

The Innovative Patient-Centered Case Study Model: CBV Protocol for Autologous Hematopoietic Stem Cell Transplant

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Learning Objectives

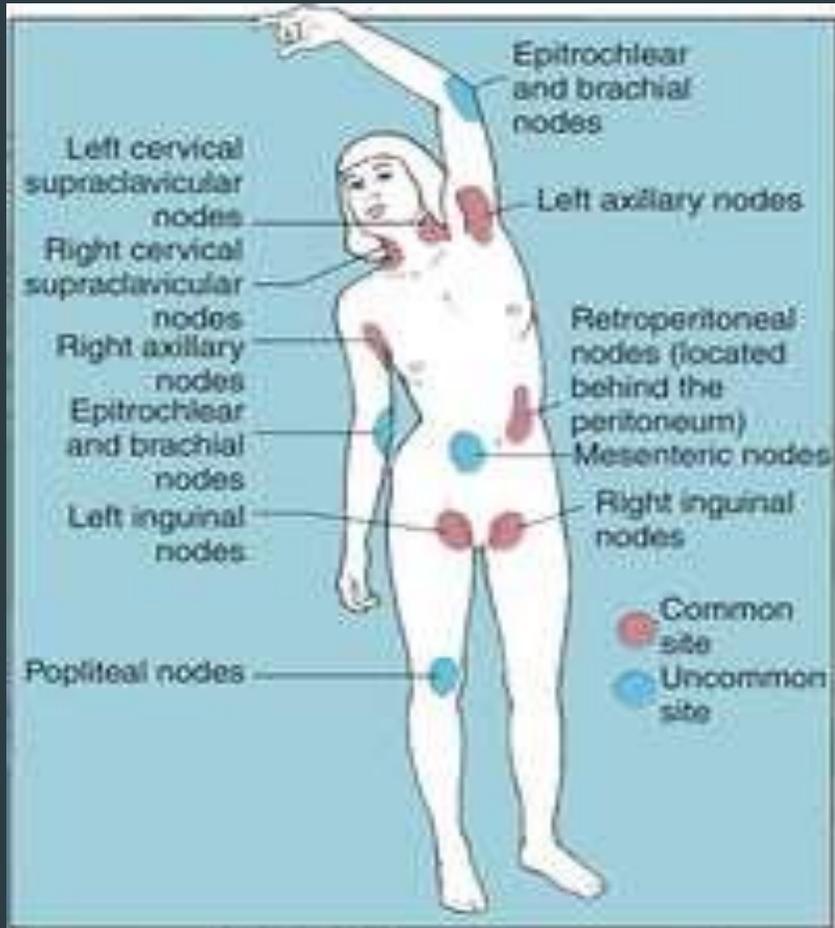
At the conclusion of this presentation, learners will be able to:

- ▶ Describe the process of autologous hematopoietic stem cell transplant
- ▶ Explain the most common side effects of and nursing management for each drug used in the transplant protocol
- ▶ Identify the most common complications experienced by patients undergoing autologous hematopoietic stem cell transplant
- ▶ Outline the requirements for discharge from an inpatient facility following autologous hematopoietic stem cell transplant and describe follow-up care
- ▶ Gain a new insight from a patients perspective on this particular protocol for autologous hematopoietic stem cell transplant

Introduction

- ▶ Hope is a 19 year-old female who presents to her primary care provider after four weeks of coughing and adenopathy in her neck and axilla
- ▶ A complete blood count (CBC) is obtained and Hope is sent home with antibiotics
- ▶ After a few days, the primary care provider calls Hope and tells her the results of her CBC are “off”
 - ▶ WBC = 28
 - ▶ Hgb = 11.6
 - ▶ Plt count = 573

Hodgkin Disease



- ▶ Type of lymphoma
- ▶ Originates in specialized WBCs called lymphocytes
 - ▶ B-lymphocytes
 - ▶ Attack pathogens by producing antibodies
 - ▶ T-lymphocytes
 - ▶ Attack pathogens directly
 - ▶ Boost or slow activity of other immune cells
- ▶ **Almost all cases of Hodgkin disease arise in B-lymphocytes!!**
- ▶ Can develop almost anywhere, but most often arises from lymph nodes in the upper part of the body [neck, chest & axilla]
- ▶ Only invades bloodstream & spreads to other parts of body in later stages

