Chemotherapy, BMT, AML Case Study Review

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Objectives

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After completing this module, the student will able to:

- Describe oncology nurses' role in safe administration of chemotherapy.
- Explain measures to prevent and/or manage common toxicities from chemotherapy drugs.
- Recognize oncologic emergencies.
- Explain difference between autologous and allogeneic blood and marrow transplantation.
- Identify common complications of blood and marrow transplantation.

Case Study

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John P.

- 67 year old man with a past medical history of HTN
- Noted some fatigue that had progressed over a few months
- PCP noted anema and down trending WBC & Platelet
- Bone marrow biopsy result consistent with AML
- Normal cardiac function at baseline
- Good performance status

Acute Myeloid Leukemia (very briefly!)

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- A type of leukemia; originates in the bone marrow due to a stem cell defect that results in uncontrolled & rapid production of leukemic cells
  - Leukemic cells do not function normally and block the production of other normal cells
  - Patients are at high risk for infection & bleeding
- “A disease of diversity”
  - Some types are sensitive to chemotherapy; there is a good chance of cure with chemotherapy alone (e.g., acute promyelocytic leukemia [APML])
  - Other types require additional treatment after initial chemotherapy such as stem cell transplantation (e.g., treatment-related AML)
  - Many tests are required (e.g., cytogenetic analysis, molecular studies) to determine the subtype and patient’s prognosis
  - Patient factors (e.g., age) will influence the treatment choice and patient’s prognosis

Case Study (John P.)

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- Considerations for older adults undergoing cancer treatments
  - Physiologic changes with aging and comorbidities may affect the ability to tolerate treatment and recover following treatment.
  - Comprehensive Geriatric Assessment (CGA): a systematic procedure to appraise objective health, including multiple comorbidities and functional status.
  - Chemotherapy toxicity risk: Cancer and Aging Research Group (CARG) Chemo Toxicity Calculator http://www.mycarg.org/Chemo_Toxicity_Calculator
- John had good performance status & cardiac function at baseline without any clinical significant comorbidities.
- Induction with “7+3” chemotherapy
  - Cytarabine 100 mg/m2 IV continuous infusion 24 hours daily on days 1-7
  - Daunorubicin 60 mg/m2 IV push daily on days 1-3

Chemotherapy

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- Targets cancer cells during their reproductive cycle or can interfere with the way the cells function.
- Many different classes of chemotherapy agents exist.
- Common chemotherapy classes/drugs are listed at https://www.cancer.org/treatment/treatments-and-side-effects/treatment-types/chemotherapy/how-chemotherapy-drugs-work.html (cancer.org -> Treatment & Support -> Treatment and Side Effects -> Types of Cancer Treatments -> Chemotherapy -> How Chemotherapy Works)
- Narrow therapeutic index = high risk!
- ONS/ASCO Chemotherapy Safety Standards: https://onf.ons.org/onf/44/1/2016-updated-american-society-clinical-oncologyoncology-nursing-society-chemotherapy (google “ONS chemotherapy safety standards”)

Various routes of administration

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- Oral
- Intravenous
- Intramuscular and Subcutaneous
- Intra-arterial
- Intraperitoneal
- Intrapleural
- Intravesicular
- Intrathecal
- Topical
- Intralesional

Oral chemotherapy

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"***Drugs don't work in patients who don't take them" - C. Everett Koop, MD***

- Adherence is important!
- Reasons for non-adherence:
  - Financial hardship
  - Side effects
  - Concerns about medication
  - Lack of perceived need
- ONS-endorsed patient education sheets available at http://oralchemoedsheets.com/

Discussion: What can we do to prevent non-adherence?

Oral chemotherapy adherence

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Zerillo et al (2018) performed a systematic review to identify oral chemotherapy intervention programs.

Interventions with statistically significant improvement:

- Nursing phone calls to contact patients within the first few days after treatment initiation.
- Standardized toxic effects management protocols.

