The Charles Drew Program in Missouri: a description of a partnership among a blood center and several hospitals to address the care of patients with sickle cell disease

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Sickle cell disease (SCD) is an inherited blood disorder which can be complicated by stroke in infancy and childhood. The primary and secondary prevention of stroke in this patient population is regular RBC transfusion therapy at least every three weeks, but there is no consensus on the ideal RBC transfusion therapy. The Charles Drew Program, a partnership among a blood center and several hospitals affiliated with academic medical centers in Missouri, provides RBCs for the care of patients with SCD. There are three basic aims: the RBC components are phenotypically matched on three minor RBC antigens, the units are less than 7 days old, and each patient has a limited number of dedicated donors, so that the donor exposure is minimized. This report describes the operational phases of this program and summarizes its performance with respect to each of these aims. ***Immunohematology* 2006;22:112–116.**

Sickle cell disease (SCD) is an inherited blood disorder that predominantly affects African Americans. Among children with sickle cell anemia (HbSS), approximately 11 percent will have a stroke and approximately 10 percent will have an elevated transcranial Doppler measurement, indicating that they are at increased risk for strokes. For both primary and secondary prevention of strokes, chronic transfusion therapy is required for an indefinite period.[1]

However, there is no consensus on the ideal chronic transfusion protocol. The lack of such a protocol results in a higher than acceptable rate of complications associated with commonly monthly RBC transfusions, such as the high rate of alloimmunization.[2] In a recent survey investigating the chronic transfusion protocols of North American laboratories, approximately two-thirds of these laboratories performed no phenotype testing beyond the required ABO and D testing, and among the institutions in the remaining one-third, approximately 85 percent performed a limited phenotype match.[3] Other components of blood transfusion therapy programs that have not been formally assessed include the potential benefit of transfusing fresh units (< 7 days) and limiting donor exposure.

Program History and Protocol

The Drew Program began in 1999 as a partnership among the Missouri/Illinois Region of the American Red Cross (ARC) and several hospitals in Missouri specializing in the care of pediatric patients. The program has three objectives. The first objective is to provide phenotypically matched, hemoglobin S (HbS)-negative, leukoreduced RBCs to all pediatric patients with sickle cell anemia who require chronic transfusion therapy and are participating in the program. All patients receive units with a limited phenotype match (C, E, and K in addition to ABO and D). Studies supporting this practice have been published in the scientific literature.[2,4] One transfusion service requests that the units also be matched for Fy^a. Any patient who develops an antibody receives units which are negative for the antigenic determinant against which the antibody is directed. The second objective is to ensure

that these units are fresh with the goal of limiting the interval from collection to transfusion to a period of five days. The third objective is to limit the number of donors to which each patient is exposed.

Recruitment Process

Blood drives are held in conjunction with donor groups with a significant African American base. When this base accounts for 30 percent of the donor group membership, the drive is designated as a Drew drive. Donor groups with this type of demographic make-up consist of churches, corporations, and schools. Before a Drew drive, a dedicated donor recruiter educates the group about the sickle cell program, its purpose, and the requirements for participation. At the time of the drive, this dedicated recruiter, or one of a few hand-picked designees, has a one-on-one interview with any donor expressing an interest in becoming a member of the program. A realistic picture of the program requirements is presented to the donor, who can then make a more informed decision about whether a commitment to the stringent requirements of the program can be made. If the donor still expresses an interest after the interview, the unit which they donate is specially tagged, so that it can be phenotyped. On the basis of the phenotype, the donor is matched with one of the patients in the program and is placed on a recruitment list for that single patient. When the patient has an upcoming appointment, the donors on the patient's list are called and asked to donate within a short window of time (commonly 5 days) before the scheduled treatment date. Donors accepting the responsibility of joining the program are expected to donate a minimum of three times per year.

Communication between Transfusion Service and Blood Center

Each transfusion service sends a list of scheduled transfusions along with the expected number of units needed for each patient to the blood center every month. This list is essential to the two departments at the blood center which coordinate most of the program activities: donor recruitment and the reference lab. The recruiters use these patient schedules to guide the selection of donors and to select an appropriate appointment date. All units intended for patients in the program are channeled to the blood center reference lab, which is ultimately responsible for appropriate distribution of the units to the transfusion services. With the first donation from a given donor, two tags are affixed to the unit at the time of distribution. The first tag indicates for whom the unit is intended; the second tag lists the confirmed antigens. Subsequent donations from the same donor are only tagged with the name of the recipient and a fax is sent to the hospital indicating the historical phenotype of the donor. The reference lab maintains an open dialogue with the hospital transfusion services during this distribution and during the period which follows. Patient issues and product issues are resolved through this open dialogue. At the conclusion of each month, the reference lab sends a complete report of all units issued during that month to every transfusion service. Next to each listed unit, the transfusion service notes whether the unit was transfused to the intended recipient and when it was transfused. The transfusion service also notes any units the patient may have received which came from a source outside of the program. The report is then returned to the reference lab, which collects all the information and generates a complete transfusion history on each of the patients in the program.

Donor Profiles

The Missouri/Illinois Region of the ARC is a large blood center that collected an average of 287,097 productive units per year (range 259,160–310,614) between July 1998 and June 2005 (Table 1). During the same period, the average number of those productive units donated by individuals identifying themselves as African Americans was 11,088 per year (range 8,616-13,420). The difference between the number of donations from African Americans from July 1998 to June 1999 and from July 2000 to June 2001 was attributed to increased minority recruitment efforts and to increased community awareness concurrent with the initiation of the Drew Program. Donation

Table 1. Productive RBC units collected by the Missouri/Illinois Region of the ARC from July 1998 through June 2005

Fiscal year	Units from all donors	Units from African American donors
7/98–6/99	285,894	8,616
7/99–6/00	285,645	12,821
7/00–6/01	298,526	13,420
7/01–6/02	310,614	12,966
7/02–6/03	282,579	10,848
7/03–6/04	287,261	9,615
7/04–6/05	259,160	9,333
	2,009,679	77,619

Table 2. Donation frequency of donors in Charles Drew Program from July 2003 through June 2005

	7/03–6/04	7/04–6/05
7 times per year	0	1
6 times per year	15	13
5 times per year	58	69
4 times per year	91	147
3 times per year	229	229
2 times per year	408	345
once per year	668	520
Total	1,469	1,324

frequency within the dedicated donor base (those donating three times per year or more) is illustrated in Table 2.

Transfusion Service and Patient Characteristics

There are four pediatric hospitals serving patients with sickle cell anemia. Among the four hospitals, there are three that participate in the Drew Program. The remaining hospital receives phenotyped units without restriction on the age of the units or the number of donor exposures. Because the three hospitals participating in the Drew Program are all affiliated with academic centers, many of the patients in the program came as referrals because of complications at outside institutions, and some of these patients had already formed antibodies before they joined the program. The current phenotypes of the patients in the program and the antibodies formed by the patients are listed in Table 3.

Table 3. Patient phenotypes and antibodies produced in patients in the Charles Drew Program

Patient phenotype	Number of patients with phenotype	Number of patients who produced antibody	Antibodies produced*	
			Common	Low frequency
C–,E–,K–	15	7	-E, -K, -S, -Jk^b	–
			-C, -K (2)	–
			-C	–
			-M	–
			–	-Co^b, -Go^a
			–	-Kp^a
C–,E–,K–,Fy(a–)	12	5	-E, -K	–
			-M	–
			-C	–
			-Fy^a	–
			–	Js^a
C–,K–	7	3	-K (2)	–
			–	Yt^b
E–,K–,Fy(a–)	7	1	–	Go^a
E–,K–	5	2	-Jk^b	–
			-D	–
C–,K–,Fy(a–)	3	0	–	–
D–,C–,E–,K–	2	1	-D, -C	–
K–	2	1	-M	–

*Each antibody was produced once unless otherwise noted.

Table 4. Transfusion protocols used to treat patients in the Charles Drew Program*

	Number of patients		
	Simple	Partial	RBC exchange
Hospital 1	0	8	10
Hospital 2	0	0	6
Hospital 3	0	15	11

*Currently, two patients have had their transfusions suspended.

In addition to the special requirements with respect to phenotype, age, and donor exposure, the donors in the program are placed on treatment protocols involving some form of exchange RBC transfusion, either partial manual exchange or RBC apheresis, to prevent the issues associated with iron overload. The distribution of patients receiving each form of treatment is outlined in Table 4.

Program Performance

From 1999 to January 2005, the program concentrated on the first objective of the protocol; implementation of the second and third objectives required a critical mass of dedicated donors. Beginning in January 2005, modifications in program design were made so that the operational progress of the program could be monitored and assessed through the use of a monthly productivity report. The productivity report requires documentation of the requested number of units, the number of scheduled donations to fill that request, the number of calls required to make those scheduled donations, and the outcome of those scheduled donations for each patient requiring transfusion therapy in that month. For all successful donations, the day of collection and the day of distribution are documented. This allows the program to maintain data on the number of patients transfused, the number of units each patient requires, the number of scheduled appointments needed to meet that commitment, the number of calls needed to make the requisite number of scheduled appointments, the number of deferrals and cancellations, the number of

Table 5. Effectiveness of the Charles Drew Program

	Units requested			Units sent			Average age of units (days)		
Date	**Hospital 1**	**Hospital 2**	**Hospital 3**	**Hospital 1**	**Hospital 2**	**Hospital 3**	**Hospital 1**	**Hospital 2**	**Hospital 3**
Aug 2005	68	15	67	57	7	65	5	6	4
Sep 2005	73	6	63	54	6	63	5	4	6
Oct 2005	58	6	60	42	6	59	5	5	5
Nov 2005	64	12	68	46	4	66	7	N/A	6
Dec 2005	70	11	82	40	6	82	6	7	5
Jan 2006	64	12	83	50	14	81	5	6	5
Feb 2006	58	27	74	45	12	73	5	6	4
Mar 2006	64	25	93	65	12	89	7	9	5
Apr 2006	60	17	76	52	17	76	6	6	5
Totals	579	131	666	451	84	654	N/A	N/A	N/A

no-shows, and the age of the units at the time of distribution. The performance of the program with respect to fill rate and age of units at distribution is illustrated in Table 5.

Because the program is still actively accruing donors, the orders from the hospitals are not always filled with units from donors who have been accepted into the program. Until the program has accrued a sufficient number of donors to meet this requirement, the balance of the order is filled with random allogeneic units which meet all the phenotyping requirements. The element missing when these random units are used is the restriction on the number of donors. For those units coming from donors participating in the program, the operational procedures are usually successful in ensuring that the units are fresh.

Beginning in February 2005, a pilot project was performed as a feasibility study to determine how successful the program could be at fulfilling the third objective of the protocol. An attempt was made to limit the donor exposure for 12 of the patients at two of the hospitals. The results of this pilot project have been submitted for publication. Overall, within the first year, donor exposure was reduced by an average of 45 percent based on the performance of the blood center. Because of additional logistic variables at the hospitals, this resulted in an overall reduction in donor exposure of 32 percent at one hospital and 37 percent at the other.

Discussion

Since its inception in 1999, the Drew Program has tried to meet three objectives in the delivery of care to the patients with sickle cell anemia who require chronic transfusion therapy. The first objective has been met, and all patients in the program receive HbS-negative, leukoreduced RBCs which are phenotypically matched. Two protocols are used. In one of the protocols, the patients receive units that are phenotypically matched for C, E, and K. In the second protocol, the units are also matched for Fy^a. On the basis of the antibody profile of the patients in the program as indicated in Table 5 and consistent with previous reporting in other publications, these two matching protocols would have prevented the majority of clinically significant antibody-related complications.[4]

The program regularly meets the second objective and the average age of the units is often 5 days. The rationale for this objective is the belief that the frequency of transfusion therapy may be reduced if the transfused RBCs are closer to the beginning of their shelf life. Since the patients require regular transfusion therapy, this objective may help to minimize the disruptions that therapy causes in the lives of these patients. While this reasoning sounds plausible, this assumption has not been investigated and validated.

The program has been working on the third objective since February 2005. The rationale behind this objective is that minimizing donor exposure may reduce the rate of alloimmunization. Transfusion is a recognized form of immunization, but in some instances, it may induce immunologic tolerance. The capacity of transfusion to induce immunologic tolerance has been used to treat women with recurrent abortions and patients receiving solid-organ transplants.[5,6] Tolerance may be the result of induction of CD4+ regulatory T cells, and there is evidence that this effect may depend on the degree of HLA-DR matching between donor and recipient, the presence of co-stimulatory molecules, and possibly on the presence of leukocytes within the transfused

component.[7,8] At this point the phenomenon is incompletely understood, and the determination of the clinical value in reducing donor exposure merits investigation and clarification. The recently completed pilot project showed that donor exposure can be significantly reduced; the clinical value of this reduction may take several years to document.

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