

Hematopoietic Stem Cell Transplantation (HSCT) Overview

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May 20, 2010

Disclosures

- I am an employee of the National Marrow Donor Program, a non-profit 501(c)3 corporation



Slide 2

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Outline

- What types of transplants are there?
- How is the matching procedure done?
- What issues are there with quality of life after HSCT?

Some terminology first...

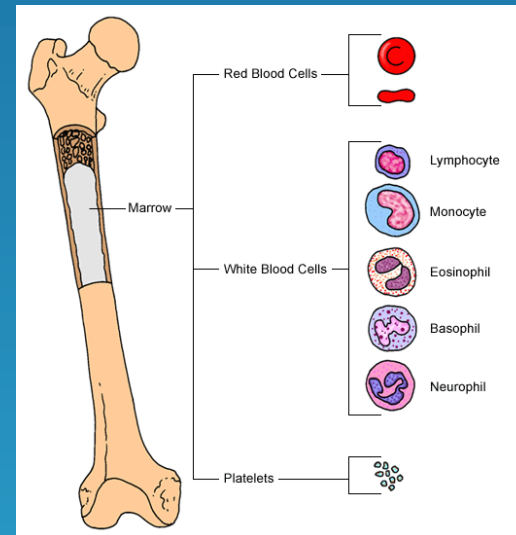
- **Global Terms for Marrow Transplant**
 - Hematopoietic Cell Transplant (HCT)
 - Hematopoietic Stem Cell Transplant (HSCT)
 - Bone Marrow Transplant
- **All these terms refer to the process of replacing the marrow after treatment with chemotherapy ± radiation**
- **Identifying the Stem Cell Source**
 - Marrow
 - Peripheral Blood Stem Cells
 - Cord Blood
- **Identifying the Individual Providing the Blood Stem Cell**
 - Allogeneic
 - Blood stem cells obtained from someone other than the patient
 - Autologous
 - Blood stem cells obtained from the patient him/herself

More Terminology--Describing the Transplant

- **Preparative or Conditioning Regimen**
 - The treatment (chemo, radiation, antibodies) used to help the new marrow take hold
- **Reduced Intensity/ Non-Myeloablative**
 - A type of allogeneic transplant in which the prep is immunosuppressive, minimally cytotoxic
- **Cytotoxicity**
 - The ability of an anticancer medication to kill cells (both good and bad cells)

And some hematology basics...

- The blood-forming system lives in the bone marrow, distributed throughout all the bones
- The immune system is inextricably linked to the blood system
- The hematopoietic system is generally the most sensitive organ to the effects of chemotherapy



What does an HSCT get you?

- It depends on the type...
 - Autologous: using cells from the patient
 - Very high doses of chemo ± radiation
 - Aim is to kill cancer cells with intermediate resistance to standard chemo doses
 - Cytotoxicity is the main benefit, no immune attack against cancer cells
 - Allogeneic: using cells from someone other than the patient
 - Immunologic effect called graft-versus-disease effect (the donor immune system battles cancer cells)
 - Cytotoxicity: depends on the prep regimen

Autologous Transplant

- Big “Bang” is from the prep regimen
- Provides a means to give very high dose chemo to kill cancer cells
 - In the process the marrow is damaged
 - Marrow is then “rescued”
- No immunologic benefit
 - But no risk of graft-versus-host disease
- Short term risks: low counts, mouth sores, skin rashes, organ damage, hair loss, taste changes, “chemo brain”
- Long term risks: secondary cancers, organ damage, sterility



Allogeneic Transplant

- Uses immunologic reaction: donor's immune system vs cancer cells
 - Can be extremely potent (and **dangerous**, when against the patient's organs [GVHD])
- Cell kill (cytotoxicity) depends on prep regimen (full vs reduced intensity)
- Short term risks (*depends on prep regimen*): infections, acute graft-versus-host disease, graft failure, relapse
- Long term risks: chronic graft-vs-host disease, infections, second cancers, organ damage, relapse, sterility

Matching and HLA

- Human Leukocyte Antigen (HLA) molecules are used by the immune system to figure out what is “self” vs foreign
- A set of HLA molecules (HLA-A, -B, -C, -DRB1, -DQ) is called a “haplotype” [half set]
- Everyone inherits two sets of HLA genes: one from mom, one from dad (so everyone has two A genes, two B genes, etc.)

