Hematopoietic Stem Cell Transplantation (HSCT) Overview

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Disclosures

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

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

The HCT Process-Collection

• The donor experience-PBSC
The HCT Process - Recipient

Day: -10 -8 -6 -4 -2 0 +9 +14 +21 +28

Prep (variable length) → Engraftment
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