Understanding Bone Marrow Transplant: Where Are We Now, and What's Coming?

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July 22, 2017

Learning objectives

Understand:

- Transplant basics
  - Difference between autologous and allogeneic transplants
  - What a donor match means
  - Haploidentical transplants
- Transplant process and how long it takes
- Graft-versus-host disease (GvHD)
- Outcomes of transplant
- Recovery and long term survivorship issues

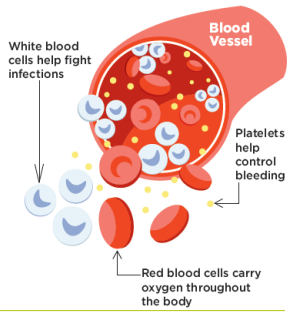
TRANSPLANT BASICS

Bone marrow transplant

- Also referred to as:
  - Blood or marrow transplant (BMT)
  - Blood stem cell transplant
  - Hematopoietic cell transplant (HCT)
  - Hematopoietic stem cell transplant (HSCT)

What is bone marrow?

- Soft tissue inside bones
- Contains blood-forming cells (stem cells)
- Makes all the cell types that go into the blood

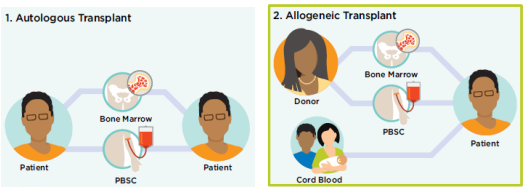


Bone marrow failure diseases

- Bone marrow failure – the bone marrow is damaged and unable to make normal blood cells
- Depending on the disease, may affect your body's ability to make:
  - White blood cells that fight infections
  - Red blood cells that carry oxygen throughout the body
  - Platelets that help control bleeding

Types of transplant and cell sources

- Two types of transplant – autologous and allogeneic
- Three sources of stem cells for transplantation – bone marrow, peripheral blood stem cells (PBSC), and cord blood



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What is a matched donor?

HLA: Genetic identity

- **H**uman **L**eukocyte **A**ntigens (HLA) are proteins on the surface of most cells in the body
- The immune system uses HLA to be sure a cell is part of the body and not foreign
- An HLA-matched donor helps decrease the risk of graft-versus-host disease (GvHD)
- There are many different HLA (HLA-A, -B, -C, -DRB1, -DQ, -DP)

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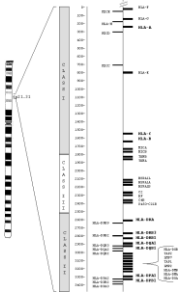
HLA proteins are grouped into haplotypes

- Possible groups are called haplotypes
  - Billions of combinations
  - Often follow ethnicity



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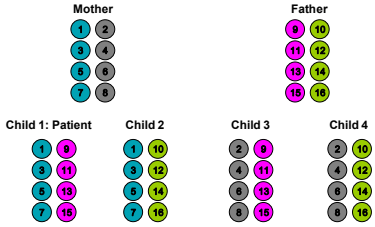
A child inherits one haplotype from each parent = 4 possible combinations



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Allogeneic donor options

- Matched sibling is first choice
- Alternatives to a sibling donor
  - Matched unrelated donor
  - Matched or partially matched umbilical cord blood
  - Haploidentical – half matched (sibling, parent, child)

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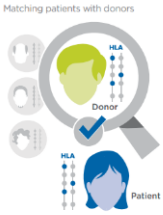
How is an unrelated donor found?

- Your transplant center is responsible for searching for a donor
- Be The Match Registry
  - 12.5 million donors and 209,000 cord blood units
  - Access to 25 million donors and 622,000 cord blood units on U.S. and global registries



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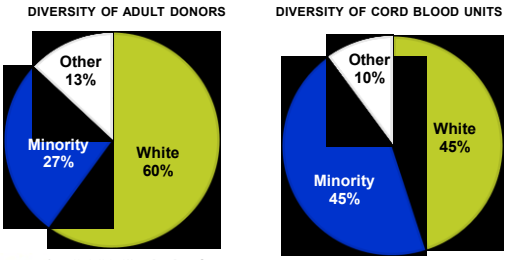
Diversity of Be The Match Registry



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What about a haploidentical transplant?

