Past and Future of Providing Matched, Unrelated Donors for Marrow Transplantation*

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ABSTRACT

Prior to 1979, bone marrow transplants were only performed with histocompatible sibling donors. Once it was established that histocompatible, unrelated donors could donate marrow for transplantation, the recruitment of such donors needed to be standardized. Blood donor centers had already identified the histocompatibility locus antigen (HLA) typing for donors who could be recruited to donate bone marrow.

Recruiting a large number of donors required systematic evaluation and testing according to defined standards which were published in 1988 by the National Marrow Donor Program (NMDP). Peripheral stem cell collection (PBS) has been added as a transplant source. It promises additional therapeutic modalities, such as gene splicing to address other than cancer therapy.

Introduction

Bone marrow transplantation has provided many patients facing death with a life-saving treatment for malignancy, which was not possible to provide prior to bone marrow transplants. Like the solid organ transplant, success of engraftment depends on patient-donor histocompatibility. Very few families today have more than 1 or 2 children, which often leaves the patient without a histocompatible sibling to donate an organ or bone marrow. Since the donation of bone marrow is not very traumatic and is easier to obtain than solid organs, the matched unrelated donor (MUD) is a solution to the problem.

To implement the process, the creation of a donor center and transplant center is very important, so that unrelated bone marrow donors would not be coerced into donating if the transplant center was in need of a donor. Donor centers had the additional advantage that these institutions are already extensively trained to serve volunteer blood donors. It was advantageous that at the same time blood centers had added histocompatibility testing for donors, providing patients with leukemia with HLA matched platelets collected by apheresis, from HLA matched volunteer donors. These skills would have to be acquired by entities that wanted to provide MUD donors for transplantation.

Standard writing organizations such as the American Association of Blood Banks (AABB) and the National Marrow Donor Program (NMDP) had not yet published standards for the process of providing MUD donors. This

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required the important aspects of the process to be defined for the Central Kentucky Blood Center (CKBC) in close cooperation with the University of Kentucky (UK) Bone Marrow Transplant Center (BMT).

Since no guidelines were available, the following steps were implemented:

1. Strict confidentiality,
2. Voluntary participation,
3. Assuring donor health,
4. Thorough counseling of the donor, and
5. Close networking with the transplant service.

In 1982, a total of 82 patients received transplants at the UK BMT with the following distribution: 80 received matched sibling donors (MSD), one a syngeneic donor, and one an autologous (AUT) donor. In 1988, CKBC provided the first MUD donor. It was a pleasure to lead the first donor through the intricate counseling process. Following the marrow collection, the donor, since it was his day off, spent it on his back underneath his automobile. This resulted in large, somewhat painful hematomas at the site of the marrow collection. No special therapy was required.

The NMDP Published Standards in December of 1988. In August 6, 1989, CKBC became an official NMDP Donor Center requiring CKBC HLA donor information transfer for those donors who agreed to be part of the NMDP.

The first NMDP donor was collected in 1991. To date, 40 individuals have been counseled, 28 had bone marrow collected at UK BMT. No donor backed out of the program. Patient death, donor deferral, or a better match found were the reasons that no donation was made. Since 1991, there has been a steady increase in MUD donor activity; if the 1997 activity continues, increasing numbers will have to be prepared to be a marrow donor (figure 1).

Over the years, transplant activity has been influenced by the transplant protocols available at the BMT units. Between 1989 and 1991, 53 percent of the transplants were provided by haplo-identical family members, such as siblings or parents (figure 2). Twenty percent were provided by MUD, and 22 percent by matched sibling donors (MSD). As already mentioned, today's family no longer has a large number of children, facilitating matched sibling donations in case of need. Looking at 63 consecutive transplants in 1995 & 1996, marked changes are revealed (figure 3). The MSD transplants have changed very little,
accounting for 29 percent; however, AUTO transplants rose sharply to 65 percent of the activity, and the use of MUD decreased to 6 percent.

The protocols for haploidentical donors have completely disappeared. New techniques, consisting mostly of peripheral blood stem cell collections (PBS) instead of marrow cells, provided autologous transplants replacing bone marrow. This is reflected in the large number of AUTO transplants being currently performed. Matched unrelated donors may also provide PBS for transplant and must meet the standards for bone marrow donors.
Standards for MUD selection for bone marrow or stem cell donations have constantly been refined. Only volunteers after full informed consent, ages 18 to 61 years, may donate. It violates the standards if HLA data are submitted without the consent of the donor. There must be the opportunity to ask questions and assurance that the donor may withdraw without prejudice. Confidentiality must be maintained. Concern about infectious diseases are the same as for blood donors, as is the testing. If a recipient is identified for a donor, additional testing is performed to assure histocompatibility. The HLA testing is also performed by the transplant center (TC) and all information is related to the coordinating center (CC). This assures maximal compatibility of donor and recipient.

Prior to the final physical examination, a donor information session is held. It is useful to make a video tape available to explain the transplant process as fully as possible. The tape made for us originally by a local television station (now replaced by NMDP tapes) frightened some donors because the bone marrow aspiration needle was distorted by the camera angle into a giant torture instrument. Bringing the aspiration needle to the counseling session so the donors could examine it, calmed the prospective donors.

If the potential donor has had a bad experience with general anesthesia, special consultation with the anesthesia professionals should be arranged. Donors handled by CKBC are examined by the outpatient facility of the UK, not the transplant service, where an anesthetist is available to answer all questions. If the medical evaluation demonstrates any abnormality, the details must be reported to the CC and TC in writing.

To collate all the test results to meet NMDP requirements, a checklist is essential, since the testing is done in a different institution. It has been our experience that results from the chest x-ray and the electrocardiogram (EKG) are most difficult to obtain in a timely fashion. All this material must be reviewed by the physician at the diagnostic center (DC) to prevent delay in transplanting. The donors height and weight are essential to assess the amount of marrow to be aspirated. It also assists to determine the feasibility of collecting the required number of autologous units. The same data are needed in preparation for stem cell collection.

The DC must make certain that the name of the donor is never used, only the NMDP number, to protect the identity of the donor.

A meeting of the donor and recipient is not encouraged. It is recommended that such meeting be postponed for a year. This meeting should only occur if both donor and recipient have a strong desire to do so and both must agree in writing. One needs to be aware of the impact a recipient’s death may have on the donor. The CKBC donor (KS), compatible with a one year old patient (BB), suffering from acute lymphoblastic leukemia, donated on 12 September 1994. The patient’s response to the transplant was excellent and one year later donor, recipient, and families met to become very close friends; they now vacation together.

The future of BM and PBS transplants is bright. Investigators are looking forward to being able to add gene splicing of autologous and unrelated PBS to correct genetic disorders. With the success in matching donors and techniques to enhance the collected cells, more patients will benefit from transplantation. A continuous, strong effort must be made to enlist potential donors, representing minorities, since the NMDP donor list clearly indi-

<table>
<thead>
<tr>
<th>Race Group</th>
<th>Number of Donors</th>
<th>Percent (%)</th>
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<tbody>
<tr>
<td>Caucasian/White</td>
<td>10,231</td>
<td>83.39</td>
</tr>
<tr>
<td>Black</td>
<td>1,839</td>
<td>14.99</td>
</tr>
<tr>
<td>Asian/Pacific Islander</td>
<td>86</td>
<td>0.70</td>
</tr>
<tr>
<td>Other</td>
<td>47</td>
<td>0.38</td>
</tr>
<tr>
<td>Hispanic/Latino</td>
<td>30</td>
<td>0.24</td>
</tr>
<tr>
<td>Native American</td>
<td>16</td>
<td>0.13</td>
</tr>
<tr>
<td>Unknown</td>
<td>13</td>
<td>0.11</td>
</tr>
<tr>
<td>Multiple Race</td>
<td>7</td>
<td>0.06</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>12,269</strong></td>
<td><strong>100.00</strong></td>
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icates underrepresentation by listing only 9 percent Black donors; CKBC has 14.99 percent registered, which is closer to the population distribution.

Summary

Experience has shown that matched unrelated donors providing bone marrow or peripheral stem cells for transplant are of great benefit to a patient in need. The donor selection process has provided safe and effective transplants which otherwise could not have been obtained, to save patients with fatal diseases.

References


CHECKLIST
STEPS NECESSARY TO CERTIFY A MATCHED UNRELATED DONOR (MUD) AND MEET REQUIREMENTS OF NATIONAL MARROW DONOR PROGRAM

1. The physician must perform a complete medical history and physical examination which includes the evaluation of the following test results:

- Complete blood count with differential and platelet count
- Urinalysis
- Electrolytes
- Urea nitrogen
- Creatinine
- Bilirubin
- EKG
- Chest x-ray
- Height
- Weight
- Pulse rate
- Blood pressure

2. Results of the donor medical history, physical examination and tests are to be forwarded in writing to the Central Kentucky Blood Center Medical Director, 330 Waller Avenue, Lexington, KY 40504.

NOTE: No name of donor is to be used. Use only NMDP ID number on all medical exam and lab forms. Perform only the requested tests in Step 1 above.