INFUSION OF HEMATOPOIETIC STEM CELLS

MEGAN STIMPSON, DNP, PCNS, RN, CPHON

STOREAGE

- Fresh cells are generally given within 24-48 hours of harvesting
  - If delayed, cells can be stored at room temp for a few hours or 4 degrees Celcius overnight
  - Discuss with Attending first
- Cryopreserved cells (Cord blood or PBSC) can be stored in DMSO for years, but are usually given within 1-4 months

***HPCs are NEVER irradiated***

TYPES OF HEMATOPOIETIC CELLS

- Peripheral Blood Stem Cells (PBSC)
  - Fresh or cryopreserved
- Cord Blood
  - Always cryopreserved
- Bone Marrow
  - Usually fresh

THINGS TO CONSIDER

- Institutional policy
- Fresh Vs Frozen
  - Pre-hydration, pre-meds, infusion length, start time
- Tubing
  - Filtered vs. non filtered, Pumped vs. gravity
- Venous Access
  - CVC preferred, required for Cryopreserved
- ABO Compatibility and Processing
  - Major vs Minor:
    - Major = antibodies to donor (ex: donor is A, recipient is O)
    - Minor = donor has antibodies to recipient (ex: Donor is O, recipient is A)
  - Red cell depletion:
    - Happens with moderate titers in Major incompatibility/Bidirectional mismatch
  - Plasma depletion:
    - Happens with high titers in Minor incompatibility/Bidirectional mismatch
  - Plasma exchange:
    - Happens when high titers in Major incompatibility (rather than in addition to red cell depleting product) The number of days of PE is based on the patient’s antibody titers

CONSIDERATIONS CONT...

- Signed consent?
- Do you have an order to infuse?
- Has it been 36 hours since the completion of chemotherapy?
- Has the patient received 24 hours (or 3 doses) of Tacrolimus or Cyclosporine doses for a non-autologous transplant?
- Teaching and Support
**Consider the Medication Schedule: Concomitant Infusions**
- No medications or fluids piggybacked
- Meds, TPN can be given through other lumen
  - *Keep fluid max in mind*
- Amphotericin, antibodies, investigational medications or blood products should not be given concomitantly
  - High risk of anaphylaxis or reaction
- HPCs cannot be infused during plasmapheresis or hemodialysis

**Day “0”**
- The day cell infusion is complete
  - There can be 2 days
- It acts as a reference point for the pre/post transplant timeline
  - Eg.: when to give day +1 MTX, immunosuppressive agents, and pre-transplant chemotherapy
- Day 0 can be inpatient or outpatient
  - Depends on cell type, conditioning regimen, supportive care needed, patient clinical status, reimbursement.

**Product Tracking Invoice**
- Stays with the cells at all times
- Documents chain of custody
- Donor information
- Recipient information
- ABO information
- Documents start and end infusion times

**Audience Response**
- Which type of HPCs are typically used in autologous transplants?
  - A: Cord Blood cells
  - B: Peripheral blood stem cells
  - C: Bone marrow
  - D: All of the above
- TRUE or FALSE? The nurse can run IV fluids through the same lumen as the HPC infusion

**Cryopreserved Cells**

**Patient Populations**
- Pediatrics
  - Neuroblastoma
  - Medulloblastoma, astrocytoma
  - Relapsed Ewings, Hodgkins Lymphoma
- Adults
  - NHL, HL, MM, MS

Cryopreserved products are autologous or cord blood transplants
**Cord Blood**

- **What it is:**
  - Donated umbilical cord and placenta blood collected after a baby is born and the cord is cut
  - Cryopreserved and saved for a matched patient
- **Why are we doing this:**
  - Alternate to bone marrow or PBSCs
  - Very rich in stem cells
  - Lower incidence of GVHD

**Expanded Cord Blood**

- **What it is:**
  - Pt receives 2 (3 for adults) UCB (Umbilical Cord Blood) infusions
  - 1st (2nd): Standard UCB
  - 2nd (3rd): Expanded/Manipulated UCB given 4 hrs post 1st infusion
- **Why are we doing this:**
  - Decrease pt infection risk - by decreasing the wait time until engraftment
- **How:**
  - When the UCB cells are expanded, they have a higher number of bone marrow progenitor cells, which engraft more quickly
  - Expanded cells are T cell depleted - thus die more quickly