Intravenous chemotherapy

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Possible complications: vesicant extravasation

- *Vesicant* is a drug that, if infiltrated, is capable of causing pain, ulceration, necrosis, and sloughing of damaged tissue.
- *Extravasation* is the inadvertent infiltration of a vesicant chemotherapy drug.
- Doxorubicin, Daunorubicin, Epirubicin, Dactinomycin, Vincristine, Mechlorethamine
- Signs of extravasation: swelling, lack of blood return, IV fluid that stops or slows, or leaking around the injection site.
- If extravasation is suspected, stop the infusion immediately, aspirate the vesicant, and initiate institutional policies for management of vesicant extravasation.
- Plastic consult may be indicated.

Other routes

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- **Intraperitoneal (IP):** Treatment of patients with peritoneal surface malignancy caused by ovarian cancer, peritoneal mesothelioma, appendiceal carcinoma, or peritoneal dissemination from pancreatic, duodenal, or gastric canner; allows delivery of chemotherapy directly to a tumor that has spread into the peritoneal cavity
- **IM and subcut**: different drugs call for different techniques; refer to the administration instruction specific to each drug.
- **Intra-arterial**: involves cannulation of the artery that provides a tumor's blood supply; drug delivery directly to the tumor bed. The primary use is via the hepatic artery for the management of liver metastasis from colorectal cancer.
- **Intravesicular**: direct instillation of chemotherapy into the bladder; effective method of controlling superficial bladder cancer. Mitomycin-C and Bacillus Calmette-Guerin (BCG).

Other routes

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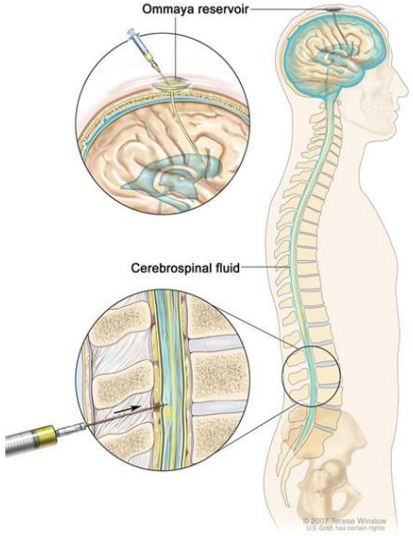
- **Intrathecal** (IT): Injection of chemotherapy directly into the cerebrospinal fluid as prophylaxis or to manage existing disease via lumbar puncture or ommaya reservoir; common drugs are methotrexate and cytarabine. Some chemotherapy drugs are lethal if erroneously administered as IT (vinca alkaloids). Measures to prevent such errors are imperative. #NCCNJustBagIt
- **Topical**: cutaneous malignant lesions.
- **Intralesional**: chemotherapy is delivered directly into tumor; dermatologic malignancies.



IT Chemo
https://www.cancer.gov/publications/dictionaries/cancer-terms/def/intrathecal-chemotherapy

Safe handling

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Many chemotherapy drugs are hazardous!

- The National Institute for Occupational Safety and Health (NIOSH) List of Hazardous Drugs.
- Protect yourself- proper PPE when administering/disconnecting hazardous drugs and when you are handling body fluids of patients who recently received hazardous drugs.
- Use closed system transfer device (CSTD) to minimize exposure during preparation & administration.
- Teach patients about safe handling at home. https://www.oncolink.org/frequently-asked-questions/cancer-resources/brown-bag-chat/caregiver-exposure-to-chemotherapy (google “Caregiver Exposure to Chemotherapy Oncolink”).

Closed System Transfer Device

Common toxicities of (mostly) cytotoxic chemotherapy

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- Bone marrow suppression
- Nausea/vomiting
- Diarrhea
- Mucositis
- Neurotoxicity
- Cardiotoxicity
- Pulmonary toxicity

Bone Marrow Suppression

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- Leukopenia/neutropenia, anemia, thrombocytopenia
- Nadir (the lowest point) is 7-14 days after cytotoxic chemotherapy
- Increased risk of infection
  - Hand hygiene
  - Educate patients about s/s of infection
  - Colony stimulating factors (G-CSF, GM-CSF) to increase production of WBCs, if indicated; NCCN Guideline for Myeloid Growth Factor, ASCO Guideline for Use of White Blood Cell Growth Factors; filgrastim, sargramostim, and their biosimilars.
- Increased risk of bleeding
  - Educate patients about s/s of bleeding (e.g., petechiae, hematuria, melena, hematemesis, gum bleeding)
  - Reinforce bleeding precautions (avoid trauma; no invasive procedures; no suppositories, enemas, or rectal temperature; use electric razor; avoid ASA/NSAIDs; soft toothbrushes; avoid tampons)

Chemotherapy induced nausea/vomiting

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- Know the emetogenic potential of chemotherapy regimen your patient is receiving: very high, high, moderate, low, very low.
- Administer the appropriate antiemetic regimen according to its emetogenic potential. Guidelines are available from National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO), and Multinational Association of Supportive Care in Cancer (MASCC).
- Common antiemetics are: **serotonin-receptor antagonists (ondansetron, palonosetron), steroid (dexamethasone), selective neurokinin-1 antagonists (aprepitant, fosaprepitant, rolapitant).**
- **Phenothiazine, metoclopramide, dexamethasone, cannabinoids, or olanzapine** may be effective agents in the treatment of breakthrough CINV.
- Also consider patient-related factors (see NCCN antiemetic guideline).
- Nausea may be acute, delayed or anticipatory.

Diarrhea

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- Assessment:
  - Number of stools per day, consistency, duration, color, onset, presence of blood
  - S/S of dehydration (lethargy, dry skin)
  - Use of antibiotics - C. difficile infection
  - Perinatal breakdown
  - Abdominal pain/cramping
  - Fever
- Antidiarrheal medicine (if indicated)
- Teach perinatal skin care - moisture barriers, sitz bath
- Monitor I/O
- Low-residue “BRATY” diet (Y = yogurt)
- Avoid lactose-containing products
- Oral hydration

Oral mucositis (stomatitis)

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- Inflammation of oral mucosa; affects 40% to 80% of patients undergoing chemotherapy
- Dry mucosa, tongue, or lips, burning sensation in the oral cavity, and decreased salivation
- Places immunosuppressed patients at much greater risk for opportunistic infection and sepsis
- Prevention and management:
  - Regular evaluation of the oral cavity & patient reported symptoms
  - Establishing good oral health prior to treatment; maintaining it by regular teeth and tongue brushing and bland mouth rinses (may be made at home using normal saline or one teaspoon of salt or baking soda in 16 ounces of water)
  - Cryotherapy
  - Avoid hot, spicy, acidic, or rough foods; smoking; and alcohol
  - If patients cannot tolerate oral intake, consider enteral feeding to avoid malnutrition
  - MASCC Oral Care Education - great patient education resources in many languages (google “MASCC oral care education”)

Neurotoxicity

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- Cerebellar (unsteady gait, nystagmus, ataxia, dizziness, seizures, confusion, coma): high dose (HD) Ifosfamide, HD Methotrexate, HD Cytarabine
- Autonomic (ileus, constipation, impotence, urinary retention, postural hypotension): Vincristine (> 2mg/m2), HD Cisplatin
- Peripheral (paresthesia of hands and feet, muscle atrophy, loss of deep tendon reflexes, muscle cramps, sensory loss, hoarseness): Taxanes (Paclitaxel, Docetaxel, Paclitaxel, protein bound [aka Abraxane], Cabazitaxel), Vinca Alkaloids (Vincristine, Vinblastine, Vinorelbine), Platinum Analogs (Oxaliplatin, Carboplatin, Cisplatin), Immunomodulating Agents (Lenalidomide, Pomalidomide), Biologic Agent (Brentuximab, Ipilimumab), and Proteasome Inhibitors (Bortezomib).

Peripheral neuropathy

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- The onset varies and the course is unpredictable; may occur 4 to 6 months after completion of the chemotherapy; while some patients may improve, others will continue to progress.
- Other risk factors: smoking history, baseline neuropathy, diabetes, and renal dysfunction.
- Evaluate Achilles tendon reflex: the loss of this reflex is frequently the first clinical feature of chemo-induced peripheral neuropathy.
- Patients should also be evaluated for diabetes to confirm the neuropathy is not related to high blood glucose.
- Significant QoL issue: a survey of 129 patients who received chemotherapy for ovarian cancer revealed that 51% experienced neuropathy symptoms up to 12 years after completing treatment, negatively impacting their health-related quality of life.

Peripheral neuropathy

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- Monitor symptoms: patient reported outcomes and QoL assessment; withhold therapy for signs/symptoms of severe toxicity
- Institute safety measures
- Avoid cold drinks and cold in general with oxaliplatin
- Managing painful peripheral neuropathy: Duloxetine, Gabapentin and Opioid Combination

Cardiotoxicity

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- Consequences of systemic chemotherapy: myocardial dysfunction, heart failure, hypertension, malignant arrhythmias, myocardial ischemia, narrowing of blood vessels.
- Cardiovascular disease is the second most common cause of long-term morbidity and mortality in cancer survivors.
- A recent study revealed that breast cancer survivors were at a higher risk of death from cardiovascular disease than from recurrent disease or the cancer itself.

Cardiotoxicity

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- **Permanent myocardial injuries** are most often induced by the anthracyclines, antimetabolites, and cyclophosphamide.
- The cardiotoxicity of anthracyclines is unpredictable - can occur within hours, weeks, or even years after exposure (survivorship considerations!).
- Patients are more likely to develop cardiomyopathy with **higher cumulative doses of anthracyclines**.
- High risk patients:
  - Extremes of age (less than 5 or more than 65),
  - Those who receive concurrent radiation treatment
  - Those with prior cardiac disease or established risk factors for heart disease (coronary artery disease, diabetes, hypertension, smoking, and obesity)

Cardiotoxicity

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- Trastuzumab exposure results in **partially reversible left ventricular dysfunction and heart failure**.
- **Hypertension** is the most frequent adverse effect of VEGF-signaling pathway inhibitors (e.g., sunitinib, sorafenib, and bevacizumab). Monitor blood pressure at every clinic visit and manage hypertension aggressively.
- **Vascular thrombosis and ischemia** are known to occur with the newer tyrosine kinase inhibitors, nilotinib, dasatinib, and ponatinib. Other studies report a higher rate of thrombotic events in multiple myeloma patients treated with combination therapy that included lenalidomide and dexamethasone.
- **QT prolongation** are associated with certain antineoplastic agents (e.g., Arsenic trioxide, Oxaliplatin). Some antiemetic agents (ondansetron, granisetron, and dolasetron) in combination with the anticancer agents can potentiate the QT interval. Review potential drug interactions. Correct electrolyte abnormalities; they can also be a cause of prolonged QT interval.

Pulmonary toxicity

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- An inflammatory-type reaction resulting in drug-induced pneumonitis.
- Can occur many years after chemotherapy is discontinued.
- Mild to progressive dyspnea, unproductive cough, bilateral basilar rales, tachypnea, and low-grade fever.
- Obtain baseline pulmonary function tests.
- Assess for pulmonary symptoms. Imaging (CT chest) may be indicated for concerning sings/symptoms.
- High risk agents: Bleomycin (lifetime cumulative dose), Carmustine, some targeted oral chemotherapy agents (e.g., PI3K inhibitors), checkpoint inhibitors.

Question

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You are about to administer 7+3 induction chemo (Daunorubicin and *** Cytarabine) to John. Which of the following are your priority nursing plans and interventions?

A. Potential for alteration in cardiac output related to acute and chronic cardiac changes: assess baseline cardiac status (e.g., baseline left ventricular ejection fraction), monitor anthracycline cumulative dose.
B. Alteration in nutrition, less than body requirements, related to nausea/vomiting/diarrhea and stomatitis: administer proper antiemetic regimen as ordered, assess fluids and electrolyte balance, assess oral mucosa, teach patient oral hygiene, assess pain and administer analgesics as needed.
C. Potential for impaired skin integrity related to drug extravasation: drug through patent IV, extravasation management if required.
D. All of above

Potential complications: Tumor lysis syndrome

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- A metabolic disturbance that occurs after cell destruction of rapidly growing tumors
- Rapid lysis of tumor cells results in the rapid release of potassium, uric acid (from nuclear acids), and phosphorus into the bloodstream. Hypocalcemia develops because of an inverse relationship between phosphorus and calcium (inverse = one increases, other decreases).
- **Look for signs/symptoms of:**
  - **Hyperkalemia**
  - Hyperuricemia
  - Hyperphosphatemia
  - **Hypocalcemia**
  - There are lots of websites that you can look up to review s/s of electrolytes imbalance, such as https://www.registerednursing.org/nclex/fluid-electrolyte-imbalances/
- TLS pathophysiology review by Andrew Wolf: https://www.youtube.com/watch?v=MuF1UgW-oJ8 (on youtube, search for "tumor lysis syndrome andrew wolf")

Tumor lysis syndrome

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- Malignancies frequently associated with TLS: **AML, ALL, myeloproliferative disease, high-grade non-Hodgkin lymphoma** (especially Burkitt lymphoma).
- Patient-related risk factors: dehydration; poor urinary output; acidic urine; bulky abdominal disease; extensive lymph node involvement; elevated WBC; elevated uric acid, potassium, and phosphorus levels; elevated LDH.

Tumor lysis syndrome

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Prevention is the cornerstone of management!

- Monitor lab values: baseline and every 8-12 hours during the first 48-72 hours of treatment
- EKG: baseline and PRN
- Hydration: begin hydration 24-48 hours prior to initiation of therapy
- Diuresis with loop diuretics or osmotic diuretics if urine flow is not maintained by hydration alone
- Allopurinol (prevents formation of uric acid - not a treatment of hyperuricemia)

Question

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You are reviewing active orders for John who just has started 7+3 induction *** therapy. You need to speak to the resident caring for John because you have questioned which of the following orders?

A. Allopurinol 300 mg PO daily
B. Continue Normal Saline 1000 mL at 150 mL/hr
C. Obtain basic metabolic panel, calcium, phosphate, uric acid, and LDH levels every 8 hours
D. Potassium supplement 40 mEq PO daily

John post-induction

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He is on day 9 of "7+3" induction. ***

Today his CBC results are: WBC 0.1K, HGB 7.7, HCT 23.0, PLT 13K. He has moderate anorexia and some mouth sores.

12N VS: Temp 38.5 C (101.3 F), P 110, BP 135/81, RR 20, O2 sat 97% RA.

What is happening to John?

a. AKI
b. TLS
c. Sepsis
d. Colitis

Sepsis

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- A systemic inflammatory response to pathogenic microorganisms and associated endotoxins in the blood.
- Can become a life-threatening oncologic emergency.
- May lead to septic shock and irreversible multiorgan dysfunction syndrome.
- Need early detection and intervention!
- Severe sepsis occurs more frequently in patients with hematologic malignancies compared to solid tumors.

Sepsis presentation

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Typically two or more of the following parameters:

- An oral temperature greater than 100.4 F (38 C) over one hour or less than 96.8 F (36 C)
- A heart rate greater than 90 beats /minute
- A respiratory rate greater than 20 breaths/minute
- A white blood cell count greater than 12K cells/mm3, less than 4K cells/mm3, or more than 10% bands in the blood

Question

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You expect which of the following orders in managing John's sepsis? ****

A. Blood culture
B. Urinalysis and culture
C. Chest X-ray
D. Initiate IV antibiotics (Cefepime 2 g IV Q8H) within 1 hour but only after obtaining cultures
E. All of above

If Sepsis does not respond to initial measures...

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- Severe sepsis: a state of organ dysfunction, hypotension, or hypoperfusion
- Septic shock: hemodynamic instability; fever, chills, tachycardia, tachypnea, mental status changes, and hypotension or hypoperfusion despite aggressive fluid challenge
    - Immediately initiate intensive therapy to maintain BP and oxygen saturation
    - ICU-level care is needed

John post-induction

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- High risk disease based on molecular studies; stem cell transplantation was considered the best option to prevent disease relapse
- Bone marrow examination post induction showed complete response
- Consolidation with Cytarabine while awaiting BMT

Overview of Stem Cell/Bone Marrow Transplant

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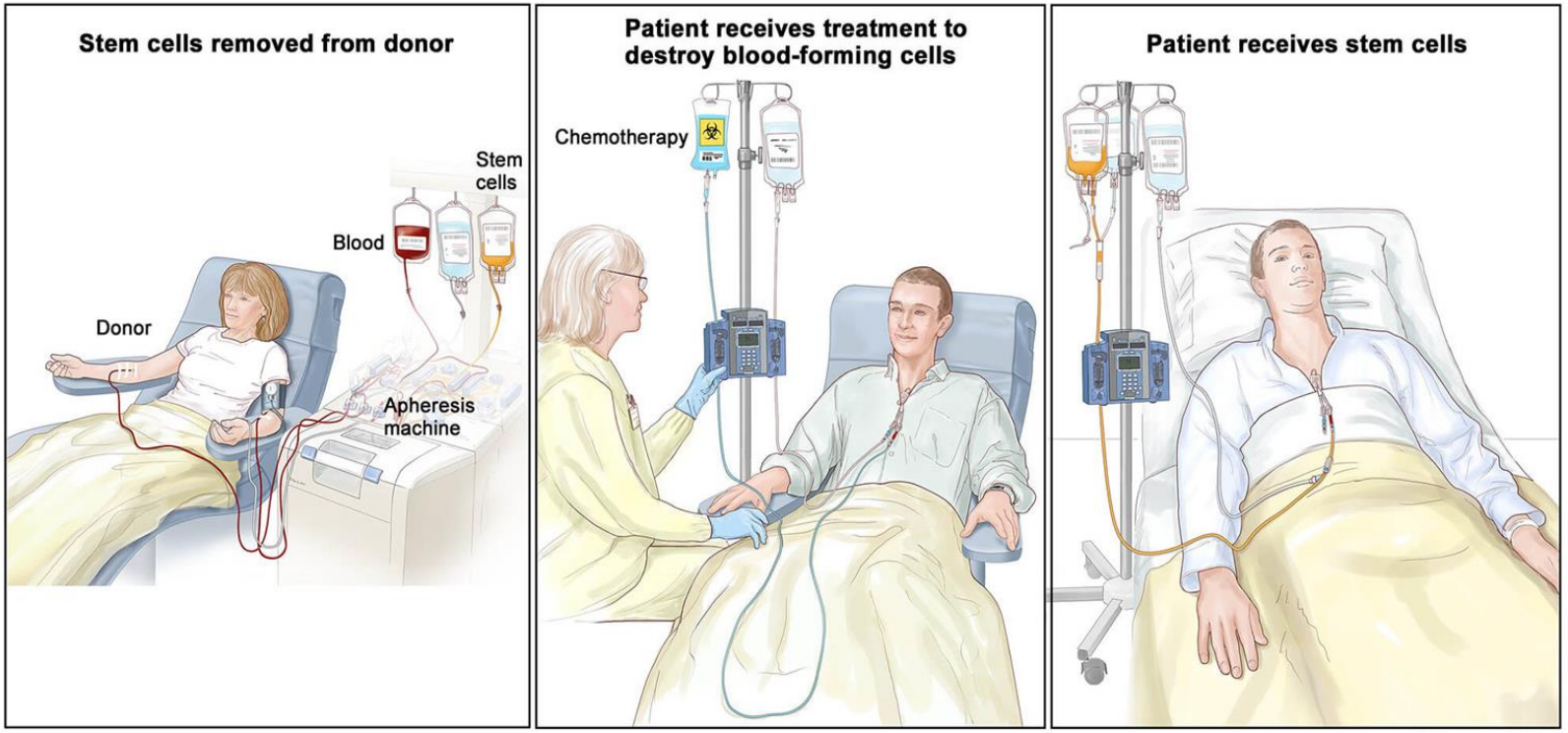

https://www.cancer.gov/about-cancer/treatment/types/stem-cell-transplant

Sources of stem cells

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- Bone marrow: collected directly from the bone marrow by bone marrow procurement or multiple needle aspiration under general anesthesia; not very common (this is a preferred source for patients with Severe Aplastic Anemia requiring BMT).
- Peripheral blood: multiple methods exist to mobilize stem cells from the bone marrow into the peripheral blood (mobilization). Once peripheral blood stem cells are in the circulation, they can be collected using a process called apheresis. Most common.
- Umbilical cord blood

Type of blood and marrow transplantation

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- Autologous Transplantation
- Syngeneic Transplantation
- Allogeneic Tranplantation
  - Donor selection
  - Myeloablative vs reduced intensity/nonmyeloablative

