. Aseptic technique must be employed.

HPC,CB must not be administered through a filter designed to remove leukocytes.

HPC,CB may be filtered through a 170 filter designed to remove clots.

HPC,CB should be mixed thoroughly before use and during infusion.

HPC,CB products must not be irradiated.

Patients should be premedicated according institution standard operating procedures 30 to 60 minutes before administration of the CB unit.

When administering double cord blood transplants, a minimum of 2 hours should elapse between the completion of the first infusion and the initiation of the second infusion.

7 Pharmacokinetics and clinical method of action

HPC,CB units administered intravenously migrate to the bone marrow, where they engraft, proliferate and mature. The mature cells are released into the bloodstream, restoring blood counts and immunity. The time from administration of HPCs to recovery of adequate normal blood counts is variable. Median time to engraftment (ANC >500 on the first of three days) for patients who receive CB stem cell transplants has been reported to vary from 21 to 35 days (4,5,6). Platelet engraftment is significantly delayed in recipients of cord blood compared to other types of stem cell transplants until more than 8 weeks (4,5,6). Allogeneic transplantation sometimes induces a graft-vs-tumor effect that is beneficial in recipients who receive a transplant for treatment of malignancies. In the case of inborn errors of metabolism the transplanted cells will produce the missing enzyme and provide correction of this error. Correction of the damage done by the metabolism error prior to transplant is variable and depends both on the disease for which the transplant is done and the condition of the patient undergoing transplant.

8 Contraindications

A known recipient immunologic sensitivity to any of the excipient components of the HPC,CB unit would require special measures before administration of the unit such as washing of the unit before administration (19).

9 Warnings and Precautions

Because HPC,CB products are derived from human blood, they may carry a risk of transmitting infectious agents including bacteria, viruses, fungi, protozoa, and prions. Donor screening and testing procedures are in place to minimize the risk of transmitting such infections but cannot

eliminate this risk. Transmission of malignant disease has been reported (1). Also, serious life-threatening septic and toxic reactions can result from administration of products containing bacterial toxins (7). In addition, HPC,CB products may contain certain immunizing substances other than those indicated on the label, such as red cells, mature white cells, platelets, and plasma proteins. Attention to the specific indications for HPC,CB must be paid to prevent inappropriate administration. Mild to moderate infusion reactions are expected and include but are not limited to: headache, fever, chills, sweats, dyspnea, nausea, vomiting, diarrhea, cramping, mild hypertension, tachycardia, bad odor on breath, fluid retention, allergic reactions. More severe reactions including respiratory distress, severe bronchospasm, hypoxia, hypotension, severe hypertension, acute renal failure, severe anaphylactic reactions may occur and must be reported.

10 Adverse reactions, side effects and hazards

Any adverse reaction defined as a suspected or proven unfavorable response to administration of HPC,CB products manifested by signs and symptoms including microbial contamination of a product or suspected disease transmission during or after product administration must be documented and reported in accordance with the facility's policies, national applicable laws and international regulations. Any such event must be reported to the Medical Director of the facility that issued the product, National Biovigilance Authority and NMDP. The user must contact the manufacturing/issuing facility for specific requirements. All entities involved in the manufacture of the product must be contacted in the investigation/reporting of an adverse reaction. The following adverse reactions, side effects and hazards may pertain to administration of HPC,CB products.

Immunologic Complications

Immediate Acute Hemolytic Reaction is one of the most severe complications of HPC,CB product administration and is usually caused by donor-recipient major ABO incompatibility. Acute hemolytic reactions characteristically begin with an increase in temperature and pulse rate. Symptoms may include chills, dyspnea, chest or back pain, abnormal bleeding, or shock. Instability of blood pressure is frequent, with the direction and magnitude of change depending upon the phase of the antigen-antibody event and the magnitude of compensatory mechanisms. Laboratory findings can include hemoglobinemia and/or hemoglobinuria, followed by elevation of serum bilirubin. Treatment includes measures to maintain or correct the blood pressure; correct the coagulopathy, if present; and promote and maintain urine flow. Signs and symptoms of acute hemolytic reactions may be immediate and include:

- Chills, fever [temperature may be 40.5 C (105 F) or higher]
- Headache
- Burning sensation along the vein
- Abnormal bleeding
- Low back pain
- Facial flushing
- Chest pain; rapid, labored respirations
- Shock

These complications can be avoided by using the post-thaw wash procedure if your facility has technical resources for this preparation step.