- Newer type of transplant using half-matched donor
- Increases number of family members who may be donors
- Very promising outcomes and more centers are performing them
- Relies on giving chemotherapy (cyclophosphamide) after transplant to prevent GvHD

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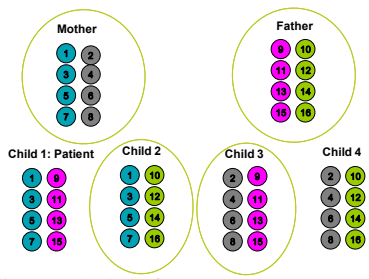
Haploidentical –half match increases number of possible family donors



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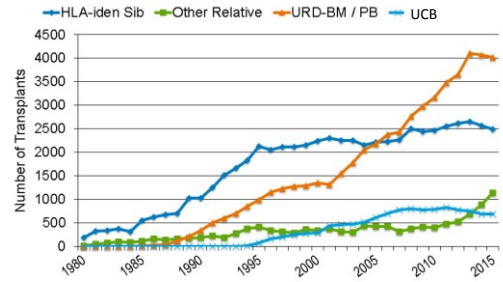
Allogeneic HCT Recipients in the US, by Donor Type



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D'Souza A, Zhu X. Current Uses and Outcomes of Hematopoietic Cell Transplantation (HCT): CIBMTR Summary Slides, 2016. Available at: http://www.cibmtr.org

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Role of BMT in bone marrow failure

- BMT can cure
- But, since BMT has potential risks, it must be used at appropriate time in disease course
- Appropriate time *may include*:
  - At diagnosis
  - When disease is causing serious complications
  - When other therapy has not worked

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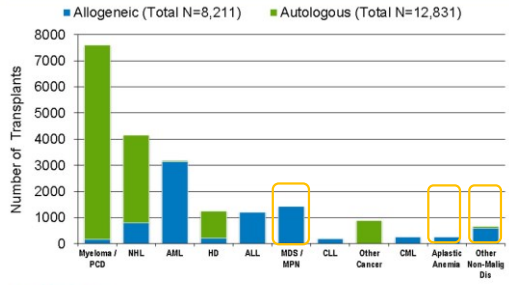
Indications for Hematopoietic Cell Transplant in the US, 2014



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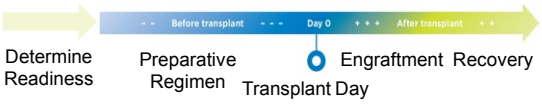
TRANSPLANT PROCESS

The transplant process



Every patient's experience is unique.

Readiness for BMT

- Is the timing right?
  - Are you well-prepared for transplant?
    - Education for you, your caregiver and family
    - Fertility preservation if appropriate
    - Emotionally and socially prepared
  - Are you healthy?
    - Tests to check organ function
  - Is your disease under control so that BMT has a good chance of helping you?

The preparative regimen

- Chemotherapy, with or without radiation
- Destroys diseased cells and as a side effect, healthy stem cells that must be replaced with a transplant
- Immune suppressing medicines to prevent graft-versus-host disease (GvHD) are started

Standard-intensity preparative regimen myeloablative transplant

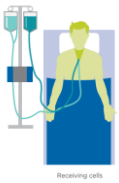
- Higher doses of chemotherapy/radiation given with goal of killing all of the patient's diseased cells
- Works for patients with:
  - MDS who are younger and overall healthy
- Usually causes more side effects than lower doses

