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On Our Cover
The International Society of Blood Transfusion Working Party on Rare Donors consists of members from those countries around the world with rare donor programs. These members work diligently to provide rare blood to their own patients in need as well as to those in other countries when requested. Each member’s donors who are negative for high-prevalence antigens are listed by phenotype on the World Health Organization International Rare Donor Panel. Providing rare blood is a collaborative worldwide effort. The cover depicts the flags of those member countries that contributed articles to Immunohematology.

Cynthia Flickinger
Introduction

The International Society of Blood Transfusion (ISBT) Working Party on Rare Donors was established in 1985 and is composed of experts in rare donor activities from many countries; its main focus is to ensure the availability of rare red blood cell (RBC) units for transfusion. Alloimmunization to RBC antigens may occur following transfusion or pregnancy.

Provision of blood may become challenging when a patient has made an alloantibody to a high-prevalence antigen or made multiple antibodies to many more common antigens. To have blood readily available for such situations requires access to an inventory of extensively phenotyped blood as well as to a database of rare donors who can be recruited for donation. One way to accomplish this is to routinely screen donors to search for rare blood types. A library of these rare donors is maintained that contains information such as their antigenic profile, demographic information for recruitment, and the RBC units that they have donated (liquid and frozen). Managers who are members of the World Health Organization (WHO) International Rare Donor Panel (IRDP) can search the WHO IRDP database and request rare blood from the members in other countries who have the blood they need. Units are then shipped according to the specifications required by both the shipping and receiving countries.

This issue of *Immunohematology* contains articles from many of the members of the ISBT Working Party on Rare Donors, detailing aspects of their country’s rare donor program(s) and their approach to making units from rare donors available for transfusion. The submitted articles appear alphabetically according to country name in issues Volume 32, Number 1, 2016, and Volume 32, Number 2, 2016, as Part I and Part II, respectively.

**Part I**
- World Health Organization
- Belgium
- Brazil
- Canada
- China
- Finland
- France
- Iran
- Israel

**Part II**
- Italy
- Japan
- Netherlands
- New Zealand
- Singapore
- South Africa
- Spain
- Switzerland, Germany, and Austria
- United Kingdom
- United States

The authors were asked to provide information on several topics. First, they were asked to give details on the type of rare donor program that exists in their country (national, regional, or local) and to outline the history of their rare donor program(s) (year started, and collaboration if regional or local programs). Second, they were asked to provide data on the number of active rare donors, the number of new rare donors added from 2012 to 2014, the number of rare units shipped (both domestically and internationally), and the number of requests for rare blood not filled. The authors were asked to review patient cases where incompatible blood had to be transfused because antigen-negative blood was not available and to provide details on the outcome, prophylaxis given, number of known cases, and other relevant details of these cases that can be shared. The authors were asked to share information about the incentives used in their country for rare donor recruitment. The Rh_null phenotype is recognized as the rarest of the rare donors in the world; the members were asked to quantify the number of such donors and provide the molecular background, if known.

In the event that the readers of *Immunohematology* are caring for patients with rare blood requirements, we hope that this collection of articles will provide an insight into the challenges of providing rare blood and allow our readers to be better informed and knowledgeable about international activities in the area of rare donor programs. The articles in this issue also serve to highlight the similarities and the differences between the programs and how they are managed in other countries.
It is incredible and reassuring to observe the international support, cooperation, and collaborative efforts that occur across geographical and political boundaries when a patient is in need, especially when the need is for very rare blood.

We thank the authors of the articles for sharing their data and experiences and the entire ISBT Working Party for their commitment to making rare blood available whenever and wherever it is needed.

