The Israeli rare donor blood program

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The National Blood Group Reference Laboratory (NBGRL) was established by Dr. Cyril Levene in 1971 to assist in the resolution of complex serology problems caused by common and rare antibodies to red blood cell (RBC) antigens throughout Israel.[1] The first rare blood unit was frozen June 24, 1975. Over the years, the NBGRL resolved unusual cases by using rare RBCs and antibodies made available through the Serum, Cells, and Rare Fluids (SCARF) program. Rare units of blood were provided by Magen David Adom National Blood Services (MDA-NBS) according to the specificity determined by the NBGRL. The NBGRL was transferred from the Ministry of Health laboratories to MDA-NBS in 1995. Since 1995, the NBGRL coordinates the testing and identification of all unresolved blood types and RBC antibodies with the provision of compatible units of blood for patients in need. This includes common antigen-negative combinations and rare units of blood. Supply of rare units of blood is either from "on the shelf" liquid units or from our frozen rare blood inventory. Donor and rare unit data are registered and secured in the MDA-NBS database.[2]

A unit of blood that is negative for a high-prevalence antigen is considered rare if the antigen's prevalence is less than 1 in 1000 in the Israeli population.[3] Throughout the years, several rare blood types such as ABTI–, JMH variant, Dr(a–), K:–22, LU:–20, and RAPH:–1 were first recognized in Israel.[1,2] These were mainly confirmed at the International Blood Group Reference Laboratory (IBGRL, Bristol, UK). Table 1 summarizes data on active rare blood donors and available frozen units through December 2014. During 2014, 136 rare units of blood were requested and 111 were issued (82%).

Most of the unfilled requests in 2014 were for one patient with anti-Yt^a (20 of 104) for whom the clinical necessity for this high-prevalence antigen negative blood was controversial.

In 2012 and 2013, 12 percent and 16 percent of requests were not completed, respectively. A lower rate (7.9%) of unfilled requests for high-prevalence antigen negative units was reported by the American Rare Donor Program.[4] Almost all the unfulfilled requests were due to the hospitals decision to postpone transfusion until a liquid unit was available or to transfuse fewer units than originally requested.

Table 1. Donors, frozen blood unit inventory, and units requested and supplied through the Israeli rare donor program as of 2014

Phenotype	Number of donors	Number of frozen units	Number of units requested	Number of units supplied
k–	79	204	12	12
Fy(a–b–)	57	148	0	0
Kp(b–)	53	240	5	5
Yt(a–)	51	108	104	84
Lu(b–)	49	145	7	5
GE:–2,3	21	42	5	3
p	12	47	0	0
Group O, D–e–	8	17	0	0
Dr(a–)	7	18	0	0
AnWj–	7	10	1	1
Group O, D–c–	6	11	0	0
P_2^k	6	10	0	0
Vel–	6*	13	2	1
K:–22	3	6	0	0
JMH–	3	24	0	0
P_1^k	3	5	0	0
Lan–	3	5	0	0
ABTI–	3	3	0	0
Js(b–)	2	2	0	0
Inab–	2	2	0	0
RAPH:–1	2	8	0	0
Group O, D–c–e–	1	1	0	0
K_0	1	10	0	0
Gy(a–)	1	5	0	0
LW(a–)	1	4	0	0
H–	1	3	0	0
$H+^w$	1	11	0	0
GE:–2,–3	1	19	0	0
Total	384	1121	136	111

*One autologous donor.

Despite the lack of a hemovigilance system, which mandates reporting on the transfusion of incompatible units, several such cases were reported to the NBGRL. In these seven cases, six patients (3 anti-Yt^a, 2 anti-Ge, 1 anti-Lu^b) were transfused with antigen-positive units following a medical decision. In these six patients, there were no known adverse clinical sequelae.

In one patient with anti-Yt^a, an increase in titer was observed (64), while being negative using an IgG1/IgG3 gel card (Bio-Rad). Because of the increase in titer, provision of Yt(a–) units was requested. Moreover, transfusion of Yt(a+) blood to patients with anti-Yt^a is regularly performed by some hospitals without reports of adverse effects. In one case, an inadvertent transfusion of AnWj+ blood was given to a newborn whose mother had anti-AnWj; this transfusion caused severe hemolysis.[5]

Rare Donor Identification

Rare blood donors are identified in a number of ways. The first is when a rare antibody specificity is identified in a patient specimen. After recovery, the patient can be considered for donation either as an autologous or an allogeneic donor. In addition, family members, especially siblings, are tested to determine whether they share the same antigenic specificity. Others are identified when a donor has an antibody to a high-prevalence antigen or while screening donor samples with certain rare antibodies. Occasionally, screening for a specific rare phenotype is performed in a targeted population.

Since 2012, screening for several rare blood types has been performed using an automated instrument (PK7200 [PK7300 since December 2013], Beckman Coulter, Nyon, Switzerland) or by manual screening. Of 20,830 donors screened with monoclonal anti-Kp^b (OSK36, kindly provided by Dr. Y. Tani from the Japanese Red Cross), 8 Kp(b–) donors were found. Two Vel– donors were identified out of 43,730 donors screened utilizing anti-Vel (Donor SP, Blood Bank Umea, diluted 1:40, kindly provided by Dr. B. Nilsson-Sojka) and were verified by genotyping. Of 3,331 donor samples screened manually with our in-house anti-Yt^a (TE diluted 1:1000), 27 were found to be Yt(a–). Among specific donor populations, we manually tested 291 samples with anti-Jr^a (OSK30, kindly provided by Dr. Y. Tani from the Japanese Red Cross); 225 samples with in-house anti-ABTI, anti-AnWj, and anti-Ge2; and 23 with anti-IFC. These screenings identified 38 new rare donors, only one of which was AnWj–.

As of 2015, no Rh_{null} patient or donor has been recorded in Israel.

A letter is sent to all rare blood donors with information on their rare blood type specificity, the importance of regular blood donations, and the opportunity for preservation of rare units of blood for themselves as well as for other patients. The letter includes an appeal for family members to be tested for the specific phenotype, a form to update donor details, and an informed consent for units to be sent abroad if needed.

A wallet-size card with the donor's name, rare blood type and antibody specificity, and recommended phenotype for transfusion is also provided.

The recruitment and retaining of rare blood donors requires special involvement of devoted personnel.[6] At the beginning of each year, greeting cards that also encourage blood donation are sent. The staff follows inventory levels and if necessary donors are called to donate for specific patients. In cases in which rare blood is needed urgently, most donors with very rare phenotypes willingly donate. A special acknowledgment letter is sent to these donors to express our gratitude for their immediate response and willingness to assist.

Our center has held two meetings for rare blood donors with patient representatives and the NBGRL staff in 2002 and 2007. The meeting program included lectures on blood types, rare blood and blood donations, a musical performance, and, most importantly, personal experiences of patients requiring rare units of blood and the rare donors who donated the units. The donor room was open to allow donors to donate blood, and samples were drawn for testing from family members.

One of our major challenges is to reach and retain rare blood donors from diverse ethnic populations that are underrepresented in our blood donor database. In these circumstances, we call the donor, his or her family physician, and religious and spiritual leaders or other influential people in the community to promote blood donations and testing. As MDA-NBS operates blood drives throughout the country, we endeavor to arrange blood drives at times and venues that are convenient for the donors. Despite all these efforts, at times, people with even very rare blood types do not donate regularly and some of them have never donated a unit of blood.

From time to time, when there is a complex unresolved case or when a rare unit is unavailable, the laboratory requests assistance from international resources. Samples are usually sent for confirmation or further investigation to the IBGRL in Bristol, UK, or to other reference laboratories.

Since 2010, nine rare units of blood were obtained through the International Rare Donor Panel operated by the IBGRL because compatible blood was not available locally. These rare units of blood were kindly provided and shipped to Israel by various contributors and included seven Vel– units: six from NHS Blood and Transplant, UK, and one from the Transfusion Center in Valencia, Spain; and two Jr(a–) units were from the Japanese Red Cross Osaka Blood Center.

The provision of blood internationally—although complex logistically and complicated by regulatory issues—is supplied within days and arrives in good condition, thanks to the efforts and dedication of all parties involved.

The main challenges facing our NBGRL are to increase awareness for blood donation among donors with rare blood types and to increase very rare blood availability [such as AnWj–, Vel–, P^k, Jr(a–)] by family testing or targeted screening using serology or molecular tools. Another important challenge is to educate physicians about the clinical significance of the antibodies associated with various rare blood types in order to improve transfusion of this very limited and unique resource.

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References

1. Levene C, Asher O, Shinar E, Yahalom V. Rare blood donors: a personal approach. Immunohematology 2006;22:64–8.
2. Yahalom V, Shinar E, Poole J, et al. The rare blood donor registry in Israel. Vox Sang 2002;83(Suppl 2):29.
3. Reesink HW, Engelfriet CP, Schennach H, et al. Donors with a rare pheno (geno) type. Vox Sang 2008;95:236–53.
4. Flickinger C. REGGI and the American Rare Donor Program. Transfus Med Hemother 2014;41:342–5.
5. Bonstein L, Yahalom V, Asher O, et al. Acute hemolysis in a newborn with maternal allo anti-AnWj. Vox Sang 2010;99(Suppl 1):365.
6. Nance ST. How to find, recruit and maintain rare blood donors. Curr Opin Hematol 2009;16:503–8.

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