Reduced-intensity preparative regimen non-myeloablative transplant

- Lower doses of chemotherapy/radiation with main goal to suppress the immune system so donor cells can grow and fight disease
- Works for patients:
  - With aplastic anemia or PNH
  - Who are less likely to tolerate the side effects of a standard regimen such as older patients with MDS

Transplant day (Day 0)

- Stem cells are collected from donor on day of transplant
  - Cord blood units shipped to transplant center before start of preparative regimen
- Stem cells taken to patient and administered like a blood transfusion
- Side effects usually the same as a blood transfusion and may include fever, chills and rash



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Many team members will care for you

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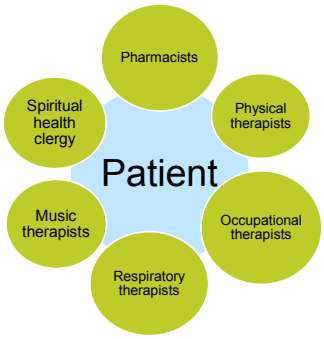
More team members!



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Advocate for yourself

- Your transplant team wants to know how you feel and what you think
- Speak up about any concern
- Take notes to help you remember what you want to tell your team
- Remember: caregivers and family are critical team members who can also advocate for you

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Early days after transplant

- At risk for life-threatening infections, bleeding, and organ damage from the preparative regimen and immune suppressing medications
- Antibiotics given to prevent and treat infection
- Blood and platelet transfusions given as needed
- Closely monitored for any complications

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Engraftment

- When the donated stem cells settle into your bone marrow and begin to grow (in order):
  - White blood cells
  - Red blood cells
  - Platelets
- Takes 2 – 4 weeks after transplant, may be longer with cord blood
- Risks from low blood counts decreases

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Getting discharged!

- You'll be discharged from the hospital when:
  - You've engrafted –absolute neutrophil count (ANC) >500
  - No active infections or other problems
  - Able to take foods and medicines by mouth
  - Able to take shower, dress, travel to outpatient clinic

After hospital discharge

- Avoid crowds to prevent getting infections
- Need caregiver for transportation, shopping, cooking, laundry
- Frequent clinic visits with possible readmission to the hospital for treatment of complications
- Don't be discouraged by re-hospitalization: it's very common

GvHD

GvHD

- Common side effect of an allogeneic transplant
- Occurs because the new cells ("graft") see your body ("host") as being different and attacks them
- Chance of happening depends on patient age, HLA match and source of stem cells
- Treated with medicines or other therapies to suppress the new immune system

Two main types of GvHD

Acute GvHD
- Early after transplant
- Affects 3 parts of the body: skin, gut, liver

Chronic GvHD
- Later after transplant
- Most common in those who had acute GvHD
- Can affect many parts of the body
  - Skin, mouth, eyes, gut
  - Most get better after 1-2 years, but some may be bothered for years

Advances in GvHD

- Prevention
  - Blood test may help predict who is at risk
  - Research testing different ways to prevent acute and chronic
- Treatment
  - Ibrutinib (pill) for chronic GvHD
  - Disease hasn't responded to prior therapy
  - Approval based on PCYC-1129 trial of 42 patients
  - 71% of patients had a response for 5 months or more

What you can do about GvHD

- Be aware of symptoms
- Tell your care team
- Take medications as instructed
- Protect your skin

RECOVERY

Life after transplant

- Typically takes up to a year to feel "closer to normal" or reach your "new normal"
- May be shorter or longer depending on any complications
- Transplant team will help guide and support you

Recovery issues that matter to patients

- What we've heard:
  - Physical health
  - Emotional health
  - Return to work/school
  - Sexual health
  - Financial health

Physical health

- Physical recovery is a slow process
- Fatigue is a common problem

- TIPS:
  - Rest up
  - Balance rest with activity
  - Eat well
  - Talk to your team about any side effects from medicines
  - Physical therapy

Emotional health

- Many people feel sad, tense or angry
- Post-traumatic stress disorder may occur
- Natural response to stress and lessens with time

- TIPS:
  - Talk to your family and care team
  - Consider seeing psychologists/psychiatrists with expertise in BMT
  - Exercise as you are able
  - Energize yourself with activities you enjoy

"Life after transplant is a different challenge than treatment. Paving the road to your new normal has its emotional ups and downs. However, if you lean on your support system and listen to your doctors, your road will be much smoother."