Diagnosis and Initial Treatment



- ▶ Diagnosed with stage IVa Hodgkin disease
- ▶ Initial treatment consists of 6 cycles of ABVD [Doxorubicin, Bleomycin, Vinblastine & Dacarbazine]
- ▶ After 2 cycles however, a PET scan reveals reactive disease, so Rituximab is added for the remaining cycles
- ▶ 2 months after the last cycle of ABVD, a follow-up PET scan shows relapsed disease
- ▶ Hope now has refractory Hodgkin disease
 - ▶ She agrees to undergo 5 cycles of ICE [Ifosfomide, Carboplatin & Etoposide] followed by autologous hematopoietic stem cell transplant (HSCT)

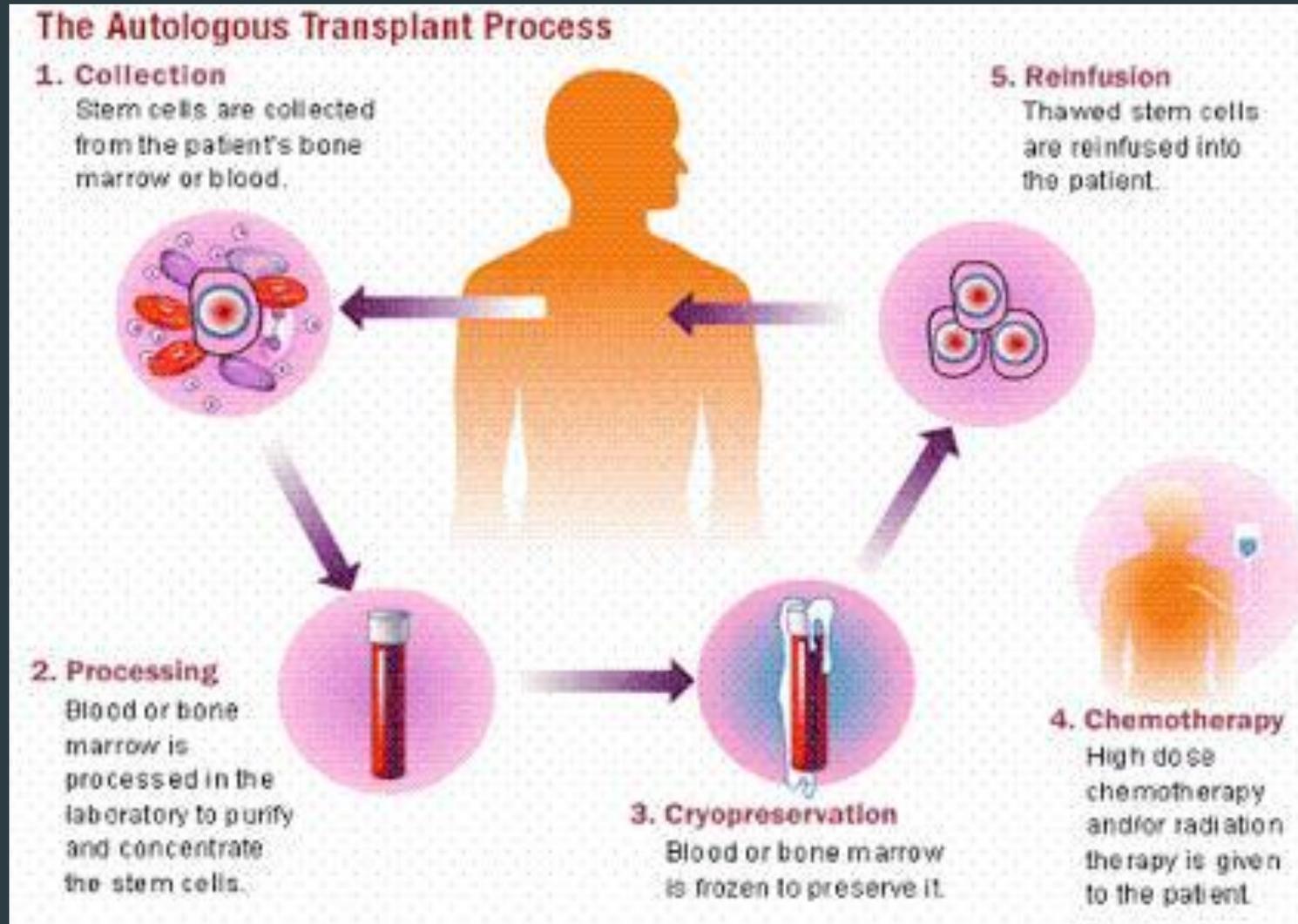
Initial PET Scan



Relapsed/Refractory PET Scan

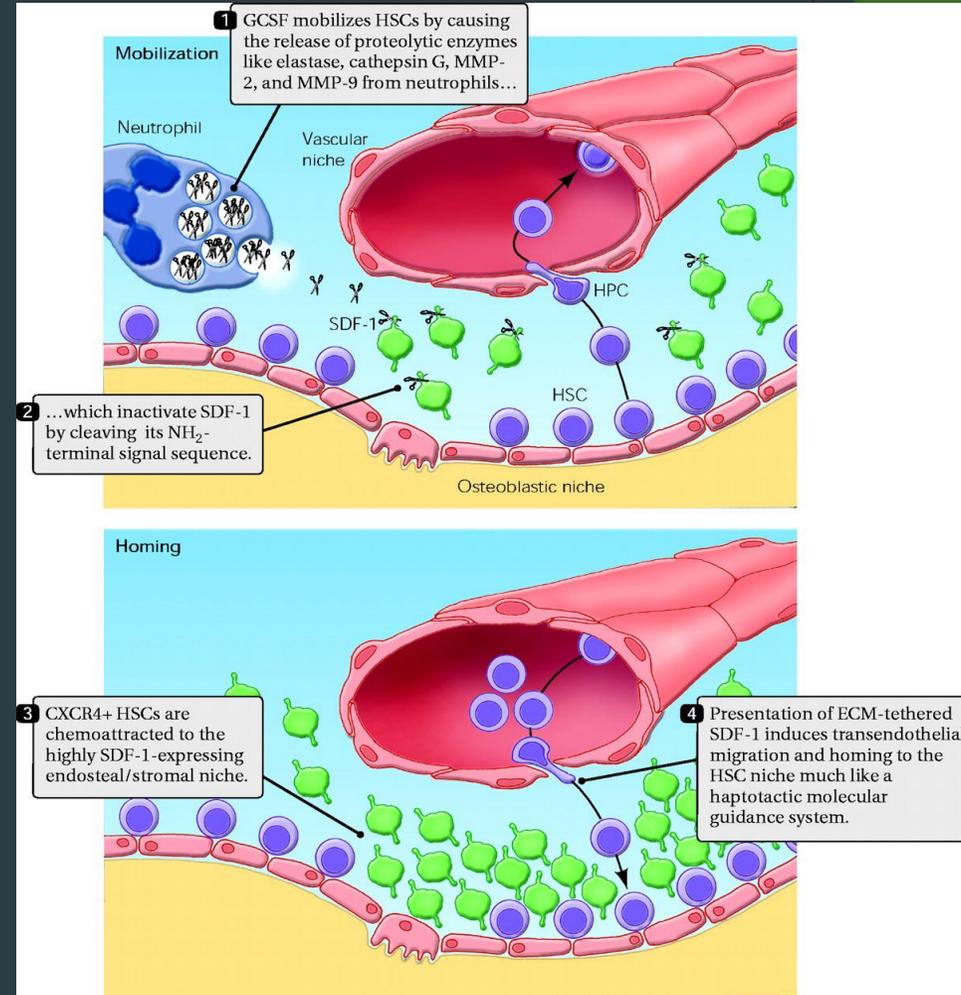


Autologous HSCT

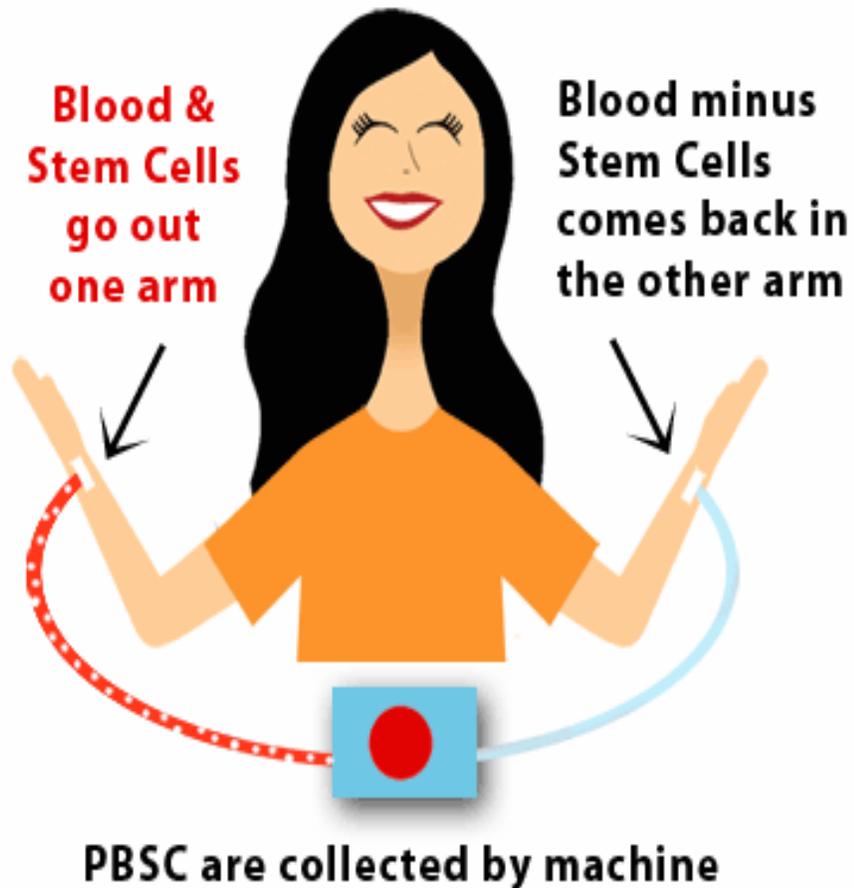