Autologous transplantation

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- The use of stem cells from (donor) and for (recipient) the same individual. Stem cells are collected from an individual and reinfused at a later date to the same individual.
- The goal is **to give high dose chemotherapy** to eradicate disease. The dose is so high that it would be lethal without stem cell rescue/reinfusion.
- Hodgkin lymphoma, non-hodgkin lymphoma, multiple myeloma, germ cell tumors.
- Mobilization (cyclophosphamide, filgrastim, plerixafor) -> collection (apheresis) -> conditioning chemo (HD Melphalan, BEAM - Carmustine, Etoposide, Cytarabine, Melphalan) -> chemo toxicity -> recovery
- Toxicities are chemo-related - bone marrow suppression, nausea/vomiting, diarrhea, mucositis, fatigue…etc.

Syngeneic Transplantation

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- The donor is an identical twin who holds the same human leukocyte antigen (HLA)
- Not common

Allogeneic transplantation

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- Primary goal is **to use donor's immune system** to eradicate host disease (Graft vs Tumor Effect) while preventing it from attacking the host organs
- Immunotherapy
- Immunosuppressants (e.g., cyclosporine, tacrolimus, mycophenolate mofetil, methotrexate)
- Acute lymphocytic leukemia, acute myeloid leukemia, myelodysplastic syndrome, non-Hodgkin lymphoma
- Conditioning regimen (chemotherapy and/or radiation) -> stem cell infusion (collected previously from the donor) -> treatment & immune related toxicities (inc. prolonged neutropenia and risk of developing serious infections) -> recovery or chronic issue

We can have a variety of donor options.

- **Matched related**: the best donor, but only a small portion of patients have a matched related donor
- **Matched unrelated**: found through a donor registry such as National Marrow Donor Program
- **Umbilical cord blood**: donated after childbirth; organized by Cord Blood Coordinating Center
- **Haploidentical**: a half-matched or partially-matched transplant. The donor is a half match for the patient (a parent or child). Need measures to prevent graft rejection & other complications.

We can make conditioning/preparatory regimens less toxic

- **Reduced intensity conditioning** (RIC)
- **Nonmyeloablative regimen**
- Do we always need high dose/ intense chemo/radiation (e.g., HD Busalfan, total body irradiation)? Can we reduce treatment-related mortality (TRM)?
- The answer is yes but not without a cost. RIC and nonmyeloablative regimen are often associated with increased relapse rate.
- We need new agents for conditioning regimen and immunosuppression that can reduce both TRM and relapse. More research is needed!

Graft vs Host Disease (GVHD)

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- Potentially a serious complication of allogeneic stem cell transplantation.
- Donor cells (“the graft”) attack the patient’s healthy tissues and organs (“the host”), which can impair the tissue or organ function or may cause it to fail altogether
- Acute GVHD
  - Usually occurs within 2 to 5 weeks following allogeneic transplant
  - Primarily presents in the skin, liver, and GI tract (rash, hyperbilirubinemia, diarrhea)
- Chronic GVHD
  - The most common late complication
  - Different pathophysiology from acute GVHD
  - Can affect the skin, liver, GI tract (but these presentations are different from acute GVHD), oral mucosa, muscles, eyes, vagina, nerves, kidneys, heart, lungs, and marrow functions.
- We need to quiet down immune attack (steroid, immunosuppressants… etc)

Question

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Who is most likely to develop GVHD? ***

A. 26 year old male with Hodgkin Lymphoma who underwent autologous stem cell transplantation 3 months ago.
B. 45 year old female without any significant PMH who is undergoing stem cell collection for her sister who needs allogeneic transplantation.
C. 58 year old female with AML who has received allogeneic stem cell transplantation from a matched unrelated donor 30 days ago (currently day +30 of allo).
D. 81 year old male with AML who is not a candidate for allogeneic stem cell transplantation and is receiving Decitabine chemotherapy.

More (free) resources

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- Leukemia Lymphoma Society Webinars: http://www.lls.org/continuing-education-programs (lls.org -> Researchers & Healthcare Professionals -> Continuing Education Programs)
- ONCC Resource Center Big Lists of Free CE: https://www.oncc.org/continuing-education/big-lists-free-ce (google “ONCC big”)
- http://www.researchtopractice.com/

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