**DMSO**

- DiMethylSulfOxide
  - Preservative for stored cells
  - Can cause histamine release and allergic reactions: pre-medicate regardless of h/o transfusion reaction.
  - Due to dose related toxicity: total cell volume not to exceed 10mL/kg/day
  - Sometimes resulting in multiple infusion days.
  - *Cells are DMSO preserved and then frozen

**ACD**

- Acid Citrate Dextrose (ACD)
  - Anti-coagulant added to cells to prevent clumping during apheresis and storage
  - Binds ionized calcium -> patient can have acute drops in calcium levels
    - Hypocalcemia: tingling, numbness, restlessness, nausea
    - IV Calcium or Tums
    - Stop/slow the infusion to allow time to recover.
    - May need to monitor baseline calcium if multiple bags expected

**Patient Prep for Infusion**

- Baseline Assessment
  - Including AM weight and abdominal girth
- Hydration
  - Pre: 2-3 hours
  - Post: 4-5 hours
- Pre-medications
  - Benadryl, Tylenol, Hydrocortisone
  - Consider anti-emetics
- Emergency medications available and oxygen ready
- Orange wedges/hard candy/lollipops

**Cryopreserved HPC Infusion Sequence**

1. Review Policy and Procedure
2. Review Patient Roadmap for correct date of infusion and determination of cell type
3. Ensure patient has signed Hematopoietic Progenitor Cell Infusion Consent and orders for Infusion
4. Infusion start time is discussed with Cellular Therapy Lab and RN
5. Let the MD/Charge RN/RN buddy know when you are starting an infusion
6. RN pre-medicates the patient 30 minutes prior
7. Obtain correct tubing for infusion and validate correct venous access
8. RN and Cellular therapy tech check patient ID and product ID on Product Tracking Invoice
9. Receipt of transfer is signed by RN and technician
**Cryopreserved HPC Sequence (cont.)**

10. CTL tech thaws initial bag of HPC (for cords, it may come already thawed)
11. Infuse HPC by gravity
   - Filter blood set with 150-260 micron filter
   - Infuse 3-5 mL/min for 10-20 mL (~ 4-5 min)
   - If tolerated, open clamp fully “wide open”
   - Bags are approx. 50 mL (takes approximately 20 minutes)
   - Flush CV with saline at completion of last bag and after tubing has been drained completely
12. Each bag is spiked and infused by the RN after thawing by CTL tech
   - Bags with the highest CD34+ will be infused 1st
   - Read label – marked with “infuse 1st”
13. Vital signs:
   - Temp, HR, P and BP at beginning of first bag
   - Q 30 minutes x 4 hours after completion of last bag
14. After infusion is completed hydration and side effect monitoring continue (4-24+hours)

**Trouble Shooting**

- Cells may run too slowly or stop dripping
  - Attach tubing “hub to hub”
  - Elevate pole
  - Un-spike the bag (open to air to eliminate vacuum effect)
  - Technician may use “stripper”
  - Flush lumen with NS
  - Use 3-way stopcock and 20cc syringe to draw cells from the tubing and inject into patient

**Monitoring**

- Side effects
- Teaching and support
- Cryopreserved monitoring: 4 hours after completion of HPC
- Cord Blood monitoring: 24 hours after completion of last bag
- Mandated documentation of how infusion is tolerated

**Side Effects:**

- **Nausea and Vomiting**
  - Why:
    - Can be caused by DMSO or granulocytes
    - May be immediate and can occur suddenly
  - What can you do:
    - Have PRN anti-emetics already ordered
    - Remember to use a separate lumen for all meds
    - Temporarily slow rate

- **Cough or Dry Tickle in Throat**
  - Why:
    - Caused by DMSO
  - What can help:
    - Slow infusion
    - Deep breathing
    - Sucking on oranges/candy/lollipop
    - Sipping on water or juice

- **Hypotension, Hypertension, Bradycardia**
  - Why:
    - Usually a response to histamine release
  - What should be done:
    - Stop Infusion
    - Check O2 sat, give oxygen if needed
    - Notify MD
    - Increase hydration/fluid bolus
  - Nursing Assessment:
    - CV changes may occur up to 6 hours post infusion
SIDE EFFECTS: RENAL DYSFUNCTION

- **Why:**
  - DMSO preserves stem cells well, but not red cells
  - As the product thaws → red cell death/hemolysis → build of DNA "slime"
    - "Slime" can clog kidneys
- **Prevention:**
  - Pre and Post hydration
- **Nursing Assessment**
  - Ensure adequate UOP
    - 2-3mL/kg/hour
  - Record Q2 hr I/O
  - Follow renal function for next few days
- **Educate:**
  - Regarding pink/red urine