HSC Mobilization

- ▶ 24 hours after completing the 3rd cycle of ICE, G-CSF (Neupogen) “priming” is initiated
- ▶ Neupogen dose = 10mcg/kg/day
 - ▶ The goal is to hyper stimulate the bone marrow so there are too many cells to be contained in the marrow space
 - ▶ Since there is not enough room in the bone marrow for all the cells that are being produced, they travel to the blood stream while still in their immature state
 - ▶ Hematopoietic Stem Cells (HSCs) = CD34+ cells
- ▶ During “priming” blood counts are monitored
- ▶ Goal for mobilization = CD34+ count >3 million cells/kg



HSC Collection



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- ▶ Once the CD34+ count is high enough, HSCs are collected through an apheresis procedure
- ▶ 5 hours is the average time allotted per collection
- ▶ During the procedure, whole peripheral blood is removed, the HSC layer is siphoned off & the remaining blood components are returned
- ▶ Once “harvested,” the HSCs are checked for contaminants & viability
- ▶ Some patients will require more than one collection

HSC Cryopreservation

- ▶ Once collected, HSCs are transferred to a storage bag containing DMSO
 - ▶ DMSO = chemical preservative used to keep HSCs viable during cryopreservation process
- ▶ Cryopreservation involves gradually freezing cell suspension in liquid nitrogen until it reaches temp $< -150^{\circ}\text{C}$
 - ▶ Places HSCs in state of “suspended animation” until ready to be reinfused



