Dear Kevin,

I enjoyed writing this technical report very much, probably more-than any other research project I have ever done. I am really interested in the topic, and I think that helped me to put my best effort into the research, writing, and polishing of this report.

The final word count for the body of the report is 3571.

The primary audience for this report is the general public, especially people who don't know much about bone marrow donation or the National Marrow Donor Program. I took a broad look at the transplantation procedure itself, as well as the effect it has on the donor and the recipient. I also gave a brief overview of The Be The Match Registry and what it does.

As you can probably tell from the word count, finding sources was pretty easy for me, as most of the information I was looking for was not too technical. I did have a hard time finding some statistics (such as survival rates for those who find a bone marrow donor versus those who don't) but I think that worked to my advantage. By not finding all the statistics I was hoping to find, I was forced to make my report more personal and less technical.

I tried to keep the report organized, but at the same time use graphics to make it less scary and scientific. I used this same approach when designing my Powerpoint presentation. I tried to relate to the audience by using pictures of people instead of charts and figures.

Thank you, and I hope you enjoy the report!

Madelyn Espinosa
BONE MARROW TRANSPLANTATION

An introduction to the National Bone Marrow Donor Program and how you could Be The Match

Scientific and Technical Communication, Spring 2011
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EXECUTIVE SUMMARY

The National Marrow Donor Program was established in 1987 to pair unrelated donors and recipients in bone marrow and peripheral blood stem cell transplants. [1] Before the NMDP’s Be The Match Registry, the only hope for those in need of a bone marrow transplant (BMT) was to find a donor in their family. Today, joining the registry is quick and painless, requiring only a few cells from the inside of the cheek. For an unknown reason, racial minorities make up a disproportionately small section of The Registry, which makes it difficult for minority recipients to find a match. [2] Regardless of race, the most commonly cited reasons for not joining include the fear of pain, the idea that registering or donating is inconvenient or time-consuming, and pre-existing health conditions. Recently, many other developed countries have begun to fund their own bone marrow registries. China now has the world’s third largest registry, founded in 2002. [5] Donation can take place in two ways: through liquid bone marrow or through peripheral blood stem cells. While physical effects are obvious for the recipient, the donor is often impacted emotionally. Many donors report feeling proud or happy of their donation, while unfortunately, some report feeling guilty if the transplant fails. [4] The health concerns associated with being a bone marrow donor are exceedingly small. [5] Ethically, the biggest concern about BMTs is the use of minor children as donors, which is common since siblings are often matches and leukemia is a cancer common to children. In addition to leukemias, Hodgkin’s lymphoma, Aplastic anemia, and many other cancers of the blood can be treated with a BMT. [6] In order for a transplant to be viable, the recipient’s own damaged bone marrow must be destroyed with chemotherapy prior to transplantation. Bone marrow cells are then given intravenously, and recovery begins. While registering to become a bone marrow donor is simple task, its effects can be life changing for both donor and recipient.
Cancer. For many people, this word is associated with chemotherapy, surgery, or worst of all, a time limit. After surgery fails, after chemotherapy fails, after radiation fails... imagine a treatment option that offers a 70-90% success rate. [7] Bone marrow transplantation is a life-saving procedure for people diagnosed with diseases of the blood, such as leukemia, Hodgkin's lymphoma, and Aplastic anemia. [6] It is often stigmatized because of misunderstanding on the part of the general public. For many people with one of these diseases, a bone marrow transplant is the last hope for recovery.

The process consists of donation, matching, and transplantation. While it may sound like a miracle cure, before the transplantation process can even begin a suitable living donor must be found. This is no small task. If a matching donor is found and willing to help, his or her marrow harvested in one of several ways. After the donor commits to make the donation, the recipient’s immune system is suppressed with drugs so that the donor’s marrow won’t be rejected after transplantation.