SIDE EFFECTS: ALLERGIC / HYPERSENSITIVITY REACTIONS

- **Why:**
  - Related to the volume of DMSO
  - Can occur despite premeds
  - Can be immediate or delayed
  - May have increased potential in Cord Blood as also preserved with Dextran
- **What to do:**
  - Stop infusion and notify MD
  - Administer anaphylaxis meds as needed
  - Watch for somnolence due to meds

SIDE EFFECTS: TAKOTSUBO (STUNNED OR BROKEN HEART) CORD BLOOD ONLY

- Mimics acute coronary syndrome – reversible left ventricular apical ballooning
  - Also called "stress cardiomyopathy"
- Transient and usually precipitated by acute stress
- Treatment would involve usual treatment for cardiomyopathy

PATIENT AND FAMILY EDUCATION

- DMSO is excreted through all body orifices and fluids
- Garlic-like odor may last up to 36 hours
- Urine may be dark red or even black due to hemolyzed red cells

AUDIENCE RESPONSE

- DMSO can cause which of the following side effects:
  - A: an unpleasant odor
  - B: an allergic reaction
  - C: renal damage
  - D: all of the above

FRESH HEMATOPOETIC CELLS
PROCESSING
- As fresh HPC are allogeneic, processing may be required for ABO incompatible transplants
- Know your donor and recipient blood types
- Be aware of any planned or possible processing

VOLUME
- Usual total = 10-15ml/kg (URD marrow may be up to 2 liters)
- For pediatric patients, notify MD if marrow volume exceeds 15ml/kg
- Inspect bag prior to spiking for clumps or visible fat droplets: return to lab

TIMING AND PREPARATION
- Less control over time of infusion
- No pre-hydration necessary
- Tubing
  - Fresh: Always pumped
  - Non-filtered (standard tubing): whole HPC marrow, plasma reduced HPC marrow
  - Filtered: PBSC, RBC Reduced Bone Marrow, donor lymphocytes, CD34 or T cell depleted marrow, fresh NK cells

PATIENT PREP FOR INFUSION
- Baseline Assessment
  - Including AM weight and abdominal girth
- Premedication
  - None, unless history of blood reactions
  - If required, then follow platelet transfusion guidelines

FRESH HPC
INFUSION SEQUENCE
1. Review Policy and Procedure
2. Review Patient Roadmap for correct date of infusion and determination of HPC type
3. Ensure patient has signed Hematopoietic Progenitor Cell Infusion Consent and orders for Infusion
4. Let the MD/Charge RN/RN buddy know when you are starting an infusion
5. RN pre-medicates the patient only if history of reaction to blood products
6. Obtain correct tubing for infusion and validate correct venous access
7. RN and Cellular therapy tech check patient ID and product ID on Product Tracking Invoice
8. Receipt of transfer is signed by RN and technician
10. Infuse HPC by pump
   - Infuse via orders (see next slide)
   - Flush CVC with saline at completion of last bag and after tubing has been drained completely
11. Each bag is spiked and infused by the RN
   - Infuse bags with highest CD34+ first, they will be labeled “infuse first”
12. Vital signs:
    - Vital signs at beginning
    - 15 minutes after start
    - Then hourly until complete
13. Document rate increases with vitals and patient tolerance
14. After infusion is completed hydration and side effect monitoring continue.
**Infusion of Marrow and PBSCs**
- Adults (PBSCs Only):
  - begin at ½ maintenance for 15 minutes, then increase to 2x maintenance
- >20kg/Adults:
  - begin at ½ maintenance for 15 minutes, then increase to 1.5x maintenance
- <20kg:
  - begin at 1ml/kg/hr for 30 minutes, then increase to by 25% of fluid maximum q15 until max; 1.5x maintenance
- Marrow infusion often take 4-8 hours

**Reactions: Volume Overload**
- Signs and Symptoms:
  - **Respiratory**: Dyspnea or tachypnea, rales, chest tightness, dry cough
  - Cyanosis
  - Decreased O<sub>2</sub> Saturation
  - **CVS**: Hypertension, JVD
  - **Neuro**: Restlessness
  - major indicator with pediatrics
- What can be done:
  - Product reduction may be required if > 20ml/kg adult weight; 15 ml/kg pediatric weight
  - Administer lasix