– Matt, transplant recipient

Return to work or school

- Depends on type of work or school
- You may get tired easily and not have the ability to concentrate as before

- TIPS:
  - Ask if you can work or attend school from home
  - Consider returning part-time at first
  - Pace yourself

Sexual health

- Isn't discussed as often as physical and emotional health, but may be just as important
- Changes in hormone production occur for both men and women
- Complications, including GvHD, affect sexual health

- TIPS:
  - Talk to your partner and care team
  - Specialists, including gynecologists and urologists, can help

Financial health

- BMT is an expensive therapy
- Few insurance plans pay for everything
  - Housing, travel, food
  - Child care
  - Medications

- TIPS:
  - Social workers can help find medication plans and grant/assistant programs
  - Fundraising before/after transplant

OUTCOMES OF TRANSPLANT

Benefits of BMT

- No longer have the disease – REMISSION
- CURE – means the disease never returns
- Extension of a good QUALITY OF LIFE (QOL)

Transplant outcomes

- Show how a group of patients has done after transplant over time
  - Survival outcomes
  - Quality of life (QOL) outcomes

Survival outcomes

How many people with a certain disease are alive after BMT

QOL outcomes

How other patients have done after BMT
- Physically
- Emotionally
- Socially

What outcomes can and can't tell you

- Can:
  - Help you make a decision
  - Tell how people with similar disease and treatment have done as a group
- Can't:
  - Tell you how you will do

Survival after BMT for bone marrow failure

- Most patients with severe aplastic anemia are cured of their disease
- Many patients with MDS are cured but the disease may recur post-transplant
- Cure of PNH depends on type of bone marrow failure (aplastic anemia or MDS)

SURVIVORSHIP ISSUES

Late effects of BMT survivors

- Late effects may include any part of the body:
  - Bone health
  - Heart and blood vessel health
  - Endocrine (glands that make hormones)
  - Eyes
  - Mouth
  - Cancer

Long term care guidelines

- More and more survivors of BMT
- Care needed depends on underlying disease, type of therapy, age, overall health and other factors
- "Takes a village" of care providers to prevent and treat late effects of BMT

Survivorship BMT clinics

- Many BMT centers have clinical teams specializing in long-term care
- Will work with you and your primary doctor to help you get care to prevent and manage late effects

After Transplant Guidelines

- *After Transplant Guidelines* mobile app
  - Customizable 6-month, 12-month and 2+ year **checkup guidelines**
  - Chronic **GVHD symptom checker**
  - **Set reminders** (appointments, medications)
- Search **"transplant guidelines"** in app stores to download
- Also available online and print at **BeTheMatch.org/patient-after**

Summary

- BMT is curative therapy for bone marrow failure diseases
- BMT use and timing varies by disease
- Many advances, but more research is needed to reduce complications and improve outcomes
- You'll work closely with your BMT team before, during and long after your transplant to help you recover and stay healthy

Be The Match: How we can assist you

Visit:
BeTheMatch.org/patient
Call:1-888-999-6743
Email: patientinfo@nmdp.org

- Confidential one-on-one support and navigation
- Tailored educational materials
- Financial resources
- Fundraising information
- Insurance appeals
- Peer-to-peer connection
- Caregiver support

Free videos: Basics of transplant

- Hear from patients, caregivers and transplant experts
- Topics such as:
  - What is a transplant?
  - What is HLA matching?
  - How does a donor search happen?
  - What is it like to be a caregiver?
  - What is life like after transplant?

BeTheMatch.org/LearnTheBasics

Thanks for listening!

Any questions?

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