In order for the transplantation to be viable, the donor and the receiving patient must be matches for one another on many genetic traits. Sometimes, a family member is found who is a suitable match. This is the best case scenario, because a family member is usually the closest genetic match, and therefore offers the best chance for a successful transplant. When a family match is not possible, a non-related donor must be sought out.

In the United States, there is a federally funded organization dedicated to matching volunteer donors to unrelated recipients...the National Marrow Donor Program and its Be The Match Registry.

**THE REGISTRY**

**History and Introduction**

The National Marrow Donor Program is an organization that matches un-related bone marrow donors and recipients. It is the first and only program of its type in America, and has inspired many other similar programs in other countries. The NMDP made its first match in 1987, a year after receiving federal funding. [1] This was a giant leap in medical advancements for people diagnosed with certain cancers and blood diseases. The Be The Match Registry relies on potential donors to volunteer to join the registry and go through the transplant process, since there is no reimbursement or monetary gain. Everyone who is on The Registry is there because they felt a sense of social or moral obligation. Since its inception, the NMDP has made over 30,000 transplants...
possible for unrelated donors and recipients. [2] In 2007, an average of over ten transplants per day took place because of The Registry. The graph below shows the number of transplants that have occurred every year since the beginning of the NMDP.

![Figure 1. Number of adult transplants by type and year [2]](image)

Prior to 1987, patients requiring a bone marrow transplant (BMT) had little hope for recovery if a match was not found within their family. Bone marrow drives could be held to test friends and acquaintances of the person in need of the transplant, but there was no comprehensive database of donors. A countless number of people passed away waiting for a donor that was never found. Now, because of the NMDP, there is hope for people diagnosed with leukemia or aplastic anemia who have no matching donors in their family.

As a side note, one can see that the number of marrow transplants has decreased and the number of PBSC, or peripheral blood stem cell transplants, has increased in the past ten years. This is because a PBSC transplant is much less invasive for the donor and is now the preferred method of donation. More detail on the types of transplants can be found in the "Donors" section of this report, under the heading "The Donation Process."

**Registration Process and Responsibility**

Getting on the Be The Match Registry is quick, easy, and 100% painless. There are no interviews, no waiting in lines, and no needles. You can sign up at a marrow donor registry drive, if there happens to be one in your area, or you can go to www.marrow.org and request a cheek swab kit be sent to you at home. Once you fill out a short online health questionnaire and provide contact information, all that’s left to do after receiving the kit is to use several cotton swabs to collect cells from the inside of your cheek, and send them to the NMDP for processing.
After returning the kit, you will receive a card in the mail with your name and the information for a donation center closest to you, in the event you are a match and agree to donate. If you match for someone on The Registry, you will be contacted by the NMDP and asked to undergo further blood testing as soon as possible, if you are willing. By joining The Registry, you are under no legal obligation to donate bone marrow if you match for someone. However, if you get “the call,” it is important to decide quickly if you would like to continue with the transplantation process. Every minute you remain undecided is a minute that the potential recipient is waiting to find a donor. If you decide not to participate quickly, the NMDP can allocate its resources to find another match.

Minority Representation

People of minority race make up a very small portion of the donor pool. Of the 15,556 transplants that have taken place because of the NMDP, only 645 were for African American patients.

Diseases like leukemia that are curable through transplant occur just as frequently in minorities as in the general public, yet minorities account for only 5% of the total number of transplants. [2] The reason that minorities are underrepresented on The Registry is currently unknown, since The National Donor Marrow Program is only 24 years old and therefore there is a lack of studies on the donor pool. Unfortunately for minorities who need a BMT, the matching process for donors and recipients is not color blind. The chances of being matched genetically with someone of another race are slim to none.

What keeps people from registering?

In this section we will explore three of the most common reasons people do not join The Be The Match Registry. Here are the three reasons, with explanations on whether or not they are valid.
#1: It’s painful!
One of the biggest reasons people don’t join The Be The Match Registry is a fear of pain. Much of the general public, and even those who work in the medical field, believe that donating bone marrow is an extremely painful procedure with a long and arduous recovery period. In reality, neither of the two methods of donation is extremely painful, or requires more than a few days for recovery. The procedure for peripheral blood stem cell donation, or PBSC, is much like donating blood. However, donors are required to give themselves several injections over the course of a few weeks prior to the donation, which boost their blood stem cell counts. These injections can cause some pain and discomfort. The other type of donation involves taking liquid marrow directly from the bones of the hip. This procedure is done under general anesthesia, and the donor feels nothing but moderate soreness for 2-3 days after. This pain can be managed with medication.

#2: It takes too long!
Another reason that people list as why they choose not to be on The Registry is that joining the registry is inconvenient and time-consuming, or that donating bone marrow would be a huge interruption to their life. In reality, joining the registry takes around 30 minutes total, including time to fill out the online questionnaire and swab the inside of the cheek. It can be done at home, and requires no wait time. The process of donating bone marrow is also much quicker than most people believe. The PBSC donation procedure takes a few hours, while donating actual marrow could take a few days, from the time of the procedure until the donor is feeling completely recovered.

#3. I’m not healthy enough to donate.
While the vast majority of people are healthy enough to safely donate bone marrow, there are some conditions that prevent potential donors from joining The Registry. First of all, you must be between 18 and 60 years of age to donate. Some of the medical conditions that prevent one from joining the registry are:

- Chronic back pain or spinal fractures
- Heart disease
- Certain breathing problems
- Hepatitis B or C
- Liver or kidney problems

Those with asthma, controlled diabetes, and epilepsy are allowed to join The Registry. Also, recent tattoos and piercings have no effect on joining The Registry. [9]

Registries Abroad

In recent years, many other developed countries have developed bone marrow registries of their own. This is important, because people most often match with others in their own ethnic group. So, while there are no restrictions preventing potential transplant recipients from searching for matches on other countries’ registries, the recipient’s chances of finding
a match there are slim. If a patient discovers
that they need a BMT and their country has no
registry, they are left with the hope to find a
match in their family, or to search on registries
abroad, which can be slow, expensive, and often
times futile.

Fortunately, the number of registered donors
worldwide is growing as new countries begin
their own registries. Today, there are over 15
million registered donors in the world. [8] China
is a great example of a country with a young registry that is proving to be wildly successful.
The Chinese Marrow Donor Program was created in 2002, with only 6000 registered
donors that year. In 2008, that number was almost a million. Today, China has the world’s
third largest registry, only nine years after its inception. As of 2008, the CMDP has
facilitated over 1000 BMTs, including 50 for overseas patients in North America, Europe,
and other parts of Asia. [3]

DONORS

The Donation Process

The bone marrow donation process is probably the most misunderstood part of bone
marrow transplantation. Much of the general public believes it to be a painful process with
a long recovery time, when in reality, the use of anesthesia and pain medication makes the
practice not nearly as painful as one would assume. There are two major ways to donate:
the first is through liquid bone marrow which is harvested from the hip, and the second is
from peripheral blood stem cells, which is similar to donating blood. [10] PBSC donation
has grown in popularity in recent years, and is more common now than liquid marrow
donation.

Peripheral Blood Stem Cell Donation consists of taking blood out of one arm, filtering it
through a machine that collects blood stem cells, and returning the rest of the blood to the
donor in the other arm. Donors must prepare
for the procedure in the five days prior by
having injections, which stimulate the body to
increase the number of blood stem cells. [11]
PBSC is much less invasive than traditional
marrow donation, and is the preferred method
for donation if it is possible. The recipient’s
doctors determine what type of donation is
best.

The second way to donate bone marrow is
through liquid marrow from the hip. The donor is asleep under general anesthesia, and doctors puncture a small hole in one of the bones of the hip and then use a needle to extract liquid marrow from the soft inside of the bone. The donor generally experiences soreness for 2-3 days, and has returned to his or her normal activities in less than a week.

**Positive Side Effects**

While the positive effects of a BMT are obvious for recipients, donors also experience many positive side effects from sharing the gift of bone marrow. There is no medical benefit for the donors, but the emotional benefits are substantial and important to understand in learning about the donation process.

A study done on donor/recipient sibling pairs was conducted by the Pediatric Oncology Branch of the National Cancer Institute in Maryland, yielded results which shed light on how sibling donors feel about their experience after giving bone marrow to a brother or sister. Two thirds of the siblings polled said that the experience was positive for them, citing a “closer relationship with family members, sense of pride for donating, and feeling good or happy about donating.” [4] This date coincides with what doctors and the families of donors already know: that donating bone marrow is a rewarding and positive experience for the donors.

**Negative Side Effects**

Negative side effects are a real concern for potential donors, though most of the negative emotions reported by donors were in regards to the outcome of the transplant. In other words, the donors that reported “negative” side effects were referring to feeling guilty that their donation didn’t heal the recipient, and not the donation process itself. A common feeling for donors is that they are somehow responsible for the outcome of the transplant, when in reality, countless medical factors can influence whether or not a transplant is successful. About one in five donors in the National Cancer Institute’s study said they regretted that their bone marrow donation did not cure their sibling of cancer, as hoped. Finding out that their donation was unsuccessful can be very disappointing for donors, especially if the person they donated to is a family member. 15% of donor siblings polled felt guilty when their sibling experienced graft versus host disease as a result of the transplant. [4]

**Risks**

**Graft versus host disease (GVHD):**

A condition that occurs in approximately 1/3 of related donor and 2/3 of unrelated donors, in which the recipient’s tissues attack the transplanted stem cells or bone marrow. Acute symptoms include: abdominal pain, fever, rash, and weight loss. GVHD can also occur chronically, causing dry eyes and mouth, hepatitis, lung and GI tract problems, and rashes. Treatment for GVHD usually consists of the use of steroid medications to control symptoms. [12]
Though rare, severe complications have been seen in bone marrow donors. A study in Europe found the death rate for donors to be less than one in 10,000. “Severe adverse events” were noticed at a rate of 7.25 / 10,000 transplants. These events include heart attacks, pulmonary embolism, stroke, and serious infections. [5] Though these complications are very serious, the chance that they will occur is exceedingly low. You are more likely to be struck by lightning in your lifetime (odds: 1/6250 vs. <1/10,000) than you are to die from donating bone marrow. [13]

Ethics

As with all medical procedures, there are ethical dilemmas faced in preparing a donor and a recipient for a bone marrow transplant. The most common ethical question faced is regarding minor siblings of someone in need of a BMT. Since the best match for a potential recipient is usually a family member, siblings are often selected to donate bone marrow. What happens when the sibling is a child, and is incapable of making his or her own medical decisions?

In normal circumstances, parents are responsible for taking their children and making medical decisions to benefit their best interests. What happens if the case where the parents are responsible for both the potential donor and the potential recipient’s best interests? Parents must take both the physical and mental health of their children into account when making these types of decisions.

While there is no medical benefit for the donor, providing bone marrow or stem cells for a BMT can be very beneficial to the donor emotionally. [14] Even in cases where the transplant eventually fails, donors feel like they did their part to try to help their sibling. This can be very empowering for a child faced with a sick family member. If the transplant succeeds, the child is not faced with losing a brother or sister. This is why, oftentimes, parents choose to go through with a BMT, even if it involves some degree of pain and discomfort for the child donor. [15]

In cases where the parents are unable to act in the best interests of the child donor, a judge may appoint a child advocate to make medical decisions in the best interests of the potential donor. A child advocate is a person trained in dealing with children, sometimes a social worker.

My Sister’s Keeper

Pop culture brings us a story on parents torn between their donor and recipient children, and what happens when what is best for one is not best for the other. Author Jodi Picoult writes a story about a young girl, Kate, who is diagnosed with leukemia as a toddler. Her parents, faced with losing Kate, decide to have another child, Anna, chosen as an embryo because her DNA closely matched her sister’s, in order to harvest stem cells from Anna’s umbilical cord at birth. The resulting transplant sends Kate into remission for a short time, but eventually Anna is asked to donate more and more in order to save Kate. The story culminates in a trial as Anna sues her parents for medical emancipation when they ask her to donate a kidney to her sister and she refuses. [16] The novel and 2009 film depict the family’s struggle, giving the audience a realistic picture of how child advocates, lawyers, doctors, and parents struggle to make the best decisions for the child donor and recipient.
worker, whose only job is to act in the best interests of the child in question.

RECIPIENTS

Treatable Conditions

Bone marrow transplantation is not just for patients with leukemia. It can be used successfully in the treatment of several other cancers of the blood, such as:

- Hodgkin's disease
- Multiple myeloma
- Sarcoma
- Aplastic anemia

The similarity in all of these diseases, and the reason they are all treatable with a bone marrow transplant, is that they are all disorders of the blood producing cells, the body's supply of bone marrow. When the body's bone marrow is not working as it should, our ability to fight off infection (white blood cells), clot (platelets), and provide our muscles with oxygen (red blood cells) is impaired. When chemotherapy and radiation fail keep the cancer in remission, doctors and patients begin the search for a bone marrow donor.

Pre-transplantation Process

If a suitable match is found for the person in need of the BMT, the recipient must then undergo a pre-transplantation process to prepare his or her body for the donor's bone marrow cells. This process can be very dangerous for the recipients, since their entire immune systems must be disabled by chemotherapy and other drugs to prevent them from attacking the donor's bone marrow. If any of the recipient's immune cells remain, they will attack the donor marrow as "foreign." If this happens on a large enough scale, the donation fails and the recipient's body rejects the new bone marrow.

Donor responsibility comes into play at this juncture in the transplantation process. While no one is ever required to donate bone marrow, it is extremely important that the potential donor be committed to donating after the recipient begins chemotherapy and the pre-transplantation process. If the recipient's immune system is destroyed in anticipation of new, healthy bone marrow and that bone marrow doesn't come, he or she is at risk for serious infections and death.

The Transplant

Whether the donation was done through PBSCs or liquid marrow, the transplant procedure is much the same for the recipient. The patient receives the marrow or stem cells through an IV placed in the chest, called a central line. To an outsider, it might look like the patient is getting a blood transfusion.

Because the pre-transplantation process is often very hard on the recipient's body, the day
of the transplant can be both joyful and difficult. The recipient’s entire immune system is about to be replaced by new bone marrow cells, which will take up residence in the bones and start producing red and white blood cells soon. The process itself is over in a few hours, but the success or failure of the bone marrow transplant can ultimately affect the recipient for the rest of his or her life. Doctors gauge outcomes for BMTs by numbering days from the transplant, starting with day of transplant as “Day 0.”

CONCLUSION

The National Marrow Donor Program is responsible for facilitating over 30,000 transplants in the twenty years since its inception in 1987. Before the NMDP, very few, if any of these patients would have been able to find matches.

Though the process of matching potential donors and recipients of bone marrow transplants is complicated, joining the National Marrow Donor Program’s Be The Match registry is not. This quick, painless process can be the difference between life and death for someone affected with leukemia, Hodgkin’s lymphoma, Aplastic anemia, and a slew of other cancers.

The National Marrow Donor Program’s mission is to educate people on the truths about becoming a living bone marrow donor, and to register as many people as possible in hopes that someday, when faced with searching for a bone marrow donor, no one will ever have to worry about not finding a match.
BIBLIOGRAPHY