Febrile, Nonhemolytic Reactions are typically manifested by a temperature elevation of at least 1 degC (2 F) occurring during, shortly after, or up to 2 hours following product administration and in the absence of any other pyretic stimulus. This may reflect the action of antibodies against white cells or the action of cytokines, either present in the infused product or generated by the recipient after product administration. Febrile reactions may accompany product administration and they occur more frequently in patients previously alloimmunized by transfusion or pregnancy. No routinely available tests are helpful in predicting or preventing these reactions. Antipyretics usually provide effective symptomatic relief.

Signs and symptoms of febrile, nonhemolytic reactions include:

- Temperature elevation of 1 C (2 F) or more
- Chills

Allergic Reactions usually occur as urticaria, but may also include wheezing or angioedema. These reactions are thought to be related to the presence of atopic substances capable of interacting with antibodies present in the donor or recipient plasma. In rare cases, anaphylaxis may occur Allergic reactions to destrano or DMSO used in cellular therapy product processing or cryopreservation may occur in sensitized patients (9,10,11,12,13,19). No laboratory procedures are available to predict or prevent these reactions, which usually respond to antihistamines or, in severe cases, corticosteroids or epinephrine.
Signs and symptoms of allergic reactions include:
• Urticaria (hives), pruritus (itching)
• Facial or glottal edema (rare)

Anaphylactoid or Anaphylactic Reactions are characterized by autonomic dysregulation, severe dyspnea, pulmonary and/or laryngeal edema, and bronchospasm and/or laryngospasm. They are rare but dangerous and potentially life-threatening complications of HPC,CB administration. Many of these reactions have been reported in IgA-deficient patients who have IgA-specific antibodies of the IgG and/ or IgE class. Such patients may develop symptoms after administration of very small amounts of IgA-containing plasma in any cellular therapy product. Anaphylactoid and anaphylactic reactions to destrano or DMSO used in cellular therapy product processing or cryopreservation may occur in sensitized or atopic patients. Patients tend to respond to fluids, corticosteroids, and epinephrine, and may require cardiorespiratory support.
Signs and symptoms of anaphylactoid reactions include:
• Bronchospasm and/or laryngospasm
• Hypotension
• Severe dyspnea
• Pulmonary and/or laryngeal edema
Other symptoms such as facial burning and flushing, abdominal pain, diaphoresis, diarrhea, and dizziness.

Transfusion-Related Acute Lung Injury (TRALI) occurs when an acutely increased permeability of the pulmonary microcirculation allows the massive leakage of fluids and protein into the alveolar spaces and interstitium. In many cases, the occurrence of TRALI is associated with the presence of leukocyte antibodies in the donor or recipient. Treatment consists of aggressive respiratory support.
In the absence of evidence for preexisting lung injury, cardiac failure, or transfusion-associated circulatory overload (TACO)*, signs and symptoms of TRALI include:
• Acute respiratory distress within 6 hours of administration
• Hypoxemia (oxygen saturation <90% on room air)
• Bilateral pulmonary infiltrates on frontal chest x-ray

Immunologic Complications, Delayed
Delayed Hemolytic Reactions may occur in two different allogeneic settings. Clinically significant antibodies to red cell antigens in previously alloimmunized patients are usually detected by preadministration testing. Antigens on infused red cells can stimulate anamnestic production of antibody from residual recipient B cells. The antibody levels may reach a significant circulating level while the infused cells are still present in the circulation. The activity of the native recipient B cells will decrease as they are replaced with the donor's immune system. The usual timeframe for reappearance of antibody is 2 to 14 days after product administration. The relatively small volume of red cells infused with HPC,CB products will typically limit this type of delayed hemolytic reaction. The potentially more serious delayed hemolytic reaction may occur in recipients who receive antibodies that are incompatible with ABO or other red cell antigens on the remaining recipient red cells. The relative small volume of plasma in the HPC,CB units will usually limit this immediate reaction. In this setting, the infused donor's B lymphocytes may produce antibodies to red cell antigen, thus destroying the recipient's own remaining red cells in the 1 to 3 weeks after HPC product administration. This reaction may be sudden, severe, and life-threatening, so at-risk recipients should be monitored for this occurrence. Treatment usually includes Group O or affected

antigen-negative red cell transfusion beginning at the time of transplantation as needed to support the patient and to begin replacement of at-risk red cells. More rapid antigen-negative red cell replacement, fluid administration, and perhaps red cell exchange may be required in more severe cases.
Signs and symptoms of delayed hemolytic reactions may include:
• Unexplained low-grade fever
• Unexplained decrease in hemoglobin/hematocrit
• Mild jaundice
• Development of a positive direct antiglobulin test (DAT)
• Elevation of lactate dehydrogenase (LDH) or bilirubin
• Hemoglobinemia and hemoglobinuria (rare)
• Symptoms of acute intravascular hemolysis (rare)

Alloimmunization to Antigens of white cells, platelets, or plasma proteins may occur unpredictably after product administration. Primary immunization does not become apparent until days or weeks after the immunizing event and does not usually cause symptoms or physiologic changes. If cellular therapy products that express the relevant antigens are subsequently administered, there may be accelerated removal of cellular elements from the circulation and/or systemic symptoms.
Alloimmunization to antigens of white cells, platelets, or plasma proteins can be detected only by specialized testing.

Graft-vs-Host Disease is an extremely serious condition that occurs frequently in recipients of allogeneic cellular therapy products.16 GVHD occurs when viable T lymphocytes in the infused product engraft in the recipient and react against tissue antigens in the recipient. GVHD can follow administration of any product that contains even small numbers of viable T lymphocytes. Severely immunocompromised recipients receiving allogeneic cellular therapy products are at greatest risk. The incidence of acute GVHD after CB transplantation is comparable to that observed with conventional donor sources, but the incidence of chronic GVHD appears to be less.

Nonimmunologic Complications

DMSO Toxicity is the most common complication of HPC,Cord Blood product administration and is caused by DMSO in thawed products that were cryopreserved with it. Symptoms result from histamine release and include flushing, rash, chest tightness, nausea and vomiting, and cardiovascular instability. Slowing the administration rate or removal of DMSO from the product by washing the cells before administration may reduce the risk of these symptoms. Premedication with antihistamines is usually effective in preventing or reducing the response. A garlic-like odor on the breath of cellular therapy product recipients may persist for 24 to 48 hours after product administration.
Signs and symptoms of DMSO toxicity include:
• Cough
• Flushing
• Rash
• Chest tightness and wheezing
• Nausea and vomiting
• Bradycardia and tachycardia
• Hypertension

Bacterial Contamination of HPC,Cord Blood products may occur, but rarely causes acute, severe, or life-threatening effects. However, the onset of high fever (>2 C or >3.5 F rise in temperature), severe chills, hypotension, or circulatory collapse during or immediately after product administration should suggest the possibility of bacterial contamination and/or the presence of endotoxin in the product. Prompt recognition of a possible septic reaction is essential. Measures should be taken to maintain adequate blood pressure, followed by evaluation of blood cultures and aggressive therapy with broad-spectrum antimicrobials. The remaining product in the container should be evaluated promptly by Gram's staining and microbial cultures.

Signs and symptoms of bacterial contamination reactions include:
• Fever with chills
• Severe hypotension
• Dry, flushed skin
• Pain in abdomen and extremities
• Vomiting
• Bloody diarrhea

Transmission of Infectious Disease may occur because HPC,Cord Blood products are collected from human blood. Disease may be caused by known agents, such as viruses, or unknown agents. All HPC, CB product donors are subjected to stringent screening procedures intended to reduce to a minimum the risk of infectious agent transmission, then the likelihood of transmitting such infections is rare, but we cannot totally eliminate this risk. Donor selection criteria are designed to screen out donors with human immunodeficiency virus (HIV), human T-cell lymphotropic virus (HTLV), hepatitis B virus (HBV), hepatitis C virus (HCV), Cytomegalovirus (CMV) and syphilis, as well as other emerging agents; additional tests are performed according to Italian Laws in case of pandemia and/or increased local risks or on demand of the Transplant Center.

Transmission of Rare Disease may occur. Because the newborn donor has scant medical history, the opportunity to identify serious diseases or genetic disorders of the donor. Six/twelve months after delivery PECBB performs a donor follow and a pediatric certificate is required stating donor health state. Furthermore, before to distribute the CBU the PeCBB performs an update of the donor and familial health state, but this information may not always available.

Malignancies of Donor Origin can appear after CB transplantation. Patients may develop post-transplant lymphoproliferative disorder (PTLD) manifested as a lymphoma-like disease favoring non nodal sites. PTLD is usually fatal if not treated. The incidence of PTLD appears to be higher in patients who have received antithymocyte globulin. The etiology is thought to be donor lymphoid cells transformed by Epstein-Barr virus (EBV). Serial monitoring of blood for EBV DNA may be warranted in high-risk groups.
Leukemia of donor origin also has been reported in HPC, Cord Blood recipients. The natural history is presumed to be the same as that for de novo leukemia [(20-22)], but some interesting trends have emerged. AML predominates as the most common type of UCBT DCL, there is also a tendency for a shorter interval between CBT and the occurrence of DCL and for a higher proportion of abnormal karyotypes involving chromosome 7 (particularly monosomy 7) was observed. These differences may be caused by the properties of the transplanted cells. Further, long-term follow-up of SCT recipients will be necessary, as CBT has a shorter history than BMT [(23-25)].

Transfusion-Associated Circulatory Overload (TACO) leading to pulmonary edema can occur after infusion of excessive volumes or at excessively rapid rates. Pulmonary edema should be promptly and aggressively treated. In patients at risk, the infusion of colloid preparations should be reduced to a minimum.

Hypothermia can be caused by rapid infusion of large volumes of cold products. Hypothermia carries a risk of cardiac arrhythmia or cardiac arrest.

Nonimmunologic Hemolysis can result from lysis of red cells in the HPC,CB which may occur at any time during processing, cryopreservation, thawing, and administration. This lysis may be caused by a number of factors. Some examples are osmotic stress, mechanical injury, shear stress, co-administration with incompatible fluids, and intrinsic red cell abnormalities such as hemoglobinopathies or enzyme deficiencies.

Graft Failure
Failure to engraft or secondary graft failure can occur (14). Primary graft failure of a cord blood unit is failure of the recipient to achieve a >500 absolute neutrophil count by day 60. It appears that

both white cell and platelet engraftment are slower compared to other sources of stem cells. Graft failure is of special concern in larger patients. Additional stem cells will not be available from the same donor to treat graft failure (14). Immunologic rejection is the primary cause of graft failure. Consider testing for HLA antibodies in order to identify patients who are alloimmunized prior to transplantation and to assist with choosing a unit with a suitable HLA type for the individual patient.Primary graft failure must be reported to the HPC,CB unit supplier.

Relapse

Relapse of the underlying disease may occur, especially in patients with advanced disease at the time of transplant. Because of the naive nature of the cord blood cells, relapse may be an increased problem in this kind of transplant. Additional stem cells will not be available from the same donor to treat graft failure (15).

11 Literature

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