

November 1992

# BONE MARROW TRANSPLANTS

## National Program Has Greatly Increased Pool of Potential Donors



147887



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**Human Resources Division**

B-249015

November 4, 1992

The Honorable Edward M. Kennedy  
Chairman, Committee on Labor and  
Human Resources  
United States Senate

The Honorable Orrin G. Hatch  
Ranking Minority Member  
Committee on Labor and Human Resources  
United States Senate

The Honorable John D. Dingell  
Chairman, Committee on Energy  
and Commerce  
House of Representatives

The Honorable Norman F. Lent  
Ranking Minority Member  
Committee on Energy and Commerce  
House of Representatives

Each year, about 12,000 people are diagnosed with leukemia and other fatal blood diseases, many of whom might die without a bone marrow transplant. A bone marrow transplant is a procedure in which marrow is collected from a donor and injected into a patient's bloodstream so that the patient can then produce healthy blood cells. About two-thirds of the patients who might benefit from such a transplant have no related donor whose tissues are compatible. Because of this, many patients seek marrow donations from unrelated volunteers.

To help patients seeking transplants find compatible unrelated donors, the Congress authorized the establishment of a national registry of volunteer donors. In 1986, the U.S. Navy funded the National Marrow Donor Program's (NMDP) establishment through a contract to the American Red Cross in collaboration with two blood bank associations. The NMDP contract is now supervised by the Secretary of Health and Human Services.

In 1990, the Congress extended funding for the NMDP for 3 years through the Transplant Amendments Act (P.L. 101-616). Because the NMDP was a relatively new program in a developing medical area, the Congress also required us to report on several issues affecting patients' searches for

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unrelated bone marrow donors. In this report we address the following issues:<sup>1</sup>

- The NMDP's progress in recruiting volunteer marrow donors;
- The rationale for typing potential donors only partially for compatibility when they volunteer for the Registry;<sup>2</sup>
- The results of patients' searches for marrow donors and the cost of these searches to patients;
- The degree to which the NMDP is incorporating changes in bone marrow research and clinical practice into its program; and
- The role of federal funding in the NMDP's progress in these areas.

We also provide information about the privately funded American Bone Marrow Donor Registry in this report. (See app. VI.)

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## Results in Brief

The NMDP increased its Registry considerably from about 72,900 donors in December 1989 to about 560,900 donors in April 1992. Moreover, the proportion of minorities more than doubled from about 5.8 percent to about 14.2 percent during this period. This larger and more racially and ethnically diverse pool of donors helped improve the odds of finding a matching donor for patients who have rarer tissue types. However, the proportion of black and Hispanic potential donors on the Registry was still considerably less than their proportion in the U.S. population as of the 1990 U.S. Census.

If cost were not a consideration, potential donors could be fully typed for compatibility when they first volunteer for the Registry. However, new donors are usually only partially typed because it is more economical, especially since only a small portion of donors on the Registry are ever contacted for full typing.<sup>3</sup> A second typing test is generally conducted later, if a potential donor is identified as a possible match for a specific patient. But while donors are being fully typed—a process that can take several months—patients may deteriorate and die or develop major complications. To help reduce the search time for patients, the NMDP in 1991 began to fully type donors whose tissue compatibility types were less

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<sup>1</sup>The remaining issues are discussed in app. VII.

<sup>2</sup>Volunteers on marrow registries are not actually donors until they match patients and undergo marrow collection.

<sup>3</sup>Because many people, especially nonminorities, have common tissue types that appear frequently on the Registry, it is not economical to fully type every donor.

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common. As of April 1992, about 20 percent of the Registry's donors were fully typed.

Between September 1987 and July 1991, about 13 percent of the 5,600 searches conducted to identify an initial list of potential donors resulted in marrow transplants, and 20 percent of the searches were still active. The charge for a patient's search for a donor depended on the number of potential donors identified, the number of compatibility tests performed, and the transplant programs' charges. The median charge for a patient's donor search was about \$20,000 when the search resulted in a transplant. Patients' search costs were mostly covered by private or public insurance.<sup>4</sup>

The National Institutes of Health (NIH) and others are conducting research on key issues affecting bone marrow transplants using unrelated donors. The NMDP is participating in such research and is beginning to incorporate preliminary research findings into its program.

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## Background

In 1979, the first bone marrow transplant with an unrelated donor was performed. Since then, at least 1,700 patients worldwide have received marrow transplants from unrelated donors. Most of these transplants have occurred over the past 5 years. Although transplants from unrelated donors were experimental in the beginning, they have become the "treatment of choice" for certain diseases when no family member matches the patient. Survival rates for transplants using unrelated donors generally depend on the patient's disease, age, stage of disease at the time of the transplant, and degree of compatibility with the donor. According to preliminary research results based on limited data, 2-year survival rates ranged from 15 to 70 percent and generally averaged about 20 to 30 percent for chronic and acute leukemia.<sup>5</sup> (See also app. V on research.)

Bone marrow creates the body's blood cells, contains the cells responsible for the immune system, and is considered a tissue. For a bone marrow transplant to be potentially successful, certain blood cell proteins of both patient and donor must match each other as closely as possible. These blood cell proteins, known as Human Leukocyte Antigens (HLA), are determined by typing the white blood cells.

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<sup>4</sup>Transplant programs assess patients' ability to pay for the donor search and transplant. Our analysis of payment sources for donor searches included only searches on behalf of patients who met transplant programs' financial criteria.

<sup>5</sup>For transplants using both related and unrelated donors, 3 to 5 year survival rates ranged from 10 to 90 percent, depending on the patient's age, disease, and phase of disease.

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If the donor's HLA antigens are not compatible with the patient's, the transplant will fail. In determining matches, the most important HLA antigens are the A and B antigens and the DR antigens. Every human being has six of these antigens—three inherited from each parent. One test determines the HLA types for both the A and B antigens; another test determines the HLA types for the DR antigens.

Finding a compatible match is difficult or impossible for many patients, because some combinations of HLA antigens are extremely rare.<sup>6</sup> Since HLA combinations are genetically inherited, they tend to follow racial and ethnic lines. Because many racial and ethnic minorities have rarer and more varied HLA combinations, they find it difficult to identify compatible donors. The odds of finding a matching donor therefore rise as the number of people from the patient's own ethnic or racial group increases on the Registry.

The overall process of matching patients with potential donors consists of separate but interdependent activities. The first is the recruitment of a large pool of potential donors who may be a suitable HLA match for current or future patients needing transplants. The second is a particular patient's search for an HLA match from among registries of donors who have already been recruited. These registries of potential donors facilitate the patient's search. Worldwide, at least 950,000 donors are listed through more than 20 registries.

In the United States, the NMDP helps patients find matching donors.<sup>7</sup> A rapidly growing organization, the NMDP recruits and HLA types volunteer marrow donors, maintains a registry of potential donors, coordinates patients' searches for donors through to transplant, follows donors through the donation process until they have recovered, and allows researchers to use its database and affiliated organizations for research. Donors are recruited through blood bank programs, community drives—often organized by patients' families—and public health programs, among others. The NMDP's Registry of potential marrow donors is now the largest in the world, accounting for about half of the world's total.

If a patient seeks a transplant, the patient's physician initiates a preliminary donor search, usually through a transplant program, which is typically located at a major hospital. At the request of either transplant

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<sup>6</sup>Patrick G. Beatty and others, "Probability of Finding HLA-Matched Unrelated Marrow Donors," *Transplantation*, Vol. 45, No. 4, Apr. 1988, pp. 717-18.

<sup>7</sup>For a discussion of the privately funded American Bone Marrow Donor Registry, see app. VI.

programs or attending physicians, the NMDP conducts a preliminary search of its Registry to identify possible donors. After potential donors are identified through the preliminary search, only an NMDP-affiliated transplant program can request a formal search. During the formal search, donors are selected for further HLA typing to determine their compatibility with the patient. The NMDP's donor centers, which are primarily blood banks, maintain records on potential donors and often help recruit donors. These centers contact the donors and arrange for blood samples to be sent to NMDP laboratories for testing. If the tissues of donor and patient are compatible and the donor agrees, then a transplant can be performed.

To carry out patients' searches for donors, the NMDP coordinates a network of about 56 hospital transplant programs, 101 donor centers, and 7 recruitment groups. As of April 26, 1992, the NMDP had coordinated 1,185 marrow transplants between patients and unrelated donors.

Donors are usually typed in two phases: first, for HLA-A,B antigens, when donors volunteer for the Registry; then later for the HLA-DR antigens, usually when a donor's HLA-A,B antigens match a patient's. There are two types of costs involved in this process: the cost to the NMDP for recruiting and typing new donors for the Registry and the cost to the patient for further typing donors who initially match the patient. The NMDP is financed by charges to patients—through transplant programs—for conducting the donor search; by federal funds; and by charitable contributions. The NMDP's total revenue grew over the past 4 years from about \$5 million in 1988-89 to about \$37 million for 1991-92. In 1992, most of the NMDP's program fees supported services for patients, while most of the \$15.1 million in federal funds supported tissue typing and recruitment.

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## Scope and Methodology

To determine the NMDP's progress on recruitment, tissue typing, and research, we interviewed officials from the NMDP and other pertinent organizations. These organizations included the National Heart, Lung, and Blood Institute (NHLBI) of NIH; NMDP donor centers, transplant programs, and laboratories; the Naval Medical Research Institute (NMRI); and the International Bone Marrow Transplant Registry.<sup>8</sup> We also analyzed contracts, policies, reports, and other documents from these organizations. (See app. VIII for more details on our methodology.) In

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<sup>8</sup>Although the NMDP originally operated under a subcontract from the Office of Naval Research to the American Red Cross, by Oct. 1990 the NMDP had separated from the American Red Cross and NHLBI had assumed direct responsibility for the NMDP contract. The Office of Naval Research and NMRI continue to oversee the NMDP's use of U.S. Navy grant funds.

addition, we interviewed officials from the privately run American Bone Marrow Donor Registry and analyzed their reports, standards and procedures, and other documents. (See app. VI on the American Registry.)

To determine search activities and costs, we analyzed data from the NMDP data base on patients and donors for the period from September 1987 to July 1991 and sent a questionnaire to all NMDP transplant programs. Wherever possible, we updated information in the report, such as the number of donors recruited and the number of transplants performed. We conducted our review from March 1991 through April 1992 in accordance with generally accepted government auditing standards.

## Federal Funds Helped NMDP Increase Donor Registry

The NMDP increased its Registry with the help of federal funds for HLA typing starting in late 1989. The U.S. Navy provided the NMDP with two grants, totaling \$11 million, to recruit and HLA-A,B tissue type new marrow donors, especially minorities; to match funds raised by families of patients to HLA-A,B tissue type new volunteers for the NMDP Registry; and to cover the DR-typing costs of potential donors so as to increase the number of fully typed donors on the Registry.<sup>9</sup> In addition, NHLBI subcontracts to donor centers provided a mixture of tissue typing equipment and funds to cover the costs of HLA-A,B typing new donors. Under the NHLBI subcontracts, potential marrow donors were to be recruited from among those who were donors to whole blood programs. Funds from the NHLBI totaled \$1.26 million for tissue typing as of March 1992. (See app. I.)

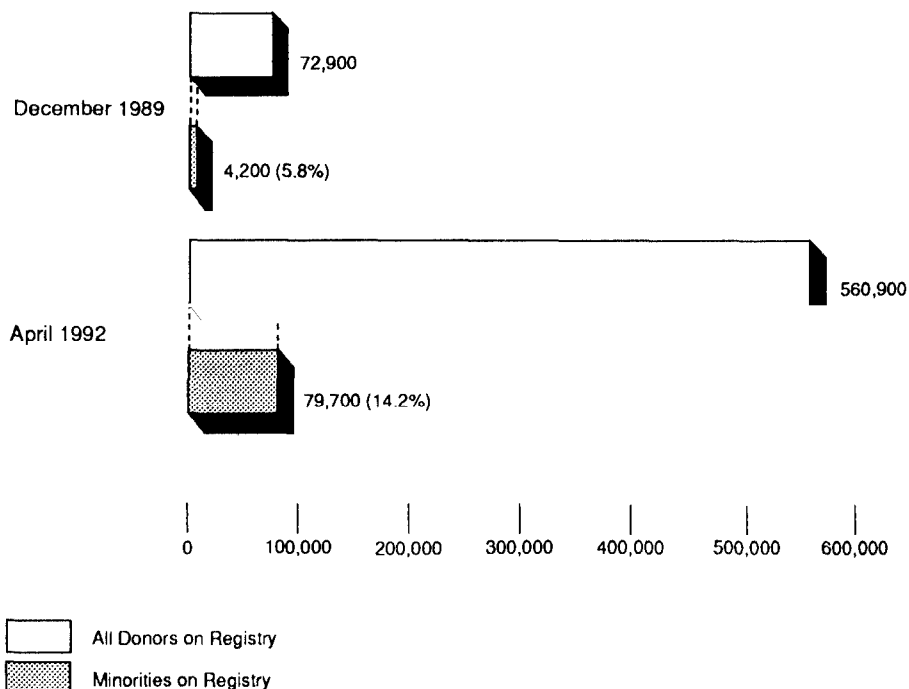
## NMDP Greatly Increased Donor Pool but Minorities Still Underrepresented

The NMDP Registry rose from 72,888 donors in December 1989 to 560,871 in April 1992. The recruitment of racial and ethnic minorities—because of the need for variety in the HLA combinations available on the Registry—represented a central focus in recruitment: the NMDP increased greatly the number of minorities on the Registry, from 4,192 donors in December 1989 to 79,743 donors in April 1992, using federal funds for HLA typing that specifically targeted minorities. Significantly, the NMDP also more than doubled the percentage of minorities on the Registry: As of April 1992, minorities constituted 14.2 percent of the Registry's 560,871 donors, up from 5.8 percent in December 1989. (See fig. 1.)

<sup>9</sup>We discuss the use of DR-typing funds in the next section of this letter.



**Figure 1: Minorities Have Increased on Registry in Both Number and Percentage Since 1989**



In April 1992, 75.6 percent of potential donors were Caucasian, 4.1 percent were black, 4.6 percent were Asian, 4.1 percent were Hispanic, 0.9 percent were Native American, and 0.6 percent were of other races.<sup>10</sup> Despite the increase in minority donors from 1989, the proportion of minority potential donors on the Registry remained less than the proportion of minorities in the U.S. census population as of 1990. This is especially true of black and Hispanic potential donors. The NMDP's goal is to recruit 1 million donors, with racial and ethnic proportions to match those in the 1990 U.S. Census. No time frame has been set for achieving this goal.

### Matching Funds Helped Recruit New Donors for Registry

More than half of the donors on the NMDP Registry were recruited through drives in communities that highlighted specific patients who sought transplants. Organized by families, friends, and community organizations, these recruitment drives also involved fund-raising to cover the costs of typing new donors for the Registry. At a congressional hearing in March 1990, patients' families testified about the pressures they had faced to raise

<sup>10</sup>These figures represent percentages of total donors. About 10 percent of potential donors either declined to identify their race or their races were unknown.

funds and recruit potential donors for the NMDP. In order to alleviate these pressures, the Transplant Amendments Act of 1990 provided funding so that the NMDP would no longer have to rely on private fund-raising drives to cover the cost of tissue typing potential donors for the Registry.

Beginning in 1990, the federal government began to provide the NMDP with dollar-for-dollar matching funds to assist such families and increase the donor Registry. These funds paid for 50 percent of the costs for A,B typing donors at such drives, up to a total of \$25,000 per family. Twenty-one families raised \$25,000 each to organize drives and A,B type new donors for the Registry. Although drives organized by families remain a key means of recruitment for the NMDP, the NMDP is beginning to sponsor more systematic drives through service, community, and special NMDP recruitment organizations.

## Partial Typing Is Economical but Slows Search for Donor

New donors are usually typed only for the HLA-A,B antigens when they volunteer for the NMDP Registry, despite the delay this approach creates later for patients, who generally need to find matching donors as soon as possible. The test for the A,B antigens provides the first level of information needed to determine compatibility. The test for the DR antigens is essential to more fully determine tissue compatibility for a transplant. (See app. II.)

There are two reasons for partially typing new donors. First, the test for the A,B antigens costs less than the test for the DR antigens. Second, it is not economical to fully type all donors to the Registry because many people have common HLA combinations—especially nonminorities. Many nonminority patients could therefore identify several donors on the Registry who would have HLA combinations to match their own. If all donors on the Registry were given both HLA-typing tests, the tissue typing costs would increase greatly, and to a certain extent unnecessarily, given the large number of people with common HLA types.

However, patients with more acute diseases or minorities with less common HLA combinations may deteriorate and die, or develop major complications, while potential donors are being DR typed during the search. The amount of time to conduct a search depends on (1) the number of potential donors who need to be DR typed to determine whether a match exists and (2) the time it takes donor centers to contact potential donors, obtain their consent, and have the DR typing performed. The DR typing phase alone can account for several months of a patient's

total search time. Other factors affecting the length of the search include the time needed to perform other compatibility tests and decisions made by the transplant program on how to proceed with the search.

## Federal Funds Helped Increase DR-Typed Donors

To help reduce the search time for patients with less common HLA types, the NMDP began in January 1991 to DR type donors—mostly minorities—who have rarer A,B combinations. Federal funds played a key role in having such donors DR typed. In addition to this approach, the NMDP began in February 1992 to collect and store extra blood from new donors for DR typing later if a donor is a potential match for a patient. Having a sample of the donor's blood at the laboratories would speed up the patient's search time because donor centers would not need to schedule appointments with donors to obtain blood samples for DR typing.

The number of DR-typed donors on the Registry doubled from 46,265 in January 1991 to 109,749 in April 1992. The percentage of DR-typed donors also increased from 17.5 percent of the donors on the Registry in January 1991 to 19.6 percent in April 1992. Federal funds covered the DR-typing costs for about 27 percent of all of the donors who were DR typed during this period.

## Donor Searches Resulted in a Small Number of Transplants

Although the number of transplants has been increasing each year, most patients who initiated preliminary searches of the Registry did not receive transplants. Of about 5,600 preliminary requests to search the Registry between September 1, 1987, and July 18, 1991,<sup>11</sup> about 3,500 searches continued formally to more fully determine the compatibility between donor and patient. Patients discontinued preliminary searches for donors for financial, genetic, medical, and personal reasons. The NMDP is currently sponsoring research to learn more about why preliminary searches were discontinued. (See app. III.)

According to our analysis of the NMDP database, of the 3,479 formal searches begun from September 1, 1987, to July 18, 1991, about 20 percent, or 724 searches, resulted in a bone marrow transplant.<sup>12</sup> About a third of the formal searches were still active as of July 18, 1991, and 47 percent, or 1,622, of the formal searches were canceled. For the 1,622 searches that

<sup>11</sup>Search outcomes are from our analysis of NMDP's database on Registry donors and on patients conducting searches in this period. (See app. VIII on our methodology.)

<sup>12</sup>As of April 6, 1992, patients initiated 9,607 preliminary searches and 5,475 formal searches that resulted in 1,168 transplants.

were canceled, 37 percent of the patients had died; 51 percent chose other treatments, such as chemotherapy; and 12 percent discontinued for personal reasons. The search for an unrelated donor generally lasted for 5 to 6 months, including DR-typing time.

## Donor Searches Cost Thousands and Were Often Covered by Insurance

The median charge<sup>13</sup> to the patient for NMDP services was about \$20,000 for searches that resulted in a transplant and about \$3,500 for searches that were canceled.<sup>14</sup> The search charges varied widely, first, because some searches were shorter and required fewer donor tests, while others took longer and required numerous tests and NMDP services, and second, because transplant programs charge patients different amounts for NMDP services. Charges for the donor search were as high as \$73,113 for one patient who received a bone marrow transplant and \$84,600 for one patient whose search was canceled. In addition to NMDP services, transplant programs also conducted further medical testing, such as confirming the patient's HLA antigens. Search charges did not include the charges to the patient for the bone marrow transplant, which were additional. The median cost of an unrelated bone marrow transplant was about \$139,000, according to a 1989 NMDP survey of its transplant programs. (See app. IV.)

## Private Insurance Paid for Many Donor Searches

During the first half of 1991, the costs of many patients' searches for donors were covered by private insurers, according to our survey of 43 transplant programs.<sup>15</sup> Private insurers paid for all or most of the charges for 50 percent of the searches initiated during the first 6 months of 1991. Other sources, such as hospitals, charitable funds, and state government funds, covered 20 percent of the searches. Medicaid and Medicare together covered 15 percent of the searches, and patients without insurance assistance paid for 10 percent of the searches. Five percent of the searches were unreimbursed during the first half of 1991.

<sup>13</sup>Charges for donor searches usually start at the formal stage, with requests for further testing of donors. A few transplant programs charge fees to initiate preliminary searches as well.

<sup>14</sup>The transplant programs we surveyed charged patients between 0 and \$31,600 for marrow procurement, which explains the higher average cost for a search resulting in a transplant.

<sup>15</sup>Most private insurers pay for bone marrow transplants, according to the Health Insurance Association of America, Insurance Coverage for Organ and Tissue Transplants (Washington, DC: Nov. 1989).

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## NMDP Is Beginning to Incorporate Research Findings

Bone marrow transplantation is an evolving treatment whose effectiveness and techniques are being studied by researchers through the NMDP, NIH, and other organizations. The NMDP participates in research by approving researchers' access to its database, member organizations, and donors. The NMDP approved research on key areas that were in line with the NMDP's research priorities and that have potential implications for the marrow donor program. These research areas were the (1) outcomes of bone marrow transplants that use unrelated donors, (2) motivation of marrow donors, (3) safety of marrow collection for donors, (4) process of searching for a donor, (5) probability of finding donors whose HLA combinations match the patients', and (6) use of deoxyribonucleic acid (DNA) technology to perform HLA-DR typing. (See app. V.)

The NMDP is responding to early research results of some projects by beginning to, or planning to, incorporate what researchers are learning about outcomes, probabilities, and other issues into the organization's policies and practices. Some research, such as using DNA technology to perform HLA-A,B typing, is promising for possibly improving match criteria and technology.

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## Conclusions

The NMDP has made significant progress in the 5 years since it began search operations in 1987. During this period, the NMDP recruited more than half a million volunteer marrow donors; increased considerably the number and proportion of minority donors on the Registry; coordinated more than 1,000 bone marrow transplants for patients using unrelated donors; sponsored research on issues directly affecting the NMDP program, patients, and donors; and revised its practices and procedures in accordance with experience and early research results. As the bone marrow transplant procedure became better known and established, the number of donor searches and the number of transplants using unrelated donors rose steadily. Federal funding for tissue typing facilitated the rise in donors since 1990 and especially the broadening of its racial and genetic distribution.

Despite the Registry's rapid growth, the proportion of black and Hispanic potential donors still lagged considerably behind their proportions in the U.S. population. The NMDP's goal is to achieve a racial and ethnic distribution equal to the proportions in the 1990 U.S. Census. To achieve this, the NMDP will have to at least double the proportion of blacks and Hispanics on the Registry. Although the number of transplants increased, the proportion of searches that culminated in a bone marrow transplant

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did not change markedly from 1987 to mid-1991. As of July 1991, 13 percent of the patients who initiated a search for a donor obtained a marrow transplant. This narrowing of the funnel occurred for many reasons—financial, genetic, medical, and personal. Research on HLA matching and other factors affecting the patients' search, such as difficulties in finding a suitable donor, may help improve the outcomes of donor searches and of marrow transplants using unrelated donors.

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## Agency Comments

We met with officials from NHLBI and discussed the report's facts and conclusions. We provided pertinent segments of the report to NHLBI, the NMDP, and the American Registry, and incorporated changes where appropriate.

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We are also sending copies of this report to the NMDP, NHLBI, the American Registry, and other interested parties. We will make copies available to others on request.

Please contact me at (202) 512-7118 if you or your staff have any questions. Major contributors to this report are listed in appendix XI.



Mark V. Nadel  
Associate Director, National and  
Public Health Issues



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**Abbreviations**

DNA	Deoxyribonucleic acid
GAO	General Accounting Office
GVIHD	Graft-versus-host disease
HLA	Human Leukocyte Antigen
IBMTR	International Bone Marrow Transplant Registry
MLC	Mixed Lymphocyte Culture
NHLBI	National Heart, Lung, and Blood Institute
NIH	National Institutes of Health
NMDP	National Marrow Donor Program
NMRI	Naval Medical Research Institute



# NMDP Greatly Increased Donors on Registry From 1989 to 1992

When the NMDP began operations in 1986, it had no resources to fund tissue typing. Because of this, the cost of typing donors' tissues was an impediment in recruiting donors for the Registry.<sup>1</sup> With the help of federal funds from the U.S. Navy and NHLBI, the NMDP increased substantially the number of HLA-A,B typed donors on the Registry, especially minority donors,<sup>2</sup> and assisted families of patients who recruited donors for the Registry.

## Recruitment Hindered Initially Because No Funds for Typing

When the NMDP was established, no funding was provided for HLA-A,B tissue typing because it was thought that apheresis<sup>3</sup> blood donors—who were already HLA typed—would serve as the primary source of the 60,000 marrow volunteers needed. Fewer apheresis donors than expected volunteered for the Registry, however, and by November 1988, the Registry had fewer than 30,000 donors recruited—far short of its 60,000 goal. In January 1989, when the NMDP began to recruit from other sources in order to enlarge the registry, the cost to A,B type donors became an issue.

## Federal Funds Provided for Hla-Typing and Recruitment

Starting in late 1989, the NMDP began to help cover the costs to HLA-A,B type new donors,<sup>4</sup> using new funding for this purpose from the federal government. NHLBI provided the NMDP with \$1.26 million from November 1989 through March 1992 to A,B type new donors.<sup>5</sup> Starting in 1990, the U.S. Navy provided the NMDP with \$11 million in grants for typing and recruitment. (See table I.1.)

<sup>1</sup>Unless otherwise noted, we will use the term "donors" in this report, instead of "potential donors," to refer to volunteers for the NMDP and other marrow registries. However, volunteers on marrow registries are not actually donors until they match patients and undergo marrow collection.

<sup>2</sup>Minorities are defined as blacks, Hispanics, Asians, and American Indians in the Navy's and NIH's contracts with the NMDP. The NMDP is considering specifying its race and ethnic categories much more broadly to help identify better HLA matches. (See app. V.)

<sup>3</sup>Apheresis is a special type of blood donation in which a portion of blood is separated out and the remainder is retransfused into the donor. Apheresis donors donate blood regularly and are well known to the blood banks. NMDP donor centers are typically affiliated with blood banks.

<sup>4</sup>See app. II for discussion of HLA laboratory typing costs.

<sup>5</sup>From May 1989 through April 1992, NHLBI provided the NMDP with \$17.1 million under the NMDP's contract with NHLBI. Other uses of the funds included program administration, payments to NMDP donor centers for recruitment activities, operating and redesigning the Registry's database tracking system, and research.

**Appendix I  
NMDP Greatly Increased Donors on  
Registry From 1989 to 1992**

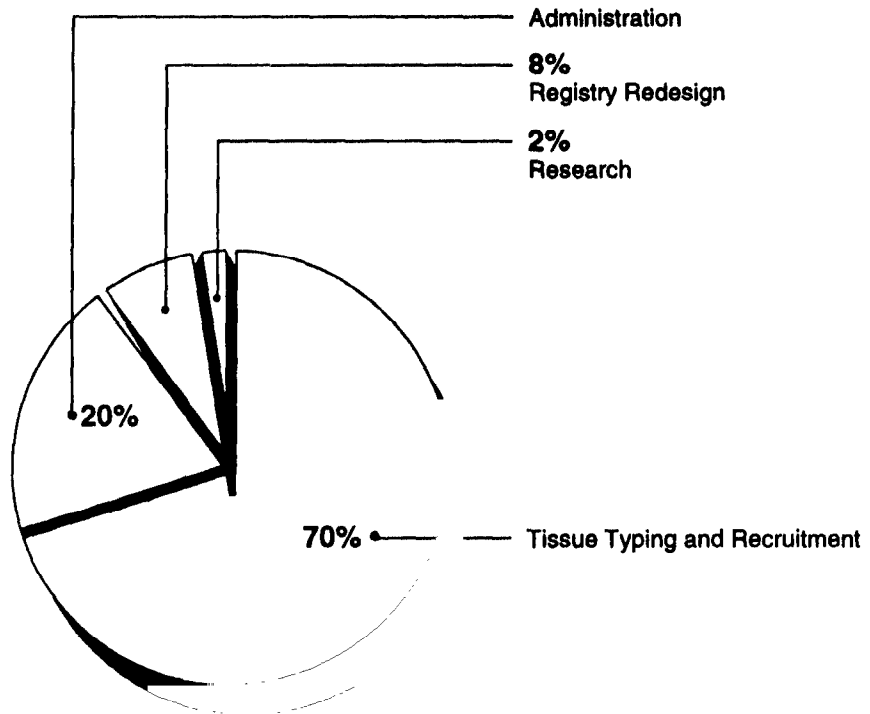
**Table I.1: Federal Funding for HLA Tissue Typing, 1989-92**

NHLBI Whole Blood Subcontracts— \$1.26 million (as of Mar. 1992)	Under these subcontracts, selected NMDP donor centers recruited and typed potential marrow donors for the Registry from the pool of regular whole blood donors at blood banks. The first subcontract ran from November 1989 to April 1991; the second, from August 1991 through April 1992. The second subcontract targeted minority donors for recruitment.
First U.S. Navy Grant—\$4.50 million (Aug. 1990-Sept. 1991)	This U.S. Navy grant provided the NMDP with funds for recruiting and A,B typing donors, especially minorities, through different means, such as family matching and corporate drives in communities. It also provided funds for DR typing donors with less common HLA combinations, especially minorities. Some administrative costs for recruitment, such as developing public education materials, were covered as well.
Second U.S. Navy Grant—\$6.50 million (Aug. 1991-Aug. 1992)	Under this U.S. Navy grant, most of the funds provided to the NMDP were for recruiting and A,B typing donors, through different means, including family matching, corporate, and community drives. It funded the DR typing of minority donors and others with less common HLA combinations, as well as a pilot program for DR typing using molecular level DNA techniques.
	The grant provided some funds for the NMDP's recruitment groups, for public education materials, and for service and community center recruitment.

From May 1, 1991, through April 30, 1992—NMDP's fiscal year 1992—70 percent of the \$15.1 million in federal funds supported donor recruitment and HLA-A,B and DR tissue typing. (See fig. I.1. Data supporting this and other figures appear in appendix IX.)

**Appendix I  
NMDP Greatly Increased Donors on  
Registry From 1989 to 1992**

**Figure I.1: Most Federal Funds Supported Tissue Typing and Recruitment in Fiscal Year 1992**



**Notes:**

1. Funds represent the NMDP's fiscal year 1992, from May 1, 1991, through April 30, 1992.
2. Federal funds consist of \$9.9 million in contracts with NHLBI and \$5.2 million in grants from the U.S. Navy.

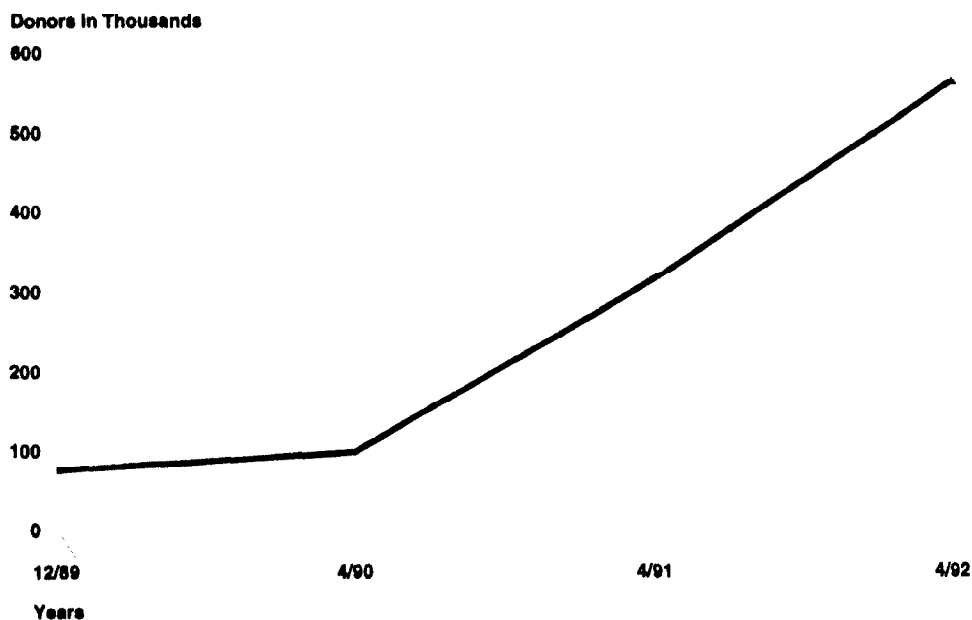
**NMDP Greatly Increased Donors on Registry, but Minorities Still Underrepresented**

With the help of federal funds,<sup>6</sup> the number of donors on the NMDP Registry rose rapidly from 72,888 donors in December 1989 to 560,871 in April 1992. (See fig. I.2.) Federal funding paid wholly or partly for the HLA-A,B typing of 168,094 donors—34.4 percent of donors who were recruited during this period.

<sup>6</sup>Other factors that contributed to this increase were physicians' increased familiarity with the treatment, media publicity about particular patients who were searching for donors, and, less directly, the Nobel Prize awarded to Dr. E. D. Thomas in 1990 for his work on bone marrow transplantation.

**Appendix I  
NMDP Greatly Increased Donors on  
Registry From 1989 to 1992**

**Figure I.2: Donor Registry Grew Rapidly From December 1989 to April 1992**



**NMDP More Than Doubled Percentage of Minorities on Registry**

Because many minorities have rarer and more varied HLA combinations and find it difficult to find compatible donors, recruiting racial and ethnic minorities is a central focus in NMDP's recruitment of donors. Minorities on the Registry rose from 4,192 donors in December 1989 to 79,743 in April 1992. During this period, the NMDP also more than doubled the percentage of minorities on the Registry, from 5.8 percent in December 1989 to 14.2 percent of the Registry's 560,871 donors in April 1992. Of these 560,871 total donors on the Registry, 75.6 percent were Caucasian, 4.1 percent were black, 4.6 percent were Asian, 4.1 percent were Hispanic, 0.9 percent were Native American, and 0.6 percent were of other races.<sup>7</sup>

Minority representation on the Registry increased largely with the help of federal funds that specifically targeted minority donors. Forty percent of typing funds from NHLBI were provided to NMDP donor centers to pay for laboratory typing materials and other costs to HLA-A,B type minority donors; two Navy grants paid for the laboratory typing costs to HLA-A,B type minority donors. Between December 1989 and early 1992, the NMDP recruited and typed 48,755 minority donors using these funds—more than half of the minorities recruited during this period. (See table I.2.)

<sup>7</sup>These figures represent percentages of total donors on the Registry. Race or ethnic group was unknown for about 10 percent of potential donors.

**Appendix I  
NMDP Greatly Increased Donors on  
Registry From 1989 to 1992**

**Table I.2: Minority Recruitment Under  
Federal Funding, 1989-92<sup>a</sup>**

<b>Type of funding</b>	<b>HLA-A,B typed</b>
NHLBI-whole blood I <sup>b</sup>	988
NHLBI-whole blood II	3,307
First Navy grant	29,073
Second Navy grant	15,387
<b>Total</b>	<b>48,755</b>

<sup>a</sup>All data are final except for the second Navy grant, for which the latest data available are from March 31, 1992. The grant ended in August 1992.

<sup>b</sup>Although NHLBI's first whole blood subcontract recruited the minorities cited here, the subcontract did not specifically target minorities in recruitment.

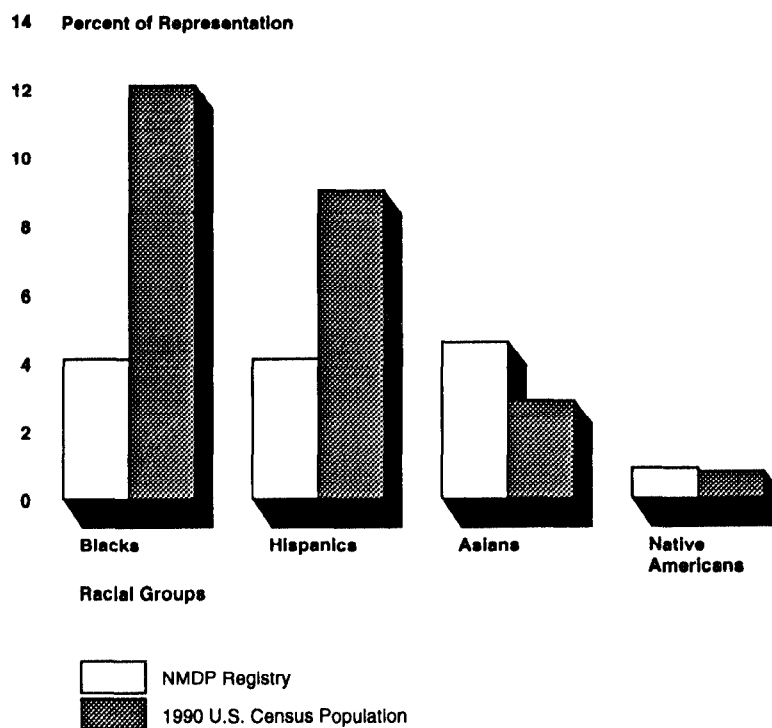
With the increase in minorities to 14.2 percent of all donors, the percentage of minorities on the Registry was close to their proportion among patients conducting formal searches for donors. Despite these gains, minorities remained underrepresented on the Registry compared with their proportions in the population. In the 1990 U.S. Census, minorities ranged from about 20 to 29 percent of the total population.<sup>8</sup> The percentage of blacks on the NMDP Registry was 4.1 percent, far lower than the 12.1 percent in the U.S. Census. Similarly, the percentage of Hispanics on the Registry was 4.1 percent, as compared to 9 percent in the U.S. Census. (See fig. I.3.)

<sup>8</sup>In the 1990 U.S. Census, nonwhite races constituted about 20 percent of the population. Hispanics were not identified in this breakdown as a race, however. In a separate breakdown of the U.S. population into persons of Hispanic and non-Hispanic origin, Hispanics constituted 9 percent of the population. Minorities in the U.S. Census could therefore represent a range of from 20 to 29 percent of the population, depending on how Hispanics classified themselves racially.



**Appendix I  
NMDP Greatly Increased Donors on  
Registry From 1989 to 1992**

**Figure I.3: Blacks and Hispanics on the Registry Are Less Than Their Percentages of the U.S. Population**



Notes:

1. Race or ethnic group was unknown for about 10 percent of potential donors on the Registry.
2. Persons of Hispanic origin may be of any race.

Because research indicates that a large, highly diverse registry is more likely to be effective in matching patients with donors,<sup>9</sup> the NMDP is continuing to target minorities in its efforts to recruit and HLA-type donors. With more than half a million donors on the Registry as of April 1992, the NMDP's goal is to recruit 1 million donors, with racial and ethnic proportions to match those in the 1990 U.S. Census. No time frame has been set for this goal.

<sup>9</sup>Since the late 1980s, the projections for the number of donors needed on a marrow registry have increased with analyses of the variability of HLA in people of different races and ethnic groups. (See app. V.)

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## **More Than Half of Donors Recruited Through Community Drives**

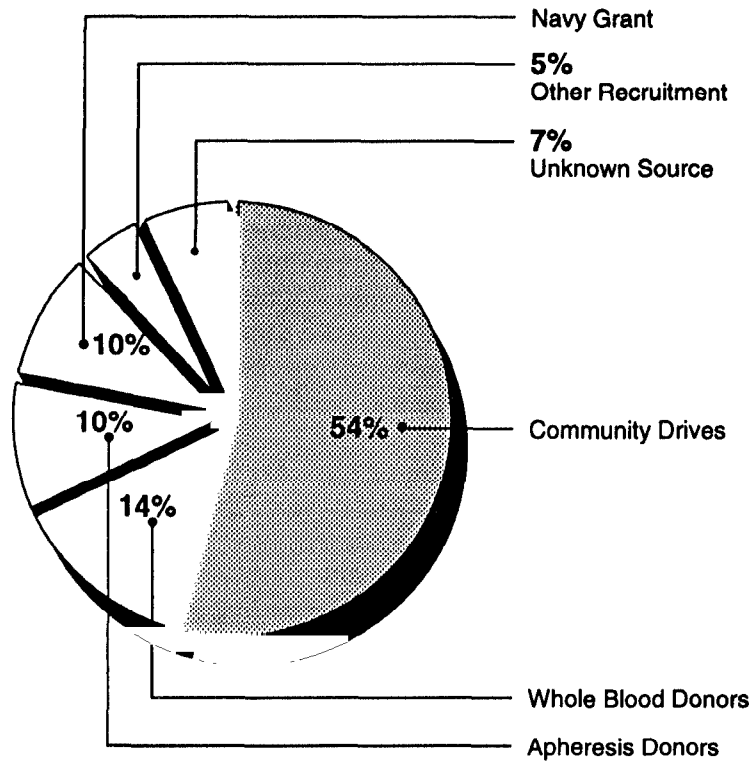
Over half of all NMDP donors were recruited through community drives from September 1987 to July 1991.<sup>10</sup> (See fig. I.4.) Community drives were initiated primarily by patients' families and friends, usually working with NMDP donor centers. In some cases, donor centers also sponsored drives featuring several local patients. Patients' families organized donor recruitment drives when no suitable match was found on the Registry. Some of these families and patients became heavily involved in fund-raising efforts to cover the costs of the initial stage of tissue typing donors for the Registry.

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<sup>10</sup>These data are based on our analysis of the NMDP's database until July 1991. See app. VIII for a description of our database methodology.

**Appendix I  
NMDP Greatly Increased Donors on  
Registry From 1989 to 1992**

**Figure I.4: More Than Half of NMDP Donors Were Recruited Through Community Drives**



**Notes:**

1. Data represent the period from September 1987 to July 18, 1991, and a total of 392,863 donors.
2. "Other" includes public health department, family, and corporations. "Navy Grant" refers primarily to minority recruitment.

In 1989, community drives represented 60.7 percent of all known sources of donors recruited in that year. Between January 1, 1991, and July 18, 1991,<sup>11</sup> the proportion of donors recruited through community drives dropped to 53.6 percent. In the same period of 1991, 26.7 percent of donors were recruited through initiatives designed to recruit minorities; 14.1 percent were recruited from whole blood and apheresis donors; and 5.6 percent represented other means of recruitment, such as through public health programs and corporate drives. A key recruitment goal for the NMDP

<sup>11</sup>July 1991 is the latest data available from our analysis of the NMDP's database. (See app. VIII.)

is “to reduce and finally eliminate the need for family crisis recruiting,” according to the NMDP.

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## Federal Matching Funds Increased New Donors on Registry

In March 1990, patients’ families testified about the pressures they had faced in raising funds and recruiting donors for the NMDP Registry when members of their families had been unable to find a matching unrelated donor. The Senate Committee believed it unacceptable for the burden of recruiting potential donors to be placed on individuals who faced life-threatening illnesses and their families. Therefore the act provided funding to the NMDP so that the NMDP would not have to rely on private fund-raising drives to cover the cost of typing potential donors for the Registry.

Beginning in 1990, the NMDP used grants from the U.S. Navy to match, dollar-for-dollar, funds that families raised to A,B type new potential donors for the NMDP Registry. Matching funds were provided if a member of the family could not find a compatible donor on the Registry and if families were willing to “go public” and sponsor drives to recruit donors to the Registry. As of June 1992, 209 families had used matching funds. Twenty-one of these families used matching funds that reached the \$25,000 grant limit for each family to organize recruitment drives for the Registry.

Most federal family matching funds were used on behalf of nonminority families. For minority families who organized community drives, the costs for typing donors were covered 100 percent under federal funding that targeted minority recruitment instead of 50 percent under the family matching program. Federal assistance to families using matching funds added 79,682 donors to the Registry by the end of March 1992.

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## Other Means of Recruitment and Fund-Raising

The NMDP has several approaches to cover typing funds and thereby increase donors on the Registry. These approaches include (1) sponsoring corporate fund-raising and recruitment drives; (2) asking donors to become apheresis or whole blood donors; (3) allowing donors to contribute the A,B typing costs themselves; and (4) recruiting through nonprofit NMDP organizations, called recruitment groups, as well as through the Marrow Foundation, a separate nonprofit entity.

Recruitment groups are nonprofit corporations that recruit donors for the NMDP Registry through individual and community recruitment drives.

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**Appendix I  
NMDP Greatly Increased Donors on  
Registry From 1989 to 1992**

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These groups are eligible to receive \$28 from the NMDP for every minority donor recruited and \$10 for every Caucasian recruited. Recruitment groups are free to raise funds to support their operational expenses. As of July, 1992, there were seven recruitment groups: the Judie Davis Marrow Donor Recruitment Program, Special and Deserving Outreach Foundation, the Asian American Donor Recruitment Program, Asians for Miracle Marrow Matches, the Bone Marrow Resource Foundation, Inc., Life-Core, and Bone Marrow Wanted International. Three of the seven groups target minorities in recruiting.

The Marrow Foundation was established in the fall of 1991 with several goals. These goals were to support the NMDP in increasing the Registry, to assist patients in financial need, and to support research on the methods and applications of marrow transplantation.

# NMDP Acts to Increase Number of Fully Typed Donors

The NMDP generally types potential volunteer donors only for the HLA-A,B antigens because it is more economical, especially since potential donors who have common HLA types may never need to be contacted as a possible match for a patient. Yet this approach creates delays later for patients during the donor search. With the help of federal funding for HLA-DR typing, the NMDP increased the number of donors on the Registry who were fully typed, especially minorities, in order to reduce the time that patients need in their search for a matched donor. As of April 1992, 19.6 percent of donors on the NMDP Registry were fully typed for the A,B and the DR antigens.<sup>1</sup> Most of these donors were DR typed in response to requests for DR typing from patients conducting searches.

## Costs Drive Two-Phase Tissue Typing

If cost were not a consideration, donors could be fully typed for the A,B and DR antigens when donors first volunteer for the NMDP because patients' physicians could then identify HLA matched donors as soon as possible. Instead, donors are generally typed only for the HLA-A,B antigens when they first register as potential donors with the NMDP. Later, if a donor's A,B antigens match a specific patient's, the donor is typed for compatibility between the patient's and the potential donor's DR antigens.

Historically, the practice of partially HLA typing new volunteer donors, and of later completing the HLA typing, occurred for several reasons. First, the typing test for the HLA-A,B antigens is less expensive than the test for the HLA-DR antigens. About twice as many donors, then, could be partially typed as fully typed, for about the same costs. Secondly, typing only for HLA-A,B antigens avoids the unnecessary costs of DR typing many donors on the Registry who have very common HLA-A,B types. Many of these donors may never be contacted for DR typing during a search to match a patient. To illustrate, about 85 percent of donors on the Registry had never been contacted for DR typing for a patient during searches conducted between September 1987 and July 1991. Finally, no federal funds were available until 1990 specifically to DR type new donors.

Typing for the A, B, and DR antigens is primarily performed using serologic<sup>2</sup> techniques. Serologic typing costs for these antigens can be reduced only to a limited extent because such typing offers few economies

<sup>1</sup>The portion of the Registry that is fully typed actually fell after January 1990, when it was 33 percent, because most efforts went to increase the number of donors on the Registry. However, the number of fully HLA-A,B, and DR typed donors quadrupled during this period, from 25,848 donors fully typed to 109,749 donors fully typed as of the end of April 1992.

<sup>2</sup>Serologic typing refers to typing tissues for the HLA antigens from the antigen-antibody reactions of cells.

of scale. Current serologic techniques require live white blood cells, are labor-intensive, need carefully trained specialists, and are not subject to automation. An additional difficulty is that serologic techniques use reagent<sup>3</sup> serum from pregnant or recently pregnant women, whose numbers are limited. The presence of antibodies specific for HLA in the serum of postpartum women is often transient as well, which makes the collection of high-quality sera an ongoing, large-scale undertaking.<sup>4</sup>

Laboratory technicians base their interpretation of the typing results on the percentage of dead cells and live cells in the test trays. DR typing costs more than A,B typing because it is more complex: DR antigens are more difficult to detect than A,B antigens using currently available typing techniques. DR typing therefore requires more interpretation and technical skill and takes longer.

Under the NMDP's 1991 subcontracts with laboratories, the costs for typing donors averaged \$55 for the HLA-A,B antigens and ranged from \$45 to \$90 per sample.<sup>5</sup> For the HLA-DR antigens, the costs to type donors averaged \$89 and ranged from \$50 to \$125 per sample.

## NMDP Increased DR-Typed Donors to Reduce Delays

Patients with less common HLA combinations—who are often from racial and ethnic minorities—have more difficulty finding an HLA match. To reduce the time needed to DR type potential donors for such patients,<sup>6</sup> in January 1991 the NMDP began DR-typing donors with less common HLA combinations for the Registry—both minorities and selected nonminorities. This action increases the likelihood that a patient with a rarer type would already have a fully HLA-typed, matching donor available at the preliminary stage of a search. The funding to support this approach comes from U.S. Navy grants. Federal funding for DR typing donors was \$674,000 under the first Navy grant, and an additional \$1,035,000 was allocated for this purpose under the second Navy grant, which ended in August 1992.

Under the first Navy grant, the NMDP DR typed 7,700 new or existing donors, most of them minorities. Under the second Navy grant, the NMDP

<sup>3</sup>Reagents are substances used to produce chemical reactions for the purpose of detecting, measuring, or producing other substances.

<sup>4</sup>See P.G. Beatty and others, "Histocompatibility 1991," *Transfusion*, Vol. 31, No. 11.

<sup>5</sup>Under the second Navy grant, the average cost for A, B typing was lower, ranging from \$50 to \$58.

<sup>6</sup>DR typing of potential donors constitutes much of the time and expense of a patient's search. (See apps. III and IV.)

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**Appendix II  
NMDP Acts to Increase Number of Fully  
Typed Donors**

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DR typed 9,600 donors, most of them newly recruited minorities, as of the end of February 1992.<sup>7</sup> The NMDP used an algorithm developed by the NMDP's Histocompatibility Committee to select typing. The NMDP's efforts in 1991 to DR type donors already on the Registry went more slowly than anticipated. Donor center staff believed that donors appeared less willing to respond when requests to have blood samples drawn for DR typing were not linked to a specific patient's need. Typing new minority donors fully for A,B and DR antigens when they joined the Registry proved more successful and has been the primary approach to DR typing under the two Navy grants.

By April 1992, the number of DR-typed donors on the Registry had doubled to 109,749, up from 46,265 in January 1991. This rise represents a small increase in percentage of the Registry as well, from 17.5 percent in January 1991 to 19.6 percent in April 1992. For about 27 percent of the donors who were DR typed between these two dates, federal funds covered the DR-typing costs, while most of the remaining donors were DR typed through patients' searches.

The NMDP also began in February 1992 to collect extra blood samples from new donors, storing samples at a central repository laboratory for later DR typing. This approach should help speed up the identification of compatible donors, if any are on the Registry, because the laboratory can DR type the blood samples without donor centers having to contact donors to collect new samples.

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<sup>7</sup>The second grant ended in August 1992. DR typing of Registry volunteers and of newly recruited minority donors was terminated in December 1991 because the funds for these projects had already been spent or committed. When a new pilot typing project, using molecular biological techniques, is completed, DR typing will resume using this technology.



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# Small Proportion of Patients Obtained Transplants

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About 13 percent of the 5,604 patients who initiated preliminary searches between September 1987 and July 1991 received bone marrow transplants. Of the about 5,600 preliminary searches, 62 percent continued formally to further test potential donors for compatibility with the patient. Of the formal searches begun during this period, about 21 percent resulted in a bone marrow transplant, about a third were still active as of July 1991, and 47 percent were canceled, primarily because other treatments were used or the patient had died. The median time for searches was about 5 to 6 months. The duration of the search and the type of disease had an impact on the number of transplants that occurred.

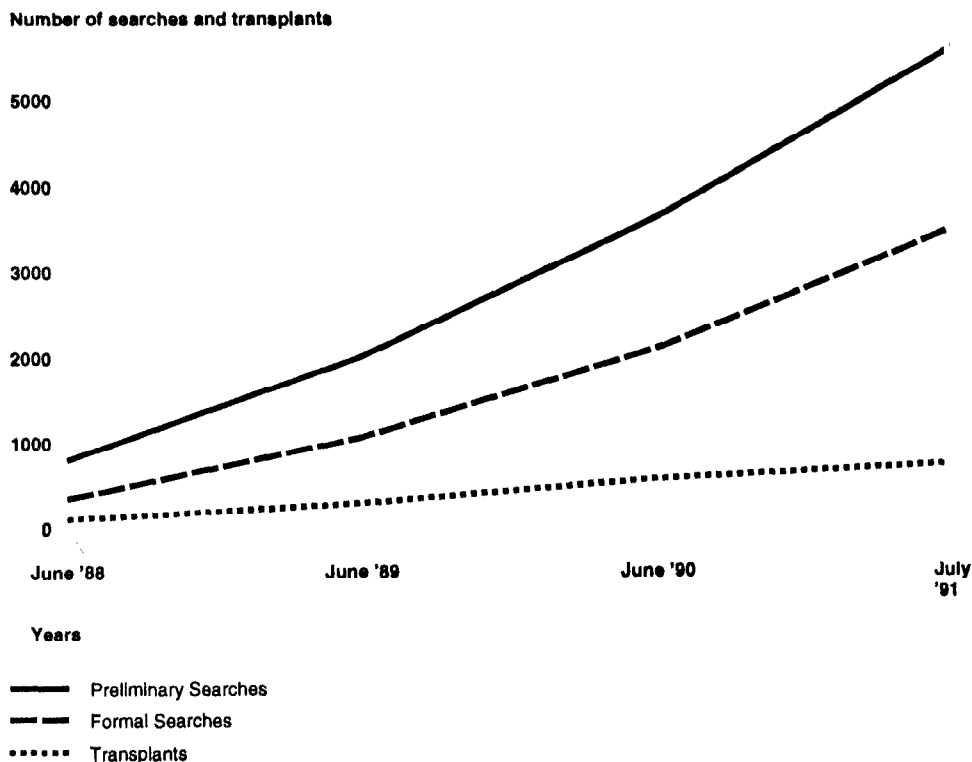
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## Searches and Transplants Have Increased Steadily

Along with the increase in Registry size from donor recruitment, both the number of searches and the number of transplants have increased since the beginning of the program, according to our analysis of the NMDP's database tracking system (fig. III.1).

**Appendix III  
Small Proportion of Patients Obtained  
Transplants**

**Figure III.1: Numbers of Searches and Transplants Have Increased**



Note: Numbers of searches and transplants are cumulative.

Source: GAO analysis of NMDP data.

**Most Searches Did Not Result in a Transplant**

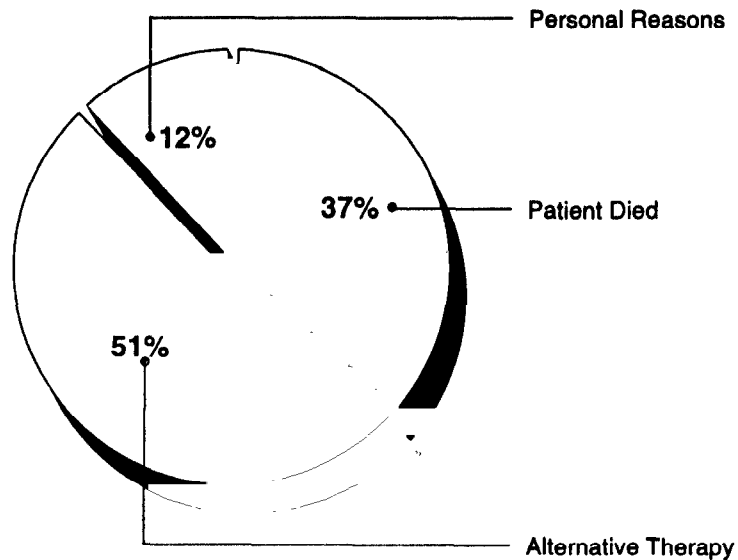
In general, a small proportion of patients received transplants. Preliminary searches were initiated for 5,604 patients from September 1, 1987, to July 18, 1991.<sup>1</sup> As of July 18, 1991, most of these searches—3,479 of them—had moved into the formal search stage. Of the 3,479 formal searches, 724 resulted in transplants, 1,133 were ongoing, and 1,622 were canceled as of July 18, 1991.<sup>2</sup> Formal searches were canceled for different reasons. (See fig. III.2.)

<sup>1</sup>September 1, 1987, was the beginning of the NMDP's patient search and follow-up data collection, and July 18, 1991, was the cutoff date for the data set.

<sup>2</sup>Most of the 1,622 searches that were canceled were canceled before a potential donor went through the final stages of the search prior to marrow collection. Only 97 of the 1,622 canceled searches—or 6 percent—included donor workup services. Donor workup, which occurs when a compatible donor has been found, includes a donor education session and a physical examination to determine the potential donor's willingness and physical ability to donate marrow.

**Appendix III  
Small Proportion of Patients Obtained  
Transplants**

**Figure III.2: Most Patients Whose Searches Were Canceled Sought Alternative Treatments or Died**



**Notes:**

1. Alternative therapy includes chemotherapy and autologous bone marrow transplants, in which patients receive their own treated marrow.
2. 1,622 searches were canceled between September 1987 and July 1991.

Source: GAO analysis of NMDP data.

In addition to seeking alternative treatments, becoming too sick, or dying, patients canceled formal searches for other reasons. For example, at one transplant program we visited, there were 110 searches initiated in 1990 for which a donor was not found. As of May 1, 1991, 14 percent of the patients chose not to proceed with an unrelated bone marrow transplant and 19 percent transferred to another transplant program,<sup>3</sup> some for insurance reasons. At another program, of 86 preliminary searches that did not continue to the formal stage as of May 1989, 14 percent of the patients withdrew from the program, with some transferring to another program, and 8 percent of the patients had no insurance or other financing. (See app. IV for further discussion of financial issues during the search.)

<sup>3</sup>Transplant programs have different criteria for performing bone marrow transplants, depending, for example, on the patient's age, disease, and degree of HLA match with the donor.

Although the number of donors on the Registry increased considerably in the time period we studied, this increase did not markedly affect the proportion of transplants that occurred. We analyzed data from two periods—formal searches before July 1, 1990, and formal searches from July 1, 1990, through July 18, 1991. At the end of the first period, in July 1990, the Registry had 154,448 donors; at the end of the second period, the Registry had 392,863 donors.<sup>4</sup> For both periods, the same proportion of formal searches resulted in bone marrow transplants, despite the different sizes of the Registry.

The NMDP is currently sponsoring research to find ways to improve its search process, especially in the period between the preliminary and formal search. Data are being collected about why searches are canceled at the preliminary search stage. Researchers are analyzing the possible roles of several factors: the difficulties of finding an HLA match, the transplant program's criteria for eligibility, the patient's financial status and degree of insurance coverage, the patient's medical condition, and other factors, such as the patient's age, diagnosis, race, and geographic region.

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## Length of Search and Disease Affected Search Outcome

How long it takes to identify a fully matched donor often affects whether a patient can proceed with a transplant. To withstand a transplant, patients must be in a relatively stable condition medically. For many patients, although a fully matched donor may be found, transplantation is no longer a viable option: patients may relapse, develop complications precluding transplantation, or die.<sup>5</sup> Many patients who do not continue to pursue a transplant receive alternative treatments.

The median time for formal searches was about 5 to 6 months.<sup>6</sup> There was little difference in median time between searches that were canceled and

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<sup>4</sup>To determine the impact of the Registry's size on the proportion of transplants, we considered the results (transplant or search cancellation) of the formal searches initiated during two periods. For the first period, 2,087 searches were initiated for donors. Of these, 552 culminated in a transplant, 1,244 were canceled, and 291 were ongoing as of June 30, 1990. For the second period, 1,392 formal searches were initiated. Of these, 172 searches culminated in a transplant, 378 were canceled, and 842 were ongoing. The same percentage—31 percent—of completed formal searches that were initiated during the two periods resulted in a transplant.

<sup>5</sup>J. Gajewski, M. Cecka, and R. Champlin, "Bone Marrow Transplantation Utilizing HLA-matched Unrelated Marrow Donors." *Blood Reviews* (1990) 4, 132-138.

<sup>6</sup>For the searches that resulted in a transplant, the median time remained relatively constant from 1987 to 1990. The median time from formalization to marrow collection was 163 days. In 1987, the median time was 171 days; in 1988, 174 days; in 1989, 180 days; and in 1990, 161 days.

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**Appendix III  
Small Proportion of Patients Obtained  
Transplants**

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searches that resulted in a transplant.<sup>7</sup> The time for formal searches ranged from zero to 1,243 days. In addition to formal search time, the median time for preliminary searches was 24 days, which included the time from when a physician requested a list of potential donors from the NMDP until the NMDP received back a list of donors selected by the physician for further testing.

The number of DR typings requested and how the donors are scheduled for testing affected the length of the search process. The median number of days from a DR request until typing results were entered into the NMDP database was 20 days.<sup>8</sup> Patients' physicians either request DR typings for all donors identified during the preliminary search or have the typings done incrementally, depending on the number of donors identified and on the patient's finances.

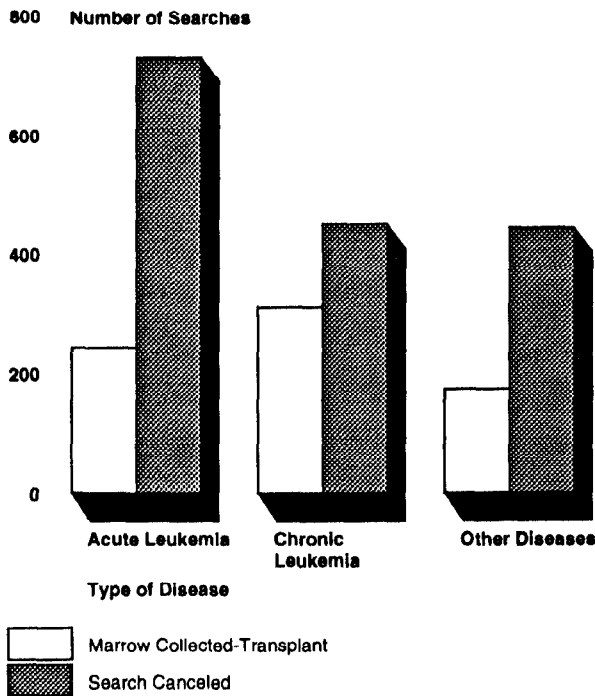
Which disease a patient has (as well as the stage of disease) has a bearing on whether a patient's search for a donor results in a transplant. According to our analysis of the results of formal searches, more patients with chronic leukemia received bone marrow transplants than did patients with acute leukemia. Searches for patients with acute leukemia were canceled more often than searches for patients with chronic leukemia. (See fig. III.3.)

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<sup>7</sup>For searches resulting in a transplant, the median time from formalization to marrow collection was 163 days, with a range of from 16 to 1,243. For canceled searches, the median time was 150 days, with a range of from 0 to 1,240.

<sup>8</sup>In addition to the DR typing of selected donors, the length of the search is also affected by the time needed to perform other search steps and a transplant program's decision on how quickly to proceed with these steps.

Figure III.3: More Patients With Acute Leukemia Cancel Formal Searches



Note: Other diseases include severe aplastic anemia, Hodgkin's lymphoma, and severe combined immunologic deficiency, among others.

Source: GAO analysis of NMDP database.

For patients with chronic leukemia, the median time from the beginning of the search to marrow collection was 203 days, with a range from 48 to 1,243. For patients with acute leukemia, the median time from the beginning of the formal search to marrow collection was 134 days, with a range from 31 to 835. Time is critical for patients with acute leukemia because the longer a patient waits, the greater the risk of dying. More acute leukemia patients died or sought alternative treatments than did chronic leukemia patients.

For some patients, regardless of the time devoted to a search, a donor cannot be located. The likelihood of finding a donor for a patient depends on the patient's HLA combinations. Finding a donor for some individuals is difficult or even impossible because of their HLA combinations.

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Regardless of the size of the donor registry, for some patients with rare HLA combinations, it will not be possible to find a compatible donor.<sup>9</sup>

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<sup>9</sup>Patrick G. Beatty and others, "Probability of Finding HLA-Matched Unrelated Marrow Donors." Transplantation, Vol. 45, Apr. 1988, pp. 714-18.

# Donor Searches Cost Thousands of Dollars and Many Were Covered by Insurance

The median charge for NMDP services for a search leading to a transplant was about \$19,600.<sup>1</sup> The median charge for canceled searches was about \$3,500 for NMDP services.<sup>2</sup> Before beginning a formal search, most transplant programs determined whether patients could pay for the bone marrow transplant and the search to find a donor. Patients who are uninsured and who have no other payment sources may not be able to obtain access to transplant programs. Private insurance, Medicaid, and Medicare paid wholly or partly for about 65 percent of the searches initiated during the first half of 1991.

## The Search for an Unrelated Donor

Preliminary searches of the NMDP Registry can be requested by NMDP-affiliated bone marrow transplant programs and by patients' oncologists and hematologists. At the request of physicians at NMDP-affiliated transplant programs, the NMDP also initiates donor searches with the international registries, such as the Anthony Nolan Research Centre in England and Greffe de Moelle in France. The international registries provide patients with access to about 430,000 additional potential donors.<sup>3</sup> In its access directory on NMDP-affiliated transplant programs, the NMDP also refers patients and physicians to another registry of donors in the United States, the American Bone Marrow Donor Registry. (See app. VI.)

Preliminary search results from the NMDP may identify several potential donors as HLA-A,B matches for the patient. These results are sent to the patient's physician. From these results, the physician either ends the search for various reasons or formally requests that selected donors be contacted through their donor centers for further testing to determine compatibility.<sup>4</sup> Further testing usually consists of DR typing and Mixed Lymphocyte Cultures (MLC).<sup>5</sup> Some potential donors were fully HLA-A,B and DR typed before the preliminary search. For these donors, the

<sup>1</sup>Analysis of NMDP searches from September 1987 through July 18, 1991. The transplant programs' charges as of June 30, 1991, were applied to all NMDP search services. (See app. VIII for methodology.)

<sup>2</sup>Search charges were computed using 698 of the 724 searches resulting in a transplant and 1,613 of the 1,622 searches that were canceled.

<sup>3</sup>Bone Marrow Donors Worldwide, Ninth Edition, June 1992, compiled by the Editorial Board of the Bone Marrow Donors Worldwide.

<sup>4</sup>Only NMDP-affiliated transplant programs can continue the formal search.

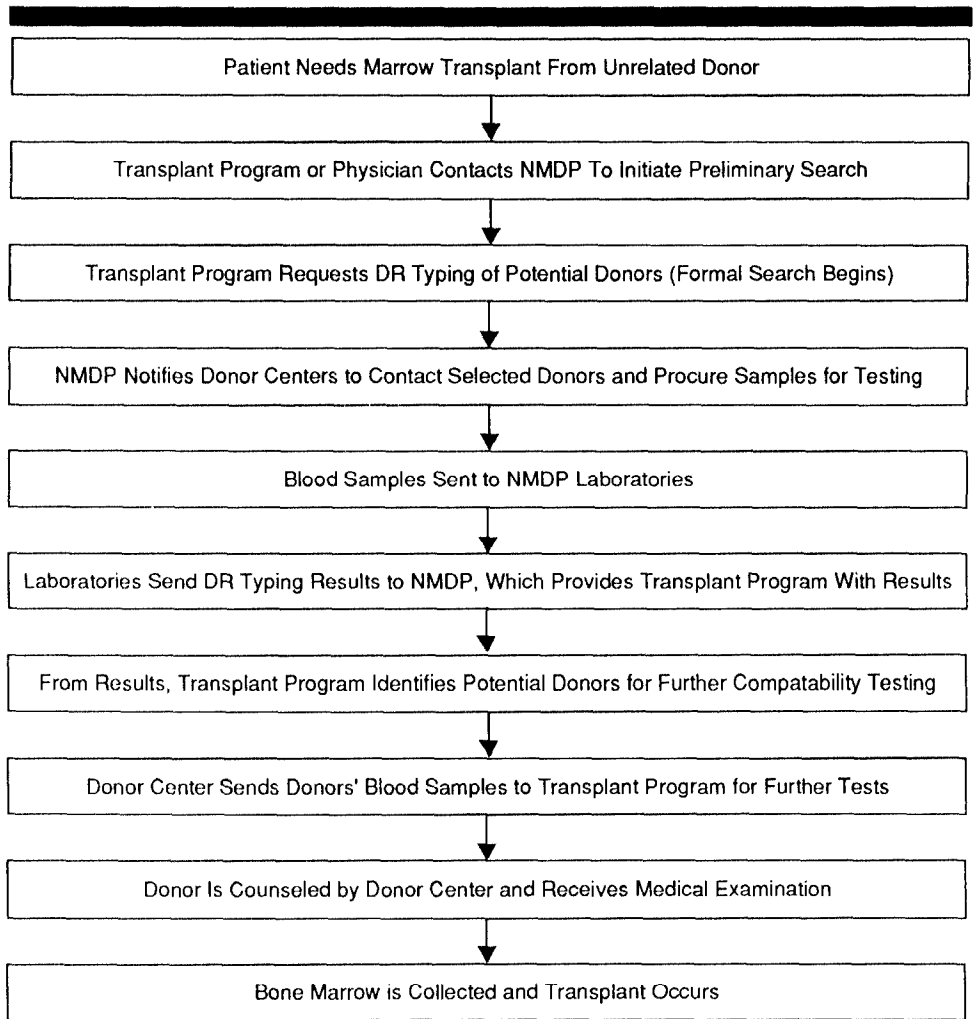
<sup>5</sup>In MLCs, the patient's and potential donor's lymphocytes, or white blood cells, are treated and mixed together in a culture. The reaction of the cells indicates if the patient and donor are compatible for transplant purposes. Because of research questioning the MLC's usefulness as a predictor of HLA tissue compatibility, as of July 1992, the NMDP stopped requiring transplant programs to conduct the MLC. (See app. V.)



transplant program instead requested a blood sample collection for MLC testing.

For DR typing, the donor center obtains a sample of the potential donor's blood, which is sent to one of the NMDP laboratories for typing. When the transplant program obtains DR results, it identifies donors, if any, for MLC testing. A blood sample from the donor is sent to the transplant program for MLC testing. After MLC testing, donors who still are viable candidates are counseled about marrow donation and assessed medically before bone marrow is collected. The marrow is then transplanted into the patient. (See fig. IV.1.)

**Figure IV.1: Patient's Search for Donor Entails Several Stages**



Note: This streamlined diagram assumes that a potential donor is compatible with the patient and that the search proceeds to a transplant. Often, however, several donors are tested and found incompatible. Until a willing and HLA-compatible donor is found, the Registry can also be searched again to find other potential donors.

## Donor Searches Cost Thousands of Dollars

The cost of a search is composed of services necessary to identify a fully compatible donor and to procure that donor's bone marrow. (See table IV.1.) The NMDP charges the transplant program for services that it

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provides to the program on behalf of a patient.<sup>7</sup> The transplant program in turn bills the patient for these services. Charges for NMDP services begin when a formal search is initiated.<sup>8</sup>

**Table IV.1: Description of NMDP Services**

Formal Search	Transplant programs activate the formal search by identifying potential donors for further testing. The NMDP tracks the patient's search through its tracking system data base.
HLA-DR Sample Procurement and Testing	The donor center (1) schedules an appointment with the donor to collect a blood sample and counsels the donor, (2) packages and ships the sample to its designated laboratory, and (3) updates the NMDP tracking system. The laboratory types the blood and conveys the results to the NMDP, which enters the donor's HLA-DR type into its tracking system.
MLC Sample Procurement	The donor center (1) contacts the donor to collect a blood sample for MLC and counsels the donor and (2) packages and ships the blood sample to the transplant program for culturing with the patient's cells. The transplant program may request an additional blood sample to confirm the MLC results.
Infectious Disease Testing	The donor center tests the donor for indications of disease, such as hepatitis, human immunodeficiency virus, and other infectious diseases. This test is repeated if more than 30 days has elapsed from MLC sample collection to scheduling of marrow collection.
Marrow Procurement	The donor attends an information session consisting of counseling and education about marrow donation. The donor is given several days to come to a final decision about donation. After a decision to proceed, a physical examination is performed. The donor receives a 1-year term life and disability insurance policy. Before marrow collection, blood is drawn from the donor and stored. This blood is used to replace blood lost during the marrow collection. Donors typically are hospitalized from 1 to 2 days for the marrow collection procedure.

Starting with the formal search, charges for NMDP services varied by transplant program. Many transplant programs charged their patients more for NMDP services than they were charged by the NMDP. The programs developed their own patient fees for NMDP services, thereby increasing the charge to the patient. Transplant programs charge for additional services, such as counseling the patient and referring physician, and administrative services, including assistance in determining degree of insurance coverage.<sup>9</sup> (See table IV.2.)

<sup>7</sup>The core of the NMDP's budget is program fees-for-service (fees charged to transplant programs), which constitutes more than half of the NMDP's revenues. The amount of program revenue the NMDP received for its donor services grew between fiscal year 1989 and fiscal year 1992 from \$3.4 million to \$19.6 million, because of the increase in donor searches.

<sup>8</sup>Although the NMDP does not charge transplant programs, hematologists, or oncologists for a preliminary search, three transplant programs did charge their patients for the service. The charges were \$55 at one program, \$83 at another, and \$300 at the third.

<sup>9</sup>Four of the 43 transplant programs did not charge their patients for any NMDP services, as of June 30, 1991, even though they were billed by and paid the NMDP for these services. The programs that did not charge include a Department of Veterans Affairs hospital, a health maintenance organization, and two programs that had not developed charges to bill the patient.

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**Table IV.2: Charges for NMDP Services  
by 39 Transplant Programs<sup>a</sup>**

<b>Service</b>	<b>Range of charges</b>
Formal search	\$0 - 1,786
DR typing	0 - 560
MLC sample procurement	0 - 550
Infectious disease testing	0 - 750
Marrow procurement	0 - 31,600

<sup>a</sup>Charges as of June 30, 1991.

In addition to variation in transplant program charges, search charges vary for searches because patients have differing numbers of matches and tests performed. For searches in which DR typings were requested that resulted in a transplant, the median number of DR typings was 10 per search, with a range from 1 to 123 donors typed.<sup>10</sup> For searches that were canceled, the median number of DR typings was 7 per search, with a range from 1 to 217 donors DR typed per search. MLC sample procurement was the second most frequent service requested. Searches that resulted in a transplant included a median of 3 MLC sample procurements per search, with a range of 1 to 21. For searches that were canceled, the median number of MLC sample procurements was 2, ranging from a low of 1 to a high of 21.

For searches that resulted in a bone marrow transplant, the median charge was \$19,630 including the charge for marrow collection, according to our analysis of the NMDP tracking system and questionnaire responses from NMDP-affiliated transplant programs. The charges ranged from zero to \$73,113. For searches that were canceled, the median charge was \$3,520, with a range from zero to \$84,600.<sup>11</sup>

The following examples illustrate the composition of the search charges for two patients. The most expensive canceled search cost \$84,600. The costs consisted of a charge for initiating a formal search (\$1,300), 217 DR typings at \$375 each (\$81,375), and 5 MLC sample collections at \$385 each (\$1,925). The most expensive search resulting in a transplant cost \$73,113. Its charges consisted of a charge for initiating a formal search (\$1,700), 123

<sup>10</sup>Only 185 of the 724 searches that resulted in a transplant requested that a donor be DR typed. Since the remaining 539 patients received marrow from a donor on the Registry, the donor was HLA-A,B, and DR typed when identified as a potential donor. This compares to DR typing requests for 1,299 of the 1,622 searches that were canceled.

<sup>11</sup>For searches resulting in a transplant, the median charges for acute leukemia, chronic leukemia, and other diseases were \$19,573, \$19,785, and \$19,610, respectively. The costliest searches were \$50,648 for acute leukemia, \$73,113 for chronic leukemia, and \$59,673 for other diseases. Similarly, for canceled searches, the charges were \$3,233, \$3,849, and \$3,829. The costliest searches were \$46,870 for acute leukemia, \$47,875 for chronic leukemia, and \$84,600 for other diseases.

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DR typings at \$400 each (\$49,200), 13 MLC sample collections and infectious disease testings at \$417 each (\$5,421), one MLC sample collection at \$212, and marrow procurement for \$16,580.

As part of the search process, transplant programs perform medical tests in addition to those performed by NMDP—for example, transplant programs often required additional laboratory tests to confirm a new patient’s tissue typing. Table IV.3 indicates the tests and charges for the transplant programs we surveyed.

**Table IV.3: Medical Tests Provided by Transplant Programs**

<b>Service</b>	<b>No. of programs performing service</b>	<b>Range of charges<sup>a</sup></b>
Patient screening before search	33	\$0 - 880
HLA-A,B,DR typing	37	0 - 1,357
MLC testing	37	0 - 2,000
Infectious disease testing	17	0 - 750
Other laboratory tests	23	0 - 1,990

<sup>a</sup>We did not determine variations in the services provided that could affect the differences in charges for these services.

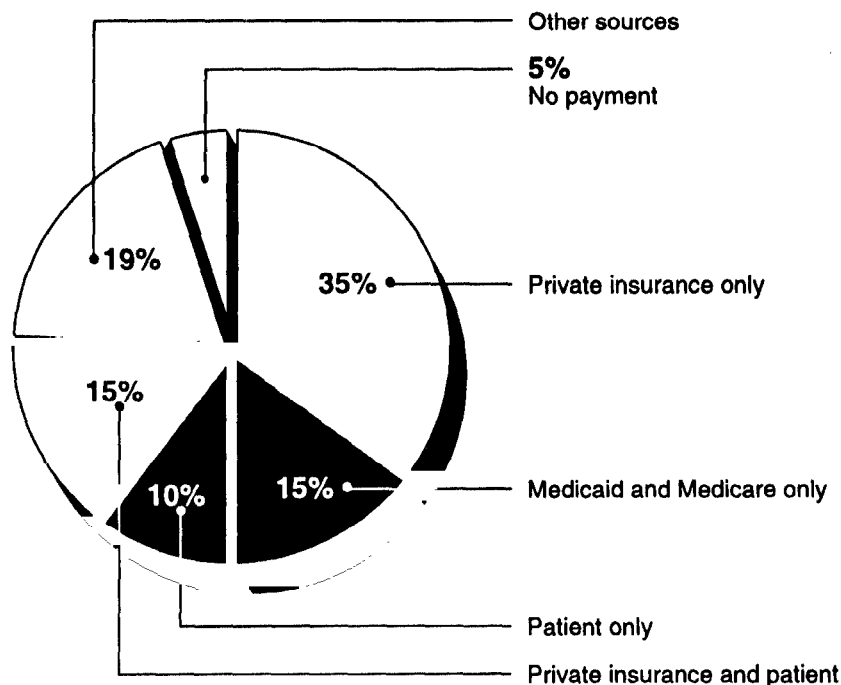
## Private Insurance Paid for Many Searches

During the first 6 months of 1991, 39 of the 43 transplant programs we surveyed requested 816 formal searches. Private insurance and public programs paid the charges for 50 percent of these searches (35 percent and 15 percent, respectively). The patient paid the charges for 10 percent of the searches, and for 15 percent of the searches, private insurance paid a portion of the charges while the patient paid the other portion. Transplant programs were not reimbursed for 5 percent of the searches. (See fig. IV.2.) For the 15 percent of the searches in which both private insurance and the patient paid, private insurance generally covered most of the charges.<sup>12</sup>

<sup>12</sup>When both the patient and private insurance covered the charges (for 139 searches occurring at 22 programs), we asked the transplant programs what portion—most, about half, or a small amount—of the charges the insurer had paid. Fourteen of the 22 programs responded to this question. For the 14 programs, 11 reported that private insurance covered most of the charges, 1 reported that it covered a small portion, and 2 reported that insurance coverage varied by search from covering most of the charges to covering a small portion.

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**Figure IV.2: Many Searches Were Covered by Private Insurance and Public Programs**



**Notes:**

1. Other sources include, for example, hospital, state, and charitable funds.
2. Sources of reimbursement do not add to 100 percent due to rounding.

According to the administrator of one transplant program, health insurers over the past 2 years have become more knowledgeable about unrelated bone marrow transplants. As a result, most of the larger insurance companies that the transplant program is familiar with now pay for the entire cost of the search. In another transplant program we visited, a review of 50 patient records showed that about one-third of these patients experienced problems with insurance covering the search charges, according to program officials. Problems included insurance not covering the search, insurance paying only a small amount of the charges, and delays before the insurer agreed to cover the search. When insurers are reluctant to or will not cover the search charges, the patient must either wait for the insurer to agree to cover the charges, seek other sources of funds, such as limited grant money, or come up with a deposit before the

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search is initiated. For patients who had no insurance or insufficient insurance coverage, some of the transplant programs we surveyed required an up-front payment. As of June 30, 1991, 27 of the 43 transplant programs had asked such patients for deposits, often of several thousand dollars, to cover search expenses.

# NMDP Is Beginning to Incorporate Research Into Program

The NMDP has been matching unrelated donors to patients for bone marrow transplants since late 1987, with the first marrow collections from donors for transplant occurring in December 1987. Because the program is relatively new, the data on patients and donors were not mature enough until recently to be used to draw research conclusions. The NMDP is beginning to incorporate preliminary results from several research projects into the organization's policies and practices.<sup>1</sup> Areas in which research is beginning to have an impact include recruiting donors and educating them about marrow donation, informing physicians during the search process about match probabilities and transplant outcomes, and improving tissue typing methods and program requirements for assessing histocompatibility.<sup>2</sup>

Research being done by NIH and other organizations also has some promising implications for the program, especially in their potential for improving HLA-A, B typing and providing alternative means of marrow collection.

## Participating in Research Is a Key NMDP Mission

Part of the NMDP's mission is to participate in research on bone marrow transplantation issues. The NMDP encourages research project ideas from researchers involved in bone marrow transplantation. The NMDP allows researchers to use information in the NMDP's database and to collect information about patients, donors, and the NMDP's affiliate organizations. These include NMDP transplant programs, marrow collection centers, donor centers, and the Irwin Memorial Blood Bank cell repository,<sup>3</sup> which retains blood samples for research.

The NMDP does not have a specific budget designated for research. Instead, the NMDP approves research on key areas that are in line with its research priorities and that have potential implications for the marrow donor program. Proposals approved by the NMDP's committees are submitted to NHLBI within NIH. NHLBI reviews and approves NMDP project proposals after

<sup>1</sup>Our discussion of preliminary research findings is largely based on research presentations delivered at the NMDP's 1991 Council Meeting, in conjunction with the research proposals themselves. We also interviewed NMDP officials and others on this subject.

<sup>2</sup>"Histocompatibility" means the mutual tolerance or compatibility that allows tissues to be grafted effectively to other tissues. The genes on the histocompatibility complex encode proteins—the HLA antigens—that are essential to the immune response, but which also present obstacles in transplantation. Because of their structure, genetic origin, and function, the HLA-A and B antigens are grouped together as Class I histocompatibility molecules while the HLA-DR antigens are considered Class II molecules.

<sup>3</sup>The Irwin Memorial cell repository in San Francisco, which is under contract to the NMDP, is a blood bank that serves as the NMDP's repository of blood samples for research.



they are approved by the NMDP's committees. NHLBI reimburses the NMDP for approved costs, such as data collection.

Current research areas are the (1) outcomes of bone marrow transplants that use unrelated donors, (2) motivation of marrow donors, (3) safety of marrow collection for donors, (4) process of searching for a donor,<sup>4</sup> (5) probability of finding donors whose HLA combinations match the patients', and (6) use of DNA technology to perform HLA-DR typing. Research represented about \$734,000, or 2 percent, of total NMDP expenditures from May 1991 through April 1992, which is the NMDP's fiscal year 1992.

In 1991 the NMDP implemented a new policy requiring its Finance Committee to review and approve proposals for research that entailed significant financial support. Previously, the Finance Committee had not examined research proposals before they were sent to the NHLBI contracting officer for approval and funding.

In addition, given the NMDP's primary mission to recruit donors and coordinate transplants, the NMDP reassessed its ability to participate in research using multi-center clinical trials. In such research, new approaches can be tested against old in a well-designed, randomized fashion. Although such basic research is important for determining, for example, the outcomes of bone marrow transplants compared to other treatments, it is also more expensive than other kinds of research. Because of this, NHLBI will sponsor basic research on marrow transplantation using clinical trials through its standard competitive bidding process.

To further improve the process by which it selects research projects from those submitted, the NMDP is surveying its committees for recommendations on what its research priorities should be over the next 2 to 3 years. The NMDP plans to use responses from its committees to reset priorities as needed on current and future research.

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## **NMDP Beginning to Incorporate Research Into Program**

Preliminary results on NMDP research projects for which data collection was completed were reported in October 1991 at the NMDP's Council Meeting of its members from donor, transplant, and collection centers.<sup>5</sup> Because of the preliminary nature of this research, the NMDP is just

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<sup>4</sup>An NMDP research project on the donor search process is discussed in app. III.

<sup>5</sup>Several researchers have submitted their study results for publication.

beginning to incorporate early research findings into the organization's policies and practices.

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### **Donors Will Receive New Data on Donation and Recovery**

According to an NMDP study on marrow donation, 77 percent of donors had the marrow collection procedure under general anaesthesia, with collection taking a median of 1 hour. Of about 500 donors who donated marrow between 1987 and November 1990, 5.9 percent experienced a complication, such as hypotension, fever, pain, or nausea, from the donation. Donors took a mean of about 2 weeks to recover from the marrow collection procedure.

Results from this study on the outcomes of marrow donation are being incorporated into an NMDP booklet for donors, to be provided to donors who are selected to donate marrow to a patient, according to an NMDP official. The booklet is expected to be issued in the fall of 1992 and will report on the donors' experiences with marrow collection and recovery.

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### **Research on Probabilities Helps Recruitment**

Research on the probability of patients' finding an A,B and DR match is helping the NMDP set better targeted recruitment goals. According to preliminary research results reported by one researcher at the council meeting, blacks, Asians, and other minorities would need to be represented on the Registry in equal proportion to Caucasians, not just in proportion to their numbers in the 1990 U.S. Census. The goal would be to help about 80 percent of patients from every racial group find a full HLA match. Because minorities often have less common or rare HLA combinations,<sup>6</sup> the researcher projected that the donor registry would need a far greater proportion of minorities on the Registry to achieve this goal than the Registry now has. Research discussed at the conference also indicated the need to recategorize Hispanic and Asian categories because Hispanic is a linguistic and cultural category, not a genetic one, and the Asian category is too broad to be scientifically useful.

The NMDP has increased its understanding of the racial and ethnic distributions of HLA combinations and their impact on donor registries as the program has progressed. Early projections by researchers on registry size were based on related transplant populations, such as tissue matching for kidney donation, and on analyses of the odds of patients finding a matching donor using projections about differently sized donor pools.

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<sup>6</sup>Some Caucasians also have less common HLA combinations and have difficulties finding a match. Most families working with the NMDP on family drives represent Caucasian patients who were unable to find matches from current donors on the Registry.

Research on such issues has played a key role in helping the NMDP determine new recruitment goals, particularly in increasing its minority recruitment target to 25 percent overall. To help improve the matching process, the NMDP is adding a field on its new Registry database to include the ethnic backgrounds of the patients' and the donors' four grandparents. The NMDP has been discussing different categorizations of the donor population in line with HLA genetics and probabilities.

According to NHLBI, which approves and funds NMDP research, more research is needed in this area because too few data are available on which to base a definitive statement on the donor pool size needed for each racial-ethnic group. Most antigens are found in most racial-ethnic groups. Some antigens are rare in any racial-ethnic group; others are rare in one group, but are more common in another. However, the frequency of A, B, and DR combinations may differ importantly among these groups. Certain combinations may be uncommon in a largely Caucasian registry, but are more common in individual minority groups, which may be more apparent as the number of minority donors increases on the NMDP Registry.

NHLBI's Office of Program Planning and Evaluation began in 1992 to determine how large the Registry should be by examining the Registry's size and the incremental costs for matching different percentages of patients with donors. That office has been working with researchers involved with NMDP research on this subject, among others.

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**Probabilities Research  
Expected to Help Search  
Strategies**

Two other studies are planned or in progress on the probabilities of patients finding a match on the NMDP Registry. This kind of research could help physicians make more informed decisions on whether to proceed with a search for a donor or to seek alternative treatments. Alternative treatments might include chemotherapy or autologous transplants, in which the patient's marrow is removed, the cancerous cells are destroyed, and the healthy marrow is reinfused after the rest of the patient's marrow has been destroyed.

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**Patient Outcome Studies  
Could Help Treatment**

The NMDP's studies on patient outcome could have an impact on referring physicians' decisions about the type and timing of treatment. In general, bone marrow transplants using unrelated donors were more successful for patients who were younger, in earlier stages of their disease, and closely HLA-matched to the donor.

In a study of a limited number of patients at one large transplant program, about 50 percent of patients with acute leukemia survived for 2 years or more if transplants were done at an early stage of the disease, such as at first remission. If the transplant was performed later, the survival rate dropped to about 20 percent. Transplants with unrelated donors were found to be at least as effective for treating acute leukemia as autologous transplants.

In a broader study of patients with chronic myelogenous leukemia, the survival rate was 30 percent after a 2-year period.<sup>7</sup> Age, stage of disease, and degree of HLA mismatch were the most important variables in post-transplant survival, according to this study, with age making the largest difference in outcome. The amount of time from diagnosis to transplant was not found to be an important variable for chronic leukemia.

These preliminary findings are expected to encourage physicians to initiate donor searches earlier in the disease cycle, especially for acute leukemia. Physicians may also use such information to better determine which therapies are best for which diseases, given the age of the patient. Early research results on the outcomes of bone marrow transplants using unrelated donors support the NMDP's attempts to shorten the search process by increasing the number of donors who are DR typed. When the research projects are completed and published, the NMDP intends to use their findings to help set reasonable expectations about patients' survival, not only for physicians and patients but also for donors before they donate. When research is published, the NMDP is planning to provide reprints of the articles to referring physicians. The NMDP has also developed several booklets on bone marrow transplant topics for referring physicians to give to patients.

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## **DNA Techniques Are Expected to Improve DR Typing**

In February 1992, the NMDP began implementing a 1-year pilot program to use molecular-level DNA technologies to HLA-DR type donors more effectively and, ultimately, faster and cheaper than serologic typing. The second U.S. Navy grant allocated about \$2 million to implement this project. Seven laboratories and 13 donor centers were participating in the DNA project as of April 1992. The Naval Medical Research Institute is closely involved with this program.

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<sup>7</sup>This rate of survival was also similar to study results reported at the NMDP conference by the International Bone Marrow Transplant Registry.

DNA typing techniques are expected to improve HLA-DR typing as well as reduce its cost. With DNA technologies, the reagents can be commercially produced, unlike with serologic typing, which requires human antisera. DNA also provides greater economies of scale because it can be partially automated. The prices for HLA-DR typing may fall as the DNA typing process becomes increasingly automated. Prices from the laboratories ranged from \$45 to \$180 per sample for DNA-DR typing.

As part of the DNA pilot's implementation, starting in February 1992, the NMDP began using DNA technology to DR type the blood samples from new donors that had been stored in the laboratory repository. As of April 1992, the NMDP donor centers began to provide blood samples from all newly recruited donors for DNA typing.

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## **NMDP Eliminated MLC as Requirement**

The reliability of using the MLC to help physicians predict the outcome<sup>8</sup> of bone marrow transplants has been under question for some time. In MLCs, the patient's and donor's white blood cells are treated and mixed together in a culture. The reaction of the cells may be one indicator of patient and donor compatibility for transplant. The use of the MLC has been controversial because there may be some correlation between a reactive MLC result and an increased risk of graft-versus-host disease (GVHD) in the patient, a major post-transplant complication. The MLC results can be difficult to interpret, especially in patients whose disease results in low cell counts or cells that grow abnormally.

An NMDP research group reassessed the usefulness of the MLC as a predictor of histocompatibility between the patient and the donor. The group concluded that the MLC was not a good predictor of compatibility because it could not determine if the donor and patient were identical at a key location on the gene complex. The group recommended that the NMDP discontinue its MLC requirement and that DNA analysis be substituted.

In July 1992, the NMDP eliminated its MLC requirement. Transplant programs can instead provide results on other tests they might perform, such as DNA typing of other locations on the gene complex. This change may shorten the search for a donor by eliminating the time to culture the MLC samples, although the donor centers would still need to test donors for infectious diseases, and transplant programs must still confirm donors' HLA typing.

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<sup>8</sup>That is, the likelihood of disease-free survival, graft failure, graft rejection, or graft-versus-host disease.

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## Other Research Is Promising in the Long-Term

Research affecting bone marrow transplantation is also being conducted by researchers at NIH, universities, and other organizations, such as the International Bone Marrow Transplant Registry (IBMTR) in Milwaukee.<sup>9</sup> Much of the research is to improve HLA typing and matching, especially for the A,B antigens, and to determine alternative means of collecting marrow.

According to NHLBI, NMDP, and other officials, other areas that are promising or needed include (1) improving treatment regimens during and after bone marrow transplants, especially to prevent or treat GVHD;<sup>10</sup> (2) improving medical understanding of the antigen groupings for ethnic and racial populations, such as Korean, about which little is known; and (3) determining which diseases can be better treated in other ways, such as through autologous transplants or chemotherapy.

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<sup>9</sup>The IBMTR is a main source of data on marrow transplants, with records that precede the NMDP's. The IBMTR was founded in the early 1970s with sources of funding that included the National Cancer Institute (NCI). The National Institute of Allergy and Infectious Disease supports part of the IBMTR through an NCI Program Project Grant. Every 3 years the IBMTR surveys teams worldwide on bone marrow transplant outcomes, receiving voluntary summary information for what is believed to be nearly 100 percent of worldwide allogeneic marrow transplants. The most recent report was published in the Annals of Internal Medicine in March 1992.

<sup>10</sup>For example, the New England Journal of Medicine reported positive results from a preliminary trial that used thalidomide experimentally to treat post-transplant patients with different degrees of GVHD. This research was sponsored by NIH. (Georgia Vogelsang and others, "Thalidomide for the Treatment of Chronic Graft-Versus-Host Disease," April 1992, Vol. 326, No. 16, pp. 1055-1058.)

# The American Registry Is Privately Funded

The American Bone Marrow Donor Registry, which had its origins in 1984, is a privately run, nonprofit organization that merged formerly independent marrow donor registries. The American Registry has four offices and eight donor centers in the United States. Its offices include a DR-MLC coordinating center in Louisiana for donors, a national donor drive coordinating center in Michigan, and a computer center in Florida. The fourth office is the Caitlin Raymond International Registry in Massachusetts, which began separately in 1986. Caitlin Raymond is the American Registry's search coordinating center and retains its international focus for donor searches.

The eight donor centers, which are run by a mix of paid and volunteer staff, range from under 500 donors to about 16,000 donors per center. The American Registry supports itself on the fees it charges to patients to conduct a search as well as through contributions from donors and the community. The American Registry uses volunteer and paid medical directors and HLA coordinators who are laboratory specialists.

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## The American Registry Has a Donor Pool of About 40,000 Donors

As of April 1992, the American Registry listed 41,543 donors in its donor center files, with about 34 percent of them minorities. About 8.4 percent of donors were HLA-A,B and DR typed. Through the international registries, the American Registry also accesses hundreds of thousands of foreign potential donors at the beginning of each search and upon further request. In its brochures for patients, the American Registry also refers patients to the NMDP's Registry.

The American Registry recruits volunteer marrow donors in the United States through its eight donor centers. To cover the costs of HLA-A,B tissue typing, the American Registry asks donors to pay \$60 as a tax-deductible contribution when they consent to join the American Registry. The organization's policy is to conduct drives for about 250 donors at a time, to allow the American Registry to educate the donors about the marrow donation process. Most of the American Registry's donor drives are conducted through communities and businesses, but the American Registry also helps families and patients organize donor drives.

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## Large Portion of American Registry Searches Originated Abroad

Searches for donors can be initiated either through patients' attending physicians or through physicians who are affiliated with transplant programs. The American Registry provides services to patients from about 50 to 60 transplant programs, most of them the same as the NMDP's. About 68 percent of the American Registry's search requests come from transplant programs. From November 1987 to May 1992, between 38 percent and 50 percent of American Registry searches originated outside the United States.

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## Search Process at the American Registry

To determine if there is an HLA-A,B match, the American Registry's search coordinating center initiates a search of the American Registry's own donor centers as well as of its affiliated foreign registries. If A,B matches are found among U.S. donors, the Louisiana office of the American Registry contacts donors through its U.S. donor centers for DR typing. Because European registries will search only at the time of the patient's initial request, searches of these registries may need to be requested more than once.

From January 1991 to May 1991, the American Registry completed 480 DR-typing tests in response to requests for typing. Of these 480 DR typings that were completed, 67 (14 percent) were DR typed within 30 days of the typing request; 145 (30 percent) were DR typed within 31 to 60 days; 168 (35 percent) were DR typed within 61 to 90 days; and 100 (21 percent) were DR typed within 90 or more days.

The next phase of compatibility testing, Mixed Lymphocyte Cultures, can only be requested through transplant programs. If a compatible donor is found and marrow collection is requested, the process of donor preparation includes a counseling session, a physical examination, and collection of autologous blood. Marrow collection is scheduled at a certified marrow transplant program geographically convenient to the donor. The donor is assigned an advocate (a person, usually a registered nurse, who is familiar with the marrow donation process) who answers questions and assists the donor with such things as appointment scheduling. The collected marrow is carried by a courier to the patient's transplant program.

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## American Registry Fees for Donor Searches

To find a potential U.S. donor through the American Registry, the American Registry charges the following fees: \$300 to initiate a search for an HLA-A,B match; \$175 for each donor DR typed; \$30 for obtaining the



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donor's blood sample for an MLC; and about \$1,700 for donor's insurance and related expenses should there be a transplant. Foreign registries without access fees are accessed immediately, according to American Registry officials. Three foreign registries with fees may be searched upon request for extra fees ranging from \$75 to \$330. If donors are obtained through European and other foreign registries, these registries have separate fees for DR typing and MLC.<sup>1</sup>

The American Registry charges patients to initiate a donor search and for DR-typing costs. These fees are sometimes waived for indigent patients, according to American Registry officials. The \$300 fee for initiating a donor search would need to be paid again in certain circumstances. These circumstances are, for example, if a physician wanted to search the foreign registries more than once, if a new registry of donors was added, or if a patient's HLA antigens were reclassified or new antigens were discovered. For other costs, such as infectious disease testing and marrow procurement, the American Registry is billed for these services and in turn charges the patient's transplant program directly for the test or procurement. The American Registry bills the patient's transplant program for the donor's transportation, insurance, disability costs, and lost wages.

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## The American Registry Coordinated Transplants for American and Foreign Patients

The American Registry has coordinated relatively few transplants with unrelated donors in the United States. As of June 1992, the American Registry reported 26 transplants in which the marrow donors came from the American Registry's donor file.<sup>2</sup> According to American Registry officials, the American Registry also facilitates transplants using donors from foreign registries, and transplants are often for patients in foreign transplant programs.

To obtain further information about American Registry transplants, we asked transplant programs to provide information on the number of marrow transplants the American Registry had facilitated through these

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<sup>1</sup>For example, the Anthony Nolan Research Centre in Great Britain charges 175 British pounds, or about \$331, to request DR typing per donor and requires a minimum payment, in advance, of 1,750 pounds (about \$3,308) for 10 DR typings, 75 pounds (about \$142) for DR typing using a form of DNA technology, and 250 pounds (about \$473) per MLC.

<sup>2</sup>American Registry officials reported that they have coordinated over 400 transplants using unrelated donors. The American Registry provided us with data showing 341 searches that resulted in transplants from November 1, 1987, to January 23, 1992. In these cases, the patient's attending physician reported to the American Registry that a donor had been identified and the patient had proceeded to a transplant. The data also indicated whether the transplants were performed at transplant programs in the United States or overseas. We asked the American Registry for clarification of its data. We were told that the American Registry could not distinguish for the transplants it had reported whether the donor was provided by the American Registry, the NMDP, or foreign registries.

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**Appendix VI**  
**The American Registry Is Privately Funded**

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programs. Between January 1990 and June 1991, the American Registry coordinated a total of 24 marrow transplants using unrelated donors, according to our survey of 43 NMDP transplant programs. The American Registry facilitated 21 transplants in 1990, and 3 transplants in the first 6 months of 1991.

# Other Issues From the Transplant Amendments Act of 1990

The Transplant Amendments Act of 1990 required that we evaluate several other issues in addition to the ones addressed in the previous appendixes. These issues included registry policies on protecting donor confidentiality, requesting second marrow donations from the same donor, and maintaining and updating donor files. We were also asked to examine the relationship between the Registries and the donor centers.

Overall, we found that (1) policies and procedures were in place and were being followed by donor centers to protect donor confidentiality and to maintain and update donor files, (2) donors were rarely asked to donate a second time for a patient, and (3) both the NMDP and the American Registry informed patients about the existence of other registries.

## Registries Have Methods to Protect Donor Confidentiality

Both the NMDP and the American Registry have policies designed to protect the identity of donors through the search process. Both Registries also allow, after a period of time, the patient and the donor to meet each other if both parties wish to do so.

To protect donors' confidentiality, the NMDP's data base and files identify the donor by code number only. Specific information about the donor's identity and location is at the donor center. The donor centers are required to limit access to this information by using locked file cabinets and locked rooms.

Each of the three donor centers we visited followed the NMDP's policy of limiting access to donor information. Donor files were kept in locked file cabinets, and access to these records was limited to certain donor center staff. In addition, staff of donor centers, transplant programs, and the NMDP Coordinating Center are required to sign a confidentiality statement. As further protection, correspondence among the NMDP, the donor center, and the transplant program identified the donor by code number.

Like the NMDP, the American Registry identifies potential donors by a code number, and donor records are to be kept locked up with limited access to them. We did not visit American Registry donor centers to observe compliance with these policies.

In two instances that donor center officials told us about, a donor's identity was made known to the patient, but in neither case was NMDP procedure at issue. In one instance, a patient was able to locate a potential donor because of local media attention. The patient subsequently began to

pressure the potential donor to make a marrow donation. In the second instance, a donor was asked to donate a second time for the same patient and had declined. Because the donor had told members of his religious community about the original donation, and the patient and donor lived in the same area, the patient's family learned the identity of the donor. This created a problem for the donor and the donor center when the family requested a second donation.

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## Both Registries Have Policies on Second Donations

For some bone marrow transplant recipients, a second marrow donation is requested for another transplant because of complications with the first transplant. According to NMDP policy, a potential donor must be allowed to consider donation and experience the donation process and post-donation period with a minimum of influence or pressure to donate marrow a second time. NMDP policy is to allow second donations under certain circumstances, such as when a second transplant would be lifesaving. According to an NMDP official, transplant programs have made few requests for donors to donate marrow a second time to the same patient. As of August 1992, six donors had donated bone marrow a second time to the same patient.

The NMDP requires four stages of approval for second donation. First, the transplant program is required to provide the NMDP with information on the patient's history and current condition, the status of the transplant, the protocol for retransplantation, the amount of marrow desired, and the reasons why alternatives to second donation were not satisfactory. The donor center's medical director, based on knowledge of the donor, decides whether the donor can be asked for a second donation. If the medical director agrees, the NMDP selects an anonymous panel of transplant program and donor center officials, as well as others not involved with bone marrow transplantation. These individuals are sent relevant information on the donor and recipient. Within 2 days, the panel members determine whether the donor should be asked to donate again. The donor can then be asked for a second donation and is free to agree or refuse.

The American Registry policy states that a donor should not be expected to provide blood components, such as platelets, for a patient after transplant. However, requests for a donor to donate to the same patient may be done 4 months after transplant. The American Registry's Coordination Center will assess whether the request should be made. On the basis of the health of the donor and the decision of the Coordination

Center, the donor can then be asked for a second donation and is free to agree or refuse.

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## Coordination Among the Registries and Donor Centers

The NMDP and the American Registry operate independently and do not coordinate search efforts for particular patients. Both registries, however, refer patients through their publications to the other registry. The NMDP refers patients to the American Registry in its Access Directory. This directory provides patients and their families and physicians with information on transplant programs and on the resources available to assist them in locating a compatible donor for a patient. The American Registry similarly provides information about the NMDP to patients in an American Registry brochure for patients when they begin a search with the American Registry.

The NMDP has policies and procedures to coordinate its network of 101 affiliated donor centers and 7 recruitment groups as of July 1992. The donor centers are required, among other things, to follow procedures in recruiting donors, having donors DR typed, and otherwise conducting the search process to identify compatible donors.

The NMDP also holds an annual meeting for members of its affiliated donor centers and transplant programs, among others, to share information, concerns, and progress in recruitment and transplantation. In October 1991, for example, sessions were held to discuss and clarify coordination among donor centers, the NMDP, and the transplant programs during the search process. Issues included the time for DR typing potential donors and communication in the period between MLC testing and marrow transplantation. Other NMDP and donor center operations were also discussed, such as the role of smaller donor centers and funding for public education about the marrow donor program.

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## Donor File Maintenance and Updates

The NMDP's central database is updated when new donors are recruited and when information on existing donors changes or donors are deleted from the Registry. Information about newly recruited donors includes a donor identification number, demographic data, and the donor's HLA type.

According to NMDP procedures, donor centers are to submit data on donors at least monthly to update the NMDP's central database. One large donor center we visited stated that it submitted this information weekly to the NMDP. According to NHLBI, the NMDP's policy is to encourage donor centers

to submit these data promptly after donors are recruited, especially from large drives. These donor data are added to the central registry within days of receipt and are promptly available for patient searches. Each month, the NMDP compiles a report summarizing the numbers and demographics of donors in the file from data sent by donor centers prior to the monthly cut-off date.

The NMDP generally obtains new information about potential donors who are on the Registry when donors are asked to come in for further testing, usually to determine compatibility with a specific patient. Every day, the NMDP sends its donor centers patients' search requests for DR and other testing. When donor centers contact donors at this point, they obtain new information about donor's willingness or ability to donate at that time and about the donor's HLA-DR type.

When DR typing tests are completed, the laboratory performing the test conveys the test results directly, through electronic mail, to the NMDP central database, which helps reduce delays in the donor search. Laboratories also send donor centers DR typing test results. Every month, the donor centers also separately confirm such test information as part of their regular reports to the NMDP.

If a donor who is contacted for DR typing or other tests no longer wants to be a potential donor or has health problems that prevent the donor from continuing in the program, the donor center will delete the donor from its records. Again, each month, the donor center sends this information to NMDP so that the donor can be deleted from the Registry's central database.

To make sure its records on donors are updated as much as possible, the NMDP published a newsletter for its potential donors in March 1992. Donor centers need current information on potential donors, such as their addresses and phone numbers, to be able to contact donors for patients' searches. Potential donors on the Registry are usually contacted primarily for DR typing, and many may have been listed on the Registry for years without having been contacted. Contacting donors through DR typing requests is not sufficient to help donor centers maintain updated lists since only a small portion of the Registry's donors—about 15 percent as of July 1991—have ever been contacted for DR typing. To update their records on potential donors, most NMDP donor centers participated in the distribution of a Registry-wide newsletter for their volunteer donors. The newsletter's address correction feature will allow donor centers to more readily contact donors for subsequent testing. By reminding donors

indirectly that they are listed on the NMDP Registry, the newsletter may also help clarify donors' interest in continuing to be listed as potential donors.

In May 1992, the NMDP revised its approach to reimbursing donor centers for maintaining files of potential marrow donors by linking its reimbursement of donor centers more directly to specific services. NMDP donor centers are responsible for maintaining files on potential donors and are reimbursed for file maintenance and other activities, such as recruiting potential donors and contacting donors for typing, that are necessary for participation in the NMDP. Before May 1, 1992, donor centers were reimbursed monthly for the number of donors registered at their center. Donor centers with more than 3,000 donors, for example, were paid 1 dollar a month for every donor. As of May 1, 1992, this form of payment was replaced with a payment to cover the salary for staff to maintain donor files.<sup>1</sup> The payment supports a clerical position, valued at \$20,000 annually, for every 40,000 donors in the donor center's file. Donor centers with fewer than 40,000 donors—or more—receive funds for clerical support proportional to the number of donors on file.<sup>2</sup> The NMDP reimburses donor centers monthly for file maintenance.

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<sup>1</sup>Beginning in the winter of 1991, the NMDP, under NHLBI's supervision, began negotiating cost-reimbursement subcontracts for 15 to 20 donor centers. These negotiations were nearly complete as of August 1992. Until they are completed, the NMDP will use current procedures for reimbursing donor centers.

<sup>2</sup>As of May 1, 1992, donor centers with fewer than 250 donors were not eligible for this monetary support.

# Scope and Methodology

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To gain an understanding of bone marrow transplantation and of the services the donor registries provide, we interviewed officials from the NMDP and from the NMDP's affiliated hospital bone marrow transplant programs, donor centers, and tissue typing laboratories. We also interviewed officials from the American Registry. Because of their funding and oversight roles, we interviewed officials from the NHLBI and the Naval Medical Research Institute as well. We also reviewed contracts, proposals, statistical reports, and other documents.

To determine the NMDP's progress in recruiting volunteer marrow donors, we interviewed NMDP officials and reviewed documents they provided, such as proposals, contracts, and reports. We also interviewed officials and reviewed documents from three donor centers located in metropolitan Washington, D.C., and metropolitan Los Angeles and from the Siegfried Foundation in metropolitan Washington, D.C., which was one of the NMDP's seven recruitment groups.

To determine the rationale for typing tissues in two phases and the cost of tissue typing, we interviewed officials from the NMDP and two NMDP HLA contract laboratories. We also interviewed the director of the tissue typing laboratory at the Naval Medical Research Institute. We reviewed documents on tissue typing from these organizations and from the donor centers we visited as well as published research articles on the subject.

To determine the cost and results of the search process, we analyzed data on patients' searches from the NMDP's database tracking system together with questionnaire responses from our survey of 43 transplant programs affiliated with the NMDP at the time of our study. (See app. X.) For each patient, we constructed the total charges for a formal donor search through the NMDP. We applied the fees that transplant programs charged as of June 1991 to all searches performed in our database period.

The NMDP tracking system contains data on donors listed with the NMDP, patients for whom search services were provided, and information about the services performed for these patients. We obtained all tracking system data between September 1, 1987, when the NMDP began collecting data on patient searches and results, and July 18, 1991, when the data set was cut off for our analysis.

Our survey of 43 NMDP bone marrow transplant programs in the United States was conducted between September 1991 and March 1992. The questionnaire was designed to collect information about the kinds of bone



marrow transplants the programs performed, the charges that programs billed to patients for the NMDP search process, the number of formal searches initiated with the NMDP from January 1991 through June 1991, and the degree and means of reimbursement for these charges. We also obtained information through this questionnaire about transplants and donor searches conducted with the American Registry and with the international registries.

To determine the extent to which the NMDP was incorporating changes in bone marrow research and clinical practice into its program, we interviewed officials from the NMDP as well as from transplant programs, donor centers, and laboratories. We also talked with officials of the NHLBI and the Naval Medical Research Institute. We obtained and reviewed research proposals sponsored by the NMDP, published journal articles on registry size, histocompatibility, and transplant outcomes, and attended sessions at the October 1991 Council Meeting that reported preliminary results from NMDP and other research.

# Data Supporting Figures in Report

Table IX.1: Data for Figure I.1

<b>NMDP activity</b>	<b>Federal funds used to support activity</b>
Tissue typing and recruitment	\$10,616,534
Registry redesign	1,146,186
Research	375,922
Administration	2,983,308

Table IX.2: Data for Figure I.2

<b>Date</b>	<b>Number of NMDP registrants</b>
December 1989	72,900
April 1990	96,000
April 1991	313,500
April 1992	560,900

Table IX.3: Data for Figure I.3

<b>Method of recruitment</b>	<b>Number of NMDP registrants</b>
Community drives	210,696
Whole blood donors	57,060
Apheresis donors	37,387
Navy grant	40,682
Other recruitment	21,256
Unknown source	25,782

Table IX.4: Data for Figure III.1

<b>Date</b>	<b>Preliminary searches</b>	<b>Formal searches</b>	<b>Transplants</b>
June 1988	786	331	89
June 1989	1,996	1,047	274
June 1990	3,621	2,087	552
July 1991	5,588	3,479	724

Table IX.5: Data for Figure III.2

<b>Reason for search cancellation</b>	<b>Number of patients</b>
Alternative therapy	567
Patient died	795
Personal reasons	187

**Appendix IX  
Data Supporting Figures in Report**

**Table IX.6: Data for Figure III.3**

<b>Disease</b>	<b>Number of searches</b>	
	<b>Marrow collected</b>	<b>Canceled</b>
Acute leukemia	242	729
Chronic leukemia	309	449
Other diseases	173	443

**Table IX.7: Data for Figure IV.2**

<b>Source of reimbursement</b>	<b>Number of formal searches</b>
Private insurance only	270
Medicaid and Medicare only	114
Patient only	79
Private insurance and patient	118
Other sources	149
No payment	38

# Results of Survey of Bone Marrow Transplant Programs

U.S. GENERAL ACCOUNTING OFFICE  
Survey of Bone Marrow Transplant Programs:  
Activities to Find An Unrelated Donor

**INTRODUCTION**

The U.S. General Accounting Office (GAO) is conducting an evaluation required under the Transplant Amendments Act of 1990, Public Law 101-616. This law requires that GAO evaluate certain aspects of bone marrow donor registries.

The purpose of this questionnaire is to gather information about (1) your transplant program activities and (2) the National Marrow Donor Program (NMDP) search process, including charge and reimbursement data. In addition, we are interested in obtaining information about other registries that transplant programs may be using to find unrelated bone marrow donors.

If you have any questions about this questionnaire, please call Roy Hogberg collect at (202) 426-0208. Please return the completed questionnaire within 2 weeks of receipt. In the event the envelope is misplaced, please send your questionnaire to the

U.S. General Accounting Office  
Mr. Roy Hogberg  
Room 1115  
330 C Street SW  
Washington, D.C. 20201

If you would like to fax your responses, our number is (202) 426-1241.

Thank you for your help.

**INSTRUCTIONS**

The questionnaire should be completed by the person most familiar with NMDP activities. This person may want to consult with others, especially for financial information. Please provide the name, title, and telephone number of the person mainly responsible for completing the questionnaire so that we may consult him or her, if necessary, for clarification and additional information.

Name of person: \_\_\_\_\_

Official title: \_\_\_\_\_

Telephone number (        ) \_\_\_\_\_

**TRANSPLANT PROGRAM ACTIVITIES**

1. In what year was the first marrow transplant (autologous or allogeneic) performed by your transplant program? (Enter year.) (N=43)

*range*  
1968-89

2. When was the first unrelated bone marrow transplant performed by your transplant program? (Enter year.) (N=42)

*range*  
1979-91

**Note:** This questionnaire was sent to the 43 bone marrow transplant programs which, at the time, were affiliated with the NMDP. All transplant programs returned the questionnaire, however some did not respond to all questions. For questions showing median and range of responses, the "N" denotes the number of transplant programs responding to that question.

**Appendix X  
Results of Survey of Bone Marrow  
Transplant Programs**

3. For each calendar year listed below, indicate the total number of each of the following kinds of marrow transplants performed by your program: (1) autologous, (2) allogeneic related donor, (3) allogeneic unrelated donor transplants. If your transplant program was not in operation, enter "NA" whenever appropriate. (Enter number or NA for each column; if no transplants were performed, enter "0.")

Calendar year	Kinds of transplants performed <i>median</i>			
	Autologous	Allogeneic related donor	Allogeneic unrelated donor	Total
a. 1987	22 (N=40)	20 (N=40)	0 (N=40)	46 (N=40)
b. 1988	26 (N=41)	19 (N=41)	0 (N=41)	52 (N=41)
c. 1989	25 (N=41)	25 (N=41)	1 (N=42)	57 (N=41)
d. 1990	30 (N=42)	20 (N=42)	4 (N=43)	60 (N=42)
e. 1991 (Jan. 1-June 30, 1991)	16 (N=42)	12 (N=42)	3 (N=43)	32 (N=42)

**SEARCH PROCESS THROUGH NMDP**

4. Now we would like to ask you a series of questions about the NMDP search process for an unrelated donor.

Consider all of the NMDP services associated with the search process. For each service listed below, please enter the total transplant program charge, including the NMDP charge, that your program billed to a patient as of June 30, 1991. (Enter amount for each NMDP service; if your program did not charge for a service, enter "0.")

Charge as of June 30, 1991

NMDP service	Total charge (NMDP + transplant program charge) per service
1. Preliminary search (that is, a search of the NMDP central computer file for a potential donor based on HLA matching.)	<i>median</i> \$ 0.00 (N=43)
2. Formal search (that is, contacting donors for further HLA testing and other activities to determine donor and patient compatibility.)	\$ 550.00 (N=43)
3. HLA DR typing of a potential donor	\$ 325.00 (N=43)
4. Mixed lymphocyte culture (MLC) sample procurement	\$ 125.00 (N=43)
5. Infectious disease testing of a potential donor	\$ 175.00 (N=43)
6. Marrow procurement	\$ 14,190.00 (N=43)
7. Donor workup services (services completed but marrow not procured)	
a. Donor information session	\$ 375.00 (N=42)
b. Donor physical examination	\$ 600.00 (N=42)
c. Donor autologous blood collection	\$ 120.00 (N=42)
d. Cancellation fee	\$ 0.00 (N=41)
8. Other NMDP service (Please specify.)	\$ 0.00 (N=43)

**Appendix X  
Results of Survey of Bone Marrow  
Transplant Programs**

5. Next we'd like you to consider transplant services associated with the search process for an unrelated donor above and beyond NMDP services.

**Part A:** For each transplant program service listed below, indicate whether or not your program usually performed the service as of June 30, 1991. (Check one.)

**Part B:** If yes in Part A, enter your program charge for the service as of June 30, 1991. (If your program did not charge for the service, please enter "0.")

Transplant program service	Part A			Part B
	Service usually performed			Transplant program charge as of June 30, 1991
	Yes	No		
1. Patient screening or consultation before the NMDP preliminary search	33	9	If yes -->	<i>median</i> \$ 132.00 (N=32)
2. HLA AB typing	24	18	If yes -->	\$ 248.00 (N=23)
3. HLA DR typing	23	19	If yes -->	\$ 302.00 (N=22)
4. HLA AB and DR typing (at the same time)	37	5	If yes -->	\$ 552.00 (N=36)
5. MLC testing	37	5	If yes -->	\$ 463.00 (N=37)
6. Dw typing	10	32	If yes -->	\$ 0.00 (N=9)
7. Infectious disease testing of a potential donor	17	25	If yes -->	\$ 202.00 (N=17)
8. Other donor laboratory test (Please specify.) _____	23		If yes -->	\$ 116.00 (N=22)
9. Other service (Please specify.) _____	17		If yes -->	\$ 158.00 (N=17)

6. In addition to the NMDP and transplant program charges you identified in questions 4 and 5, would physicians bill the patient for services--such as reading lab results or providing patient counseling--that they provided as of June 30, 1991? (Check one.)

1. [20] Yes
2. [23] No

**Appendix X  
Results of Survey of Bone Marrow  
Transplant Programs**

7. How many formal searches did your transplant program activate from January 1 through June 30, 1991?  
(Enter number.) (N=42)

range  
0-169 Formal searches activated January 1-June 30, 1991

8. About what percentage of formal searches activated from January 1 through June 30, 1991, were paid for in each of the following ways? (Enter percentage for each.)

Payment source	Percentage of formal searches from Jan. 1-June 30, 1991
1. Private insurance only	<u>range</u> 0-100 % (N=41)
2. Private insurance and patient	0- 87 % (N=41)
3. Patient only	0- 75 % (N=41)
4. Medicaid only	0- 50 % (N=41)
5. Medicaid and patient	0- 10 % (N=41)
6. Medicare only	0- 10 % (N=41)
7. Medicare and patient	0- 6 % (N=41)
8. Medicare, private insurance, and patient	0- 20 % (N=41)
9a. Other source (Please specify.) _____	0-100 % (N=42)
9b. Other (Please specify.) _____	0- 43 % (N=41)
10. No payment received	0-100 % (N=41)
	100 %

**Appendix X  
Results of Survey of Bone Marrow  
Transplant Programs**

9. Were any of the searches your transplant program activated from January 1 through June 30, 1991, paid for, at least in part, by private insurance? (Check one.)

- 1. [34] Yes
- 2. [8] No ----> (Skip to question 12.)

10. In any of the searches paid for by private insurance, did the patient make out-of-pocket payments for part of the charges? (Check one.)

- 1. [17] Yes
- 2. [16] No ----> (Skip to question 12.)

11. Consider only those formal searches activated from January through June 30, 1991, in which charges were partly covered by private insurance and partly by the patient. In about what percentage of these searches did the private insurance cover almost all, most, about half, some, or almost none of the charges? (Enter percentage for each.)

**Jan. 1-June 30, 1991 Searches whose charges were paid by both patient and private insurance**

Percentage of these searches in which private insurance paid..... (N=15)

- |                               |                  |
|-------------------------------|------------------|
|                               | <del>ENTER</del> |
| 1. almost all charges         | 0-100%           |
| 2. most charges               | 0-100%           |
| 3. about half of the charges  | 0-20%            |
| 4. some charges               | 0-100%           |
| 5. almost none of the charges | 0-40%<br>100%    |

12. Did your transplant program accept Medicaid payment for unrelated donor search charges as of June 30, 1991? (Check one.)

- 1. [28] Yes ---> From which states does your program accept Medicaid payment?
- 
- 

- 2. [14] No

13. Did your program usually ask a patient for a deposit to pay for unrelated donor search activity charges before initiating a search as of June 30, 1991? (Check one.)

- 1. [14] Yes --> (Skip to question 15.)
- 2. [28] No

14. Has your program asked any patient for a deposit as of June 30, 1991? (Check one.)

- 1. [14] Yes
- 2. [14] No --> (Skip to question 17.)



**Appendix X  
Results of Survey of Bone Marrow  
Transplant Programs**

15. Under what circumstances has your program asked for a deposit? (Check one for each.)

	Yes	No
1. Patient has no third-party coverage	22	5
2. Patient has third-party coverage but that coverage will not pay for all search activities	24	4
3. Other (Please specify)	6	

16. Was the deposit about the same for all patients? (Check one.) *median*

1. [10] Yes --> What was the deposit? \$ 2,500.00  
(N=10)

2. [17] No --> What was the range of deposits?

\$ 1,750.00 to \$ 8,000.00  
(N=16) (N=15)

17. After a formal search is activated, does your transplant program charge a fee over and above the activation charge (that is, an additional fee exclusive of charges for search activities such as HLA typing) to keep that search active? (Check one.)

1. [0] Yes

2. [43] No ---> (Skip to question 21.)

18. How many months after the formal search has been activated does your transplant program begin charging this fee? (Check one.)

1. [<sup>8</sup>] 1 month

2. [ ] 2 months

3. [ ] 3 months

4. [ ] 6 months

5. [ ] 12 months (1 year)

6. [ ] Other (Please specify.)  
\_\_\_\_\_

19. What fee does your transplant program charge? (Enter amount.)

\$ \_\_\_\_\_ .00

20. What period of time does this fee cover? (Check one.)

1. [ ] A monthly period

2. [ ] A yearly period

3. [ ] Other (Please specify.)  
\_\_\_\_\_

21. Once your transplant program activates a formal search, are limits placed on the length of time for conducting the search process? (Check one.)

1. [1] Yes ---> How long can the search process continue? 6 (months)

2. [42] No

**Note:** No response to items 18, 19, and 20; see item 17.

**Appendix X  
Results of Survey of Bone Marrow  
Transplant Programs**

**SEARCH PROCESS THROUGH OTHER REGISTRIES**

22. Has your transplant program ever used a marrow donor registry other than the NMDP? (Check one.)

- 1. [34] Yes
- 2. [ 9] No ----> (Skip to question 36.)

23. Have you ever contacted or been contacted by the American Bone Marrow Donor Registry (American Registry)? (Check one.)

- 1. [31] Yes
- 2. [ 3] No ----> (Skip to question 33.)

24. Now consider the 18 months from January 1, 1990 through June 30, 1991. During this time period, did your transplant program contact the American Registry requesting that it search its registry for a potential donor? (Check one.)

- 1. [23] Yes
- 2. [ 8] No --> (Skip to question 26.)

25. Please enter in the numbers, as follows, for Parts A and B:

**Part A:** The number of contacts your transplant program made with the American Registry during the time periods listed below. (Enter number for each column; if none, enter "0".)

**Part B:** The number of transplants that had resulted from the contacts in Part A as of June 30, 1991. (Enter number for each column; if none, enter "0".) *median*

	Part A	Part B
	Contacts made by your transplant program	Transplants that resulted from these contacts as of June 30, 1991
1. Calendar year 1990	4 (N=22)	0 (N=23)
2. Jan. 1-June 30, 1991	1 (N=23)	0 (N=23)

26. Consider again the 18 months from January 1, 1990 through June 30, 1991. During this time period, was your transplant program contacted by the American Registry on behalf of a patient who already had an identified donor? (Check one.)

- 1. [ 7] Yes
- 2. [24] No --> (Skip to question 28.)

**Appendix X  
Results of Survey of Bone Marrow  
Transplant Programs**

27. Please enter in the numbers, as follows, for Parts A and B:

**Part A:** The number of contacts the American Registry made to your transplant program during the time periods listed below. (Enter number for each column; if none, enter "0".)

**Part B:** The number of transplants that had resulted from the contacts in Part A as of June 30, 1991. (Enter number for each column; if none, enter "0".) (N=7) median

	Part A Contacts made by the American Registry	Part B Transplants that resulted from these contacts as of June 30, 1991
1. Calendar year 1990	1	0
2. Jan. 1-June 30, 1991	2	0

28. Now we would like you to think about all of the American Registry services associated with the search process for an unrelated donor. For each service listed below, please enter the total transplant program charge, which may include the American Registry charge, that your program billed to a patient as of June 30, 1991. (Enter amount for each service; if your program does not charge for the service, enter "0".)

American Registry service	<u>median</u> Charge as of June 30, 1991 Total service charge (American Registry + transplant program charge)
1. Donor search	\$ 300.00 (N=30)
2. HLA DR typing of a potential donor	\$ 88.00 (N=30)
3. Mixed lymphocyte culture (MLC) sample procurement	\$ 0.00 (N=28)
4. Infectious disease testing of a potential donor	\$ 0.00 (N=27)
5. Donor information session	\$ 0.00 (N=27)
6. Donor physical examination	\$ 0.00 (N=27)
7. Donor insurance	
a. Disability insurance	\$ 0.00 (N=28)
b. Life insurance	\$ 0.00 (N=28)
c. Medical insurance	\$ 0.00 (N=28)
9. Donor autologous blood	\$ 0.00 (N=27)
10. Marrow transport from collection center to your transplant program	\$ 0.00 (N=27)
11. Marrow procurement	\$ 0.00 (N=28)
12. Other American Registry service (Please specify.) _____	\$ 0.00 (N=30)

Appendix X  
Results of Survey of Bone Marrow  
Transplant Programs

29. After a donor search is initiated by the American Registry, does your transplant program charge a fee over and above the activation charge, (that is, an additional fee exclusive of charges for search activities such as HLA typing) to keep that search active? (Check one.)

1.  Yes
2.  No ---> (Skip to question 33.)

30. How many months after a donor search is initiated by the American Registry does your transplant program begin charging the fee? (Check one.)

1.  1 month
2.  2 months
3.  3 months
4.  6 months
5.  12 months (1 year)
6.  Other (Please specify.) \_\_\_\_\_

31. What fee does your transplant program charge? (Enter amount.)

\$ \_\_\_\_\_ .00

32. What period of time does this fee cover? (Check one.)

1.  A monthly period
2.  A yearly period
3.  Other (Please specify.) \_\_\_\_\_

33. Has your transplant program ever initiated a search with an international registry? [For example, Anthony Nolan (UK), Greffe de Moelle (France), Sheba Medical Center (Israel), Belgium National Registry (Belgium)]. (Check one.)

1.  Yes
2.  No ---> (Skip to question 36.)

Note: No response to items 30, 31, and 32; see item 29.

**Appendix X  
Results of Survey of Bone Marrow  
Transplant Programs**

34. Does your transplant program access the international registry (registries) directly, or indirectly through the NMDP, Caitlin Raymond (American Registry), or some other organization?

*(Check one for each.)*

Ways to access registry	Yes	No
1. Directly	16	15
2. Through NMDP	30	2
3. Through Caitlin Raymond (American Registry)	21	11
4. Through another organization <i>(Please specify.)</i> _____	1	

35. From January 1 through June 30, 1991, how many times did your transplant program contacted an international registry (registries) to initiate a search? *(Enter number; if none, enter "0.") (N=31)*

median

7 Contacts made

**COMMENTS**

36. If you have any comments about these questions or about NMDP or other registry activities, please write them in the space provided below.

Thank you for your help.

HRD/SLS/9-91  
(108794)

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