Sandra Nance, Immediate Past Chair (corresponding author), ISBT Working Party on Rare Donors, American Red Cross, 700 Spring Garden Street, Philadelphia, PA 19123; Christine Lomas-Francis, Chair, ISBT Working Party of Rare Donors, New York Blood Center, Laboratory of Immunohematology and Genomics, Long Island, NY.
The International Rare Donor Panel (IRDP) has been in existence for almost 50 years and is now a worldwide collaboration involving 27 countries, with approximately 8000 rare donors listed. The Red Cell Reference Department of the International Blood Group Reference Laboratory (IBGRL) has compiled and maintained the panel since it began. The purpose of the panel is to locate and facilitate the exchange of rare blood between countries, when blood cannot be sourced nationally for a specified patient.

History

The pioneering work for the organization and compilation of the IRDP was carried out in the early to mid 1960s. The act of exchanging rare blood between countries was in place prior to that, however, as evidenced in The Lister Institute annual report of 1957, which in part describes highlights of the activities of the IBGRL and states:

[Dr. Parkin's] previous discovery of a family in England and Ireland with the exceedingly rare "Bombay" blood group (apparent red-cell group O, with anti-O in serum) made it possible for the laboratory to arrange for the transfusion of a baby in Holland with blood from one of the only two potential donors in Europe.1

In 1964 the then-director of the IBGRL, Dr. Arthur E. Mourant, presented a proposal for the organization of an international panel of blood donors of rare types at the General Assembly of the International Society of Blood Transfusion (ISBT) in Stockholm.2 Following this, in 1965, the IRDP was established as an ISBT initiative in collaboration with the World Health Organization. The purpose of the panel was to locate and facilitate exchange of rare blood units between countries for patients in need. The organization and maintenance of the panel were allocated to the IBGRL, and the inaugural meeting of the newly formed ISBT Advisory Committee for the IRDP took place on February 9, 1966, at the IBGRL in London.3 It was decided at this meeting that the panel should consist of two categories: the first category included group O donors whose red blood cells (RBCs) lacked antigens to a range of antibodies commonly encountered, therefore making them useful for transfusion to patients with multiple antibodies; the second category included donors whose RBCs lacked a high-prevalence antigen. The first panel was published in 1968 and consisted of almost 300 donors from 10 countries.4 The panel was typed and copies were distributed by mail, accompanied by an introductory letter (Fig. 1).

Since then, the panel has organically adapted with advances in technology and the discovery of more and more blood groups. In 1981, the panel was compiled on a computer for

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1. The Lister Institute annual report of 1957
2. Dr. Arthur E. Mourant, then-director of the IBGRL
3. ISBT Advisory Committee for the IRDP
4. First edition of the International Rare Donor Panel

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Fig. 1 Accompanying letter to the first edition of the International Rare Donor Panel.
the first time, although the technology only had the capability to enter and print information in capital letters, which was not ideal when dealing with RBC antigens. To deal with the issue, the word “little” was used to denote when a lowercase letter was indicated (Fig. 2). Around this time, the decision was made to remove the first of the original two categories of donors from the IRDP, since donors lacking common antigens could generally be provided locally. The panel was printed on large reams of paper (Fig. 2) and continued to be sent out by mail. When the 1985 panel was compiled and distributed in this way, it consisted of approximately 1500 donors from 22 countries and was sent to 110 blood centers around the world.

In 1991, the panel was compiled on an in-house computer at IBGRL (Fig. 3), which made adding and deleting donors a more continuous process. It was at this time that modem access was made available, which meant 24-hour password-protected access to the panel was now possible for those blood centers with modem capability. Then, in 1999, the panel was made accessible via the Internet. Information technology development and the beginning of the Internet age changed the usability of the IRDP significantly, although it was probably not exactly what Dr. Mourant had envisaged in 1964 when he wrote,

“The scheme would be organized by an International Central Office and Laboratory, which would collate, edit, and publish a list of donors of rare types... This proposal does not exclude ultimate transfer of lists to mechanical or electronic selector systems, but I am sure that we must begin with printed or stencilled lists.”