Day -6 Admission to HSCU



- ▶ Admission process
 - ▶ Obtain baseline height & weight per policy + vital signs
 - ▶ Transplant educated RN:
 - ▶ Performs initial head-to-toe assessment
 - ▶ Completes 1st check of chemotherapy + transplant orders & releases order set in Beacon
 - ▶ Asks another transplant educated RN to perform 2nd check of chemotherapy + transplant orders
 - ▶ Writes chemotherapy plan on whiteboard & makes sure room has necessary supplies for safe handling of contaminated body fluids
 - ▶ Reviews hospital routines & provides admission packet from Charge RN
 - ▶ Completes admission paperwork

Day -6 Carmustine (BCNU)

Plan of Care Outlined on Hope's Whiteboard for Day -6

Action	Time	Duration
Pre-hydration	1800	NS @ 250ml/hr x 4hrs
Pre- medications for nausea	2100	Ondansetron 16mg PO q12hrs
Carmustine (BCNU) 550mg/m ²	2200	Continuous IV over 3hrs
Post-hydration	0100	NS @ 200ml/hr x 2hrs

- ▶ Mixed in alcohol
- ▶ Side effects include:
 - ▶ Nausea/vomiting
 - ▶ Facial flushing
 - ▶ Headache
 - ▶ Increased emotions
 - ▶ “Hungover” feeling
- ▶ Administered over 3 hours
 - ▶ Given at night so pts can sleep off the effects
- ▶ **CANNOT BE GIVEN IF THE PT HAS TAKEN ACETAMINOPHEN WITHIN THE PAST 72 HRS**

Day -4 Etoposide

Plan of Care Outlined on Hope's Whiteboard for Day -4

Action	Time	Duration
Pre-medications for hypersensitivity prior to the dose; repeated 2 hours after starting Etoposide	1330 & 1600	Diphenhydramine 25mg IV Hydrocortisone 1mg/kg over 30 min
Hydration to start concurrently with Etoposide	1400	NS @ 1000ml/hr x 4hrs
Etoposide 60mg/kg	1400	Continuous IV over 4 hrs
Post-hydration	1800	NS @ 500ml/hr x 30min, NS @ 250ml/hr x 30min, NS @ 125ml/hr x 3hrs

- ▶ Plant alkaloid
 - ▶ Derived from chemical compound (podophyllotoxins) found in May apple plant
- ▶ Side effects include:
 - ▶ Type I hypersensitivity reactions
 - ▶ Can occur during OR shortly after drug administration
 - ▶ Hypotension
 - ▶ Nausea/vomiting
 - ▶ Diarrhea
 - ▶ Mucositis
 - ▶ Peripheral neuropathy
- ▶ Administered concurrently with large volumes of IV fluids over 4 hrs
 - ▶ Give 20mg furosemide IV if pt. exhibits s/s of pulmonary edema

Day -2 Cytoxan

Plan of Care Outlined on Hope's Whiteboard for Day -2

Action	Time	Duration
Pre-medications for nausea	1100	Palonosetron 0.25mg IV Aprepitant 125mg oral
Hydration	1100	NS @ 250ml/hr continue at least 6 hrs after Cytoxan complete or 24 hrs after
Mesna to prevent hemorrhagic cystitis 60mg/kg (use actual weight)	1100	Continuous IV every 12 hrs beginning 1 hr before Cytoxan for two doses
Cyclophosphamide 100mg/kg	1200	Administer over two hrs

- ▶ Alkylating agent
 - ▶ Related to nitrogen mustard
- ▶ Side effects include:
 - ▶ Hemorrhagic cystitis
 - ▶ Delayed nausea/vomiting
 - ▶ Cardiotoxicity
 - ▶ Mucositis
 - ▶ Diarrhea
- ▶ EKG MUST be obtained & signed-off on by MD before proceeding
 - ▶ Drug will be held if EKG is abnormal
- ▶ Mesna and hydration are used to prevent hemorrhagic cystitis
 - ▶ Also, patient must void within 2hrs of receiving drug or else Lasix is given
- ▶ UA at baseline and then every 24hrs for the first 2-3 days after administration