**Reactions: Hemolytic Transfusion**
- Why:
  - May be secondary to ABO incompatible transplants
- Signs and Symptoms:
  - Sudden onset nausea or vomiting
  - “Sense of doom”/Anxiety
  - Fever ≥ 1° or chills
  - Severe lower back or flank pain
  - Anuria
- Prevention:
  - Red cell depletion or plasma exchange can prevent reactions

**Reactions: Febrile**
- Why:
  - May be related to history of transfusion reactions
- Signs and Symptoms:
  - Fever ≥ 1°
  - Chills or rigors
  - Headache
  - Flank pain
- Tx:
  - Tylenol and Benadryl

**Reactions: Allergic**
- Signs and Symptoms:
  - Fever
  - Chills
  - Hives
  - Wheezing, bronchospasm
  - Flushing
  - Emesis
- What to do:
  - Treatment same as with platelets
  - Anaphylaxis meds if needed

***The product MUST BE GIVEN***

**Reactions: Pulmonary Micro-embolism**
- Why:
  - Caused by fat particles, particularly in marrow
- Signs and Symptoms:
  - Chest pain
  - Cough
- What to do:
  - Slowing rate of infusion and use of O<sub>2</sub> may alleviate mild symptoms
- Prevention:
  - Excessive fat can be removed by Cellular Therapy
REACTIONS: EXCESSIVE ANTICOAGULATION

- Why:
  - HPCs are anti-coagulated with heparin and or acid citrate dextrose
- Result:
  - Rapid or large volumes can cause transient anticoagulation of patient
- Nursing Assessment:
  - Monitor for bleeding

IMMEDIATE ACTIONS:

- Stop the infusion
- Re-check the product
- Notify MD immediately
- Have anaphylaxis medications available
- Refer to FHCRC standard of practice or institutional guidelines

AUDIENCE RESPONSE

- Is the volume of a fresh bone marrow infusion typically larger than a cord blood infusion?
  - A: YES
  - B: NO
- Which of the following side effects is not typically seen in fresh bone marrow infusions?
  - A: Volume Overload
  - B: Coughing
  - C: Unpleasant Odor
  - D: Fever

DOCUMENTATION

- Clearly document
  - Pre/post assessment
  - Vital signs
  - Weight
  - Start and stop times
  - Reactions/adverse effects
  - Any actions taken/medications given
  - Total volume

WHERE TO DOCUMENT

SCA: HPC band in the transfusion section of I & O

SCCA/UWMC:

MONITORING POST INFUSION

- Cord Blood Units – Green Monitoring Form
  - Monitor for 24 hours post infusion for adverse events
- Cryopreserved Units – Yellow Monitoring Form
  - Monitor for 4 hours post infusion
- Fresh Units – yellow Monitoring Form
  - Monitor for 2 hours post infusion
- Fax Monitoring Form to CTL as soon as completed and no later than 24 hours post infusion
- File form in Unit specific location – do not place in patient chart or dispose
**CTL Documentation**

- **HPC Infusion Monitoring Form**
  - Sections 1 (Completed by lab and cellular therapy personnel)
  - Sections 2, 3 & 4
    - Completed by nursing personnel on ALL patients
    - Includes start/stop dates and times - needs to match chart documentation
    - Total volume infused
    - Number of bags used
  - Check box for absence or presence of adverse reactions, what you did about them and the response to interventions
  - Form MUST be completed and **faxed** to CTL at end of infusion and monitoring time

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**Cord Blood Units**

**WHAT HAPPENS WHEN INFUSION IS COMPLETE?**

- Product bags must be saved
  - Cryopreserved product
    - Cellular therapy personnel will take after infusion complete
  - Fresh cells
    - If adverse event/reaction occurs:
      - Complete section 2B of HPC infusion monitoring form and return bags in zip-lock bag provided with form
      - If no adverse event/reaction noted:
        - Keep empty bags for 2 hours, then discard.

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**Fresh/Cryopreserved Units**

**TAKE-HOME POINTS**

- **Cryopreserved Products**:
  - Can be either cord blood or PBSCs
  - Need to be careful with DMSO side effects
- **Fresh Products**:
  - Mainly bone marrow or PBSCs – always allogenic
  - Watch for fluid overload
  - Use a buddy to prep for infusion
  - Utilize your resources (policy, standard practice, algorithm, etc.)
- Documentation is **VERY** important
- The product must always be given!

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**ANY QUESTIONS?**

Thank you!

megan.stimpson@seattlechildrens.org