**Table 1. Rare donor listings of the International Rare Donor Panel, 2015**

<table>
<thead>
<tr>
<th>Number of donors</th>
<th>&gt;500</th>
<th>250–500</th>
<th>100–249</th>
<th>50–99</th>
<th>25–49</th>
<th>10–24</th>
<th>5–9</th>
<th>0–4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fy(a–b–)</td>
<td>S–s–U–</td>
<td>Js(a+b–)</td>
<td>Kc</td>
<td>Ge–</td>
<td>RH:–51 (MAR–)</td>
<td>SC:–1</td>
<td>Cr(a–)</td>
<td></td>
</tr>
<tr>
<td>Jr(a–)</td>
<td>Co(a–b+)</td>
<td>Jk(a–b–)</td>
<td>O(a,Bombay)</td>
<td>LW(a–b+)</td>
<td>CDE/CDE (R,r)</td>
<td>Ok(a–)</td>
<td>K11–</td>
<td></td>
</tr>
<tr>
<td>D(b–)</td>
<td>Yt(a–)</td>
<td>I–</td>
<td>P</td>
<td>Gy(a–)</td>
<td>JMH–</td>
<td>En(a–)</td>
<td>Er(a–)</td>
<td></td>
</tr>
<tr>
<td>Lu(a+b–)</td>
<td>Vel–</td>
<td>D–</td>
<td>S–s–U+var</td>
<td>Rhnull</td>
<td>In(b–)</td>
<td>RH:–46 (Sec–)</td>
<td>Co(a–b–)</td>
<td></td>
</tr>
<tr>
<td>Lu(a–b–)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Co(a–b–)</td>
<td></td>
</tr>
<tr>
<td>Kp(a+b–)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Cw/D–/CwD–</td>
<td></td>
</tr>
</tbody>
</table>

**Fig. 2** Front page of the 1985 printed International Rare Donor Panel.

**Fig. 3** Compiling the International Rare Donor Panel on a computer at the International Blood Group Reference Laboratory in the early 1990s.
In 2007, a new IRDP database was developed by the National Health Service (NHS) Blood and Transplant Center for IBGRL and included functionality to search on multiple criteria, including ABO group and other antigen-negative requirements in addition to the rare phenotype. This database has been updated periodically and remains in use today (Fig. 4).

Figures 5–8 provide additional information from the early days of the IRDP.

**The IRDP Today**

Currently, the IRDP has approximately 8000 donors listed from 27 countries. The IRDP is only intended for use when blood cannot be sourced nationally; therefore, the rarities listed represent those that are the hardest to find in most populations. Some categories are still rarer than others, as shown in Table 1. In addition to individually listed donors, the IRDP includes the frozen inventories of blood banks from around the world. A number of these contributing institutions choose only to list the number of frozen units according to ABO and rarity; therefore, the number of actual donors will be greater in the respective categories.

The IBGRL, now located in Bristol at the NHS Blood and Transplant Filton center, continues to compile and maintain the IRDP. The role of the IBGRL is to receive rare donor lists, provided by the contributing countries, and update the IRDP database according to the additions and/or deletions provided on the lists. Some contributors send samples to IBGRL for confirmatory testing of newly identified donors, although this is not a requirement for inclusion of a donor to the panel. Donors are assigned a unique number by their contributing country and are listed by this number on the IRDP; therefore,
no personal donor data are held in the database. Most IRDP contributors maintain a national donor registry, but in countries where a national registry is not established, there may be a number of individual contributing institutions from the same country. All contributors are required to provide IBGRL with any amendments to their designated contact personnel details. This step is very important to ensure the appropriate person/department can always be contacted to inquire about rare donor availability. The IBGRL makes all this information available via the Internet, and authorized users can access the panel at https://rare.blood.co.uk/RareDonor/Login/Default.aspx. Access requests can be made by medical professionals, who may be required to source rare blood for clinical use only. All access requests should be made to the IBGRL by e-mailing rare.donor@nhsbt.nhs.uk. The staff of the IBGRL Red Cell Reference Department is also available to carry out searches when required, and search requests can be sent to the same e-mail address.