Day -5, -3, and -1 Rest



- ▶ No chemotherapy given
- ▶ Supportive care

Preparing for Stem Cell Administration

- ▶ Stem cells cannot be given until at least 36 hours after the completion of cyclophosphamide
- ▶ RN must call Cellular Therapy the day before stem cells are to be administered to verify the timing of the infusion as well as the total number of stem cells to be given
 - ▶ Administering too many bags/syringes at once can result in adverse reactions. This can be due to:
 - ▶ DMSO toxicity
 - ▶ Lysis of red blood cells
 - ▶ Infusing high numbers of damaged granulocytes
 - ▶ If a high number of bags/syringes are to be re-infused, they will be divided into 2 separate administrations, both given on Day 0, several hours apart, with additional hydration in between

Day 0 Stem Cell Administration

- ▶ Autologous SCT is not a *true* transplant
 - ▶ It is myeloablative chemotherapy followed by stem cell rescue
- ▶ Almost all of the potential complications associated with the procedure are DMSO-related
 - ▶ These complications can include:
 - ▶ Nausea/vomiting
 - ▶ Changes in blood pressure [hypotension or hypertension]
 - ▶ Abdominal cramps
 - ▶ Flushing
 - ▶ Chills
 - ▶ Garlic-like taste and odor
 - ▶ Cough or tickle in the back of the throat
 - ▶ Tight feeling across the chest
 - ▶ Seizures
- ▶ Water bath
 - ▶ Used to thaw frozen stem cells at bedside
- ▶ Pre-medication with Tylenol & Benadryl
 - ▶ Used to prevent DMSO-related complications
- ▶ Pre-hydration and post-hydration
 - ▶ Used to prevent DMSO-related complications
- ▶ Prior to the procedure, a baseline set of vital signs is obtained & recorded
 - ▶ Vital signs are taken every 5 mins during the procedure to assess the patient for DMSO-related complications
- ▶ Once thawed, stem cells are administered through a free-flowing line of 0.9% saline
- ▶ Each syringe is given over 5 mins - no more, no less
 - ▶ DMSO is toxic to thawed stem cells
- ▶ Have the room stocked with emergency equipment - just in case!



Frozen stem cells getting ready for thawing in the warm water bath



Thawed stem cells getting ready to be drawn up in 60ml syringe for infusion





Complications of Autologous HSCT

Common Complications of Autologous HSCT:

Fluid Overload:

- ▶ Risk for Pulmonary edema
 - ▶ BID weights
 - ▶ PRN Lasix

Electrolyte Abnormalities:

- ▶ Assess for s/s of electrolyte disturbances
- ▶ Monitor serum electrolytes daily & replete per Electrolyte Replacement guidelines

Mucosistis:

- ▶ Prevention is key!!
 - ▶ Up to 80% of patients who receive CBV conditioning will develop mucositis
- ▶ Nursing interventions:
 - ▶ Administer Caphasol QID
 - ▶ Administer pain medications prn
 - ▶ Work with MD & Pharmacy to change PO meds to IV when appropriate

Anemia:

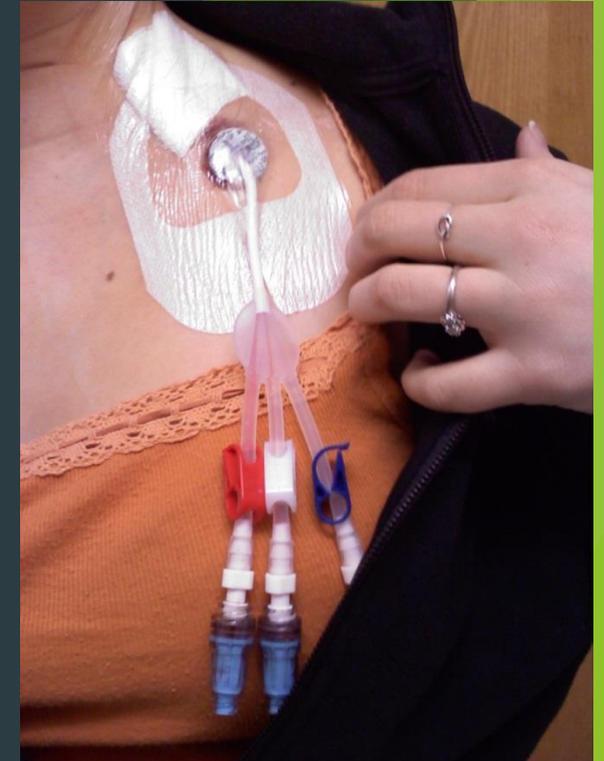
- ▶ Symptoms include:
 - ▶ pallor, fatigue, dyspnea on exertion, tachycardia, tachypnea, decreased oxygen saturation levels, cold extremities, headaches, nausea, and decreased urine output.
- ▶ Live for 90 days

Thrombocytopenia:

- ▶ Bleeding precautions typically initiated when platelet count falls below 50
- ▶ Live for 8-10 days

Infection Prevention and Management During Neutropenia

- ▶ Prophylactic Anti Infectives
 - ▶ An antiviral = Acyclovir
 - ▶ An antifungal = Fluconazole
 - ▶ An antibiotic = Levofloxacin
- ▶ Neutropenic diet- focus on standard safe food handling
- ▶ Monitoring
 - ▶ VS Q4
 - ▶ Thorough nursing and provider staff assessment
 - ▶ Close Central Line monitoring and complacence with CLABSI prevention bundle
- ▶ QUICK ACTION!



Complications of Autologous HSCT - Infertility

- ▶ How chemo affects fertility is dependent on the type of drug being used
 - ▶ Alkylating agents (like cyclophosphamide) carry a high risk of ovarian damage
- ▶ Oocyte cryopreservation now used to preserve fertility after chemotherapy
 - ▶ Not dependent on the menstrual cycle, so only 2-4 weeks are required
 - ▶ Similar rate of live birth compared to embryo cryopreservation
- ▶ Most female transplant recipients receive some form of long-term contraception



Suppression and Management of Menstrual Bleeding During HSCT

Patient population:

1. All female bone marrow transplant (BMT) patients that are:
 - a. Pre-menopausal
 - b. Have no documentation of surgical oophorectomy/hysterectomy
 - c. Actively menstruating

Pre-transplant:

1. Lupron depot (Leuprolide) 11.25mg is administered one month prior to the initiation of high-dose chemotherapy
2. Lupron injections should be given within the 1st few days of the cycle or at day 21
3. If Lupron injection is not initiated prior to admission for transplant:
 - a. Injection is administered on the 1st day of admission
 - b. Document injection in the electronic medical record (this is to notify staff that patient may experience menstrual bleeding while thrombocytopenic)

Additional treatment:

1. If heavy vaginal bleeding develops during the period of thrombocytopenia:
 - a. Increase platelet transfusion parameters (transfuse if platelet count <20K)
2. If the patient develops acute episodes of vaginal bleeding - start Aygestin (Norethindrone)

Initiation of G-CSF and Engraftment

- ▶ Granulocyte Colony Stimulating Factor (G-CSF)
 - ▶ Used to limit the severity & duration of neutropenia
 - ▶ Accelerates the recovery of neutrophils
 - ▶ Reduces infection
 - ▶ Decreases length of stay
 - ▶ Starts on Day +5
 - ▶ Dose = 5mcg/kg SQ daily
 - ▶ Given till ANC >1,500 cells/mm³ on 2 consecutive days OR >5,000 cells/mm³ once post-engraftment
 - ▶ Most common side effects:
 - ▶ Bone pain
 - ▶ Fever
- ▶ Engraftment = bone marrow recovery (period during which bone marrow begins producing white blood cells, red blood cells, and platelets)
 - ▶ Usually occurs 10-14 days AFTER stem cells are given
 - ▶ 1st cell line to engraft = WBCs
 - ▶ Monocytes 1st
 - ▶ Neutrophils 2nd
 - ▶ 2nd cell line to engraft = RBCs
 - ▶ 3rd cell line to engraft = Platelets

Discharge Teaching and Criteria

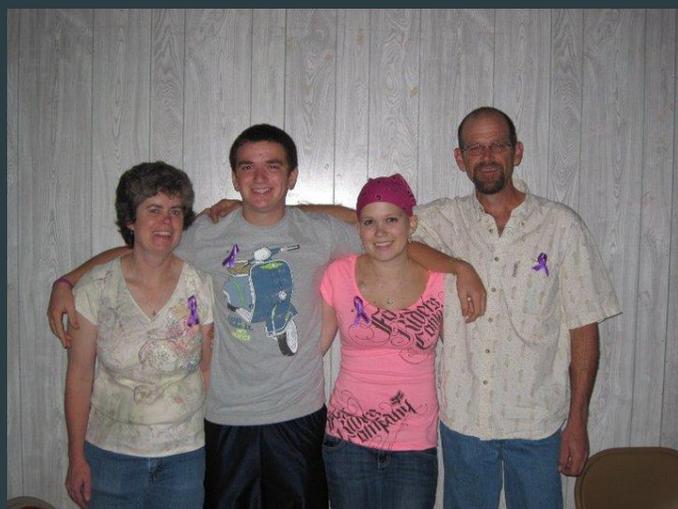
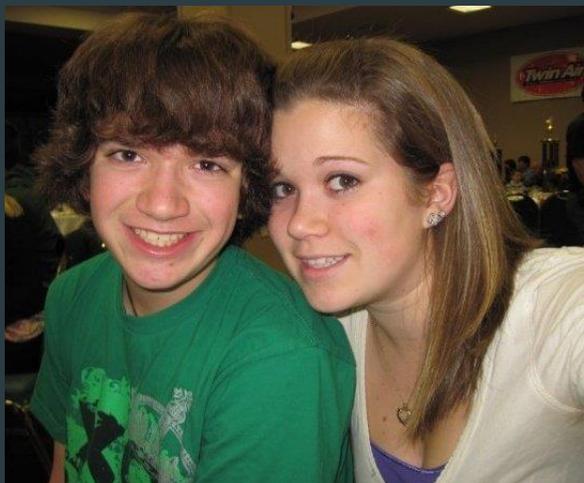
- ▶ Discharge teaching begins before admission!!
 - ▶ Pts receive packet of discharge info from BMT coordinators during pre-transplant work-up
 - ▶ Reinforce discharge teaching starting on Day +2
 - ▶ See Discharge Packet for full discharge instructions
- ▶ Discharge criteria:
 - ▶ ANC >500
 - ▶ Afebrile for 24hrs off prophylactic antibiotics
 - ▶ Able to take PO medications
 - ▶ Eating
 - ▶ Drinking 2-3L per day
 - ▶ Understands need for ongoing follow-up & has dedicated caregiver



Post-Transplant Care and Follow-Up

- ▶ Full immune reconstitution following autologous SCT doesn't usually occur until 12-18 months post-transplant
 - ▶ This means pts are at increased risk of infection for a prolonged period of time
- ▶ Other complications following autologous SCT include:
 - ▶ Relapsed disease
 - ▶ Regimen-related toxicity
 - ▶ Bone disease
 - ▶ Fertility issues
 - ▶ Development of secondary malignancies
- ▶ Post-transplant pts are usually seen in the outpatient clinic within 2-5 days of discharge, then weekly/monthly thereafter as needed
 - ▶ Formal post-transplant evaluations occur:
 - ▶ Day +100
 - ▶ Day +180
 - ▶ Day +365
 - ▶ Then annually
- ▶ Labs, complete H&P, & other diagnostic tests are obtained at each outpatient appointment to monitor for:
 - ▶ Engraftment
 - ▶ Infection
 - ▶ Treatment-related toxicities
 - ▶ Disease status
 - ▶ Overall clinical condition
- ▶ Myeloablative nature of conditioning regimen means pts must be re-vaccinated

Patient Perspective: Life after Transplant



Patient Reflective Thoughts:

- ▶ “There’s no archetypal response to cancer. Patients have different responses. This woman’s or this man’s struggle - this child’s struggle - is his or her own. As family members, as loved ones, as physicians we might be able to witness it **but it’s not ours.**” -Siddhartha Mukherjee, MD, PhD (author of *The Emperor of All Maladies*)
The 2nd Episode Of Ken Burns Documentary: 'Emperor Of All Maladies

The End: Comments and Questions



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