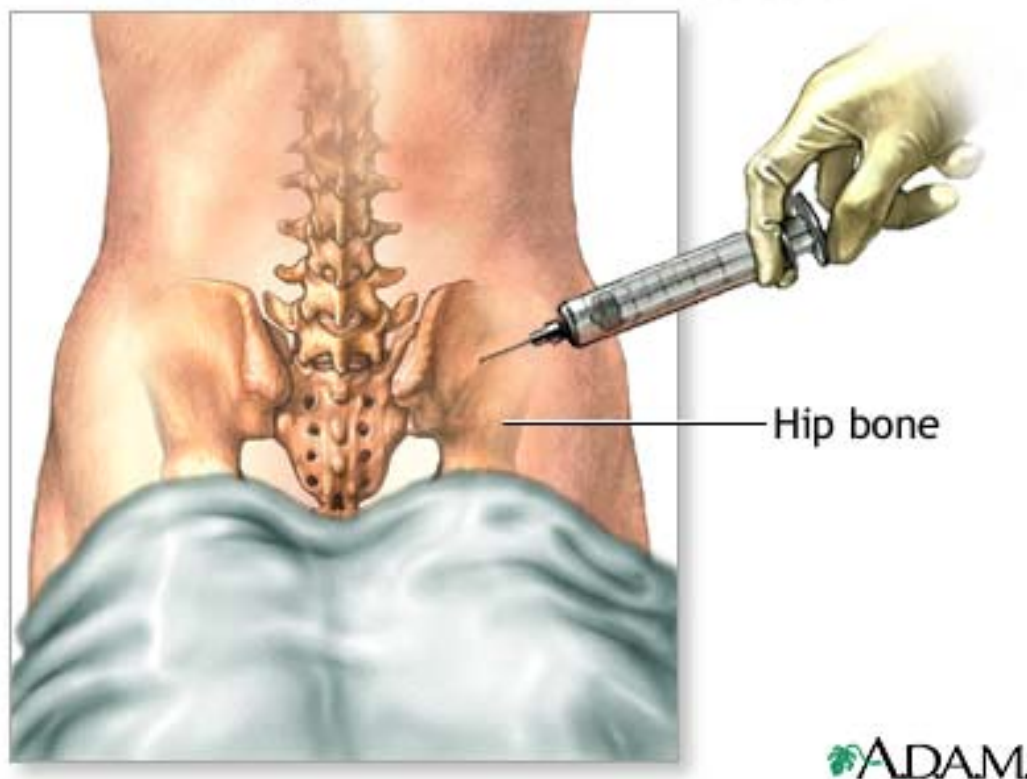
		Mom	
		C	D
Dad	A	AC	AD
	B	BC	BD

- In looking for an HLA match, the chance any one sib will match is 25%
- For the roughly 70% of pts without a sib match, the NMDP will facilitate obtaining cells from a matched donor

The HCT Process-Collection

- The donor experience-marrow harvest

Harvesting bone marrow from the donor



http://commons.wikimedia.org/wiki/File:Bone_marrow_biopsy.jpg

<http://www.walgreens.com/marketing/library/contents.html?docid=000122&doctype=10>

The HCT Process-Collection

- The donor experience-PBSC



The HCT Process-Recipient



Prep (variable
length)

Engraftment

Day -10 -8 -6 -4 -2 0

+9 +14 +21 +28

Quality of Life Issues

- **Depends on the type of transplant performed**
 - Autologous: predominantly due to high dose chemotherapy
 - Short term side effects
 - Fatigue, hair loss, taste changes, skin dryness and pigment changes, organ damage
 - Long term side effects
 - Risk of second cancers, effects of organ damage
 - Allogeneic: much more complicated because of graft-versus-host risk, slower immune system recovery
 - Some allogeneic transplants use less intense chemo, results in decreased chemo-related side effects; some use full intensity and have similar effects as an autologous HCT
 - Graft-versus-host: short term can cause organ damage, in the longer term, often behaves like an autoimmune disease
 - Risk of GVHD is related to the degree of HLA match