When a search of the IRDP has been carried out and possible rare donors identified, the requestor is provided with the contact details for the relevant contributing institutions. It is then the responsibility of the requestor to contact the contributors to inquire about donor availability and to discuss the logistics associated with obtaining blood from another country, including mandatory testing practice, shipment, customs requirements, and price. The IBGRL works closely with the ISBT Rare Donor Working Party to ensure that the IRDP functions as optimally as possible. An “International Shipment of Rare Blood Response Form” was devised by the Working Party to capture useful information regarding the outcome of any rare blood shipments that have occurred as a result of searching the IRDP. This information helps us to understand rare blood demand and to ensure that the IRDP process runs without problems; it also helps to capture any logistical issues that may need addressing by the Working Party.

The Future of the IRDP

It is important that the IRDP evolves with the changing demands for blood of rare types. These changes not only coincide with discovery of new blood groups, but also with scientific and information technology developments. DNA-based testing to find rare donors is already being used in some countries, and it is likely that the potential to scale up rare donor screening will be realized as high-throughput genotyping platforms become more economical. This scenario will bring new challenges for the IRDP. The IRDP database
WHO International Rare Donor Panel

is currently undergoing an upgrade that will provide new functionality to enable remote upload of donor lists and updates to contributor contact details. This functionality will make the panel maintenance more efficient, and it is hoped that more regular updates will be possible.

Summary

Over the past 50 years, the IRDP has evolved and developed to meet international rare blood needs. Although the definition of a rare donor has changed since the early days of the panel, the purpose of the IRDP has always remained the same: to locate and facilitate exchange of rare blood for patients in need. It is important to remember that rare blood is required rarely, but when it is needed, the worldwide collaboration of the IRDP ensures that every effort can be made to find blood for patients with even the rarest of blood types. Although it is difficult to predict what the next 50 years might bring, no matter what format the IRDP takes, the purpose of the panel is unlikely to change.

Acknowledgments

The author would like to thank all those who contribute to the IRDP for the wonderful worldwide collaboration. Most of all, we must thank the rare donors of the IRDP; their selfless generosity to save the lives of others, regardless of where they may be in the world, is remarkable.

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3. ISBT Advisory Committee for the International Panel of Donors of Rare Types. Minutes of a meeting held at the Blood Group Reference Laboratory. [Minutes of meeting held 9 February.] London, 1966 (Unpublished).

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For information concerning the National Reference Laboratory for Blood Group Serology, including the American Rare Donor Program, contact Sandra Nance, by phone at (215) 451-4362, by fax at (215) 451-2538, or by e-mail at Sandra.Nance@redcross.org.

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Belgium has two frozen blood banks: Dienst voor het Bloed (DvB) in the northern part of the country and Service du Sang (SdS) in the southern part of the country. A regional rare donor program was established in both services; we do not have a national program. Our goal is to obtain a national inventory and to list the rare donors of our country on the World Health Organization (WHO) International Rare Donor Panel (IRDP).

The frozen blood bank at DvB began preserving rare blood units in 1985 in collaboration with the reference laboratory of immunohematology, where identification of rare antibodies is performed. The frozen blood bank at SdS began preserving rare blood units in 1980. Preservation at both centers was initially performed in liquid nitrogen, but since 2005–2006, storage is in high-concentration glycerol at −80°C with a conservation limit of 10 years, as defined by Belgian law.

A donor is considered rare if his phenotype prevalence is 1 in 1000 or less. Most of the rare donors in our services have been detected by random phenotyping campaigns of regular donors (from group O or A with determination of antigens in the RH, KEL, FY, JK, and MNS blood group systems) or in family members of patients immunized against high-prevalence antigens. As for all donors in Belgium, rare donors must comply with national legal standards for blood donations.

The total number of allogeneic units in the frozen inventory of the DvB consists of 136 units from approximately 40 active rare donors; between 2012 and 2014, seven new rare donors were added. For SdS, the total number of allogeneic units consists of 155 units; between 2010 and 2014, 103 frozen red blood cell (RBC) units were added. Table 1 provides an overview of rare donors and the frozen rare RBC unit inventory in Belgium.

In the DvB donor population, most of the donors are of European descent; there is not a wide variation of rare donor antigen profiles because of the small variation of ethnicity in northern Belgium. Significant demographic differences in the donor population of the SdS (larger urban areas with mixed ethnic groups) means that their antigen profiles are more extended—especially with donors from African communities.

The most difficult types to find are GE:–2,–3, Lan–, Jk(a–b–), K0, Co(a–b–), P–, I–, U–, Rhnull, and Oh (Bombay). The use of autologous storage from directed donations is discouraged unless for planned surgery. One Oh (Bombay) patient was detected in 1991, and between 1991 and 1999, was requested to provide five autologous donations to be frozen in liquid nitrogen. This donor has been invited to give blood in early 2015 to obtain more recent donations to be stored at −80°C.

In Belgium, we handle 1–13 requests for frozen rare RBC units per year, with a total of 48 units in the last 5 years. Almost all units are supplied from our own frozen blood banks. Only four orders have been placed to international frozen blood banks (National Health Service [NHS] in the United Kingdom, National Reference Center for Blood Groups [CNRGS] in France, and the European Blood Bank of Frozen Blood of Rare Groups [Sanquin] in Amsterdam) in the last 4 years.

The most required specificities for rare blood units for our patient population are K+k–, Yt(a–), U–, Vel–, Lu(b–), Kp(b–), and Fy(a–b–).

We do not have exact data on the number of incompatible transfusions; in some rare cases when no rare blood was available, prophylaxis was given with steroids and intravenous immunoglobulin. Further work is necessary to follow up with patients transfused with the provided rare donor units and to retain a record of the transfusion outcome of these patients. In addition, we plan to begin monitoring the outcome of incompatible transfusion cases when no appropriate blood is available.

In the future, we want to increase the number of rare donors through mass antigen screening of regular donors with automated molecular methods.

As noted earlier, most of our donors are of European descent—our challenge is to expand the recruitment of donors with different ethnic backgrounds to enlarge our database with other specificities of rare blood groups.

An Rhnull donor has not been encountered either in our regular donor population or in patients for whom we have received a request.

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A. Vanhonsebrouck and T. Najdovski

Table 1. Overview of rare donors and frozen rare unit inventory in Belgium

<table>
<thead>
<tr>
<th>Phenotype</th>
<th>Number of donors</th>
<th>Number of units</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A+</td>
<td>A-</td>
</tr>
<tr>
<td>Lu(a+b-)</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Yt(a-)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>r’r’</td>
<td>0</td>
<td>13</td>
</tr>
<tr>
<td>R_0 R_0, Fy(a-b-)</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>r’r’</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>Vel-</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>Other Rh*, Fy(a-b-)</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>R_0,</td>
<td>15</td>
<td>0</td>
</tr>
<tr>
<td>R_0, R_0, K-Fy(a-b-), Jk(b-) S-</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>S-s-U-</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Co(a-)</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>r, Fy(a-b-)</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>U-</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>D-</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>D(c)-</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>S-s-U+</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Kp(a+b-)</td>
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<td>1</td>
</tr>
<tr>
<td>Lu(a-b-)</td>
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<td>0</td>
</tr>
<tr>
<td>Jr(a-)</td>
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<td>0</td>
</tr>
<tr>
<td>Jk(a-b-)</td>
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<td>0</td>
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<tr>
<td>Lan-</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>60</td>
<td>38</td>
</tr>
</tbody>
</table>

DvB = Dienst voor het Bloed (blood bank in northern Belgium); SdS = Service du Sang (blood bank in southern Belgium).
*Other Rh = Rh different than R_0 R_0 or rr.
Brazil is a large country with approximately 200 million inhabitants and has 27 states in a total area of approximately 8 million square kilometers. The distance from north to south is 3,645 km and from west to east is 3,577 km. The Brazilian population is of heterogeneous ethnic origin, with an intense process of miscegenation and a high degree of admixture between people of European, African, and Native American descent. Therefore, finding compatible blood to meet the needs of patients requiring rare blood has been a significant challenge in Brazil.

It is estimated that 3 million units of blood are collected per year in Brazil, with approximately 70 percent of donations collected through the public system. Despite numerous efforts performed by different institutions and professionals, until 2014, there was no Brazilian national panel of rare donors—although local programs, including private and public blood centers, have their own donor panels. The frozen stocks of rare units are kept in two centers with consolidated testing laboratories—the Albert Einstein Hospital and the Sírio Libanês Blood Center.

In a multi-ethnic population such as Brazil, the prevalence of the different blood group antigens vary significantly, and it is necessary to have a range of rare blood types available. Our main difficulty is in importing rare units through international rare donor registries, because Brazilian customs procedures are restrictive and bureaucratic. Because of this, collaborations between regional and local programs have helped us to meet the needs of the patients with a rare phenotype; for example, the local program run by the Sírio Libanês Hospital Blood Bank in São Paulo holds a special inventory of liquid and frozen red blood cell (RBC) units and has helped to fulfill many requests.

To meet most of the needs of patients, and considering the importance of having a national panel of rare donors in a large country like Brazil, in 2012, the Ministry of Health, through the General Coordination of Blood and Blood Products (CGSH), started and sponsored a project in partnership with the Albert Einstein Hospital to support three public blood centers located in strategic regions (south, north, and southeast Brazil). These centers have the potential to screen large numbers of donors for rare blood group antigens and platelets using serology and DNA typing and can freeze rare units. To encourage this initiative, and also as an incentive for the establishment of a national rare donor program, in November 2013, the Brazilian Association of Hematology and Hemotherapy, in conjunction with the International Society of Blood Transfusion (ISBT), organized an Academy Day on rare donors during the Brazilian Congress of Hematology and Cell Therapy (HEMO 2013), with positive repercussions throughout the country.

In May 2014, the Brazilian Ministry of Health, through the CGSH, established a technical committee to provide support for the implementation of a national rare donor program. At present, four blood centers located in strategic regions (Campinas, Florianópolis, Manaus, and Rio de Janeiro) were tasked with screening and freezing of rare red cells and platelets. Currently, these centers are starting the validation of cryopreservation procedures. A strategy for searching for and freezing rare units is being established by these four public blood centers and an extensive screening program for regional blood centers is being developed. Education of personnel, development of software, and creation of a process for requesting and shipping rare units have also been discussed. The role of the Brazilian national program, established by the CGSH, is to compile information on rare donors who have been identified at all blood centers in Brazil and to make this information available when rare blood is needed.

To start a national registry of rare donors, the CGSH conducted a survey at 17 public blood banks, which represent half of the Brazilian network of public blood centers. These regional blood banks do not have a screening program in place, but according to this survey, they have more than 1000 active donors whose RBCs lack high-prevalence antigens, with more than 200 new rare donors identified between 2012 and 2014. In this scenario, it is important to remember that the national program is still in the early phase and we are just implementing a rare donor database. We believe that the incentive from the government, together with the availability of resources for screening programs and the implementation of a countrywide network to establish the national rare donor registry, will significantly increase this database.

Surprisingly, we have five Rhnull donors identified in Brazil, including two group A sisters in the South of Brazil, two group O donors in Rio de Janeiro, and one group O donor in São Paulo. Sequencing of RH and RHAG of four of these donors showed that the two sisters have a deletion in RHCE*ce
(960–963 delG), one donor has the RHAG*01N.09 allele, and the other donor has the novel RHAG*01N.16 allele leading to a premature stop codon (Gln104Stop).

The rare units shipped domestically between 2012 and 2014 are listed in Table 1. During this period, five requests were not fulfilled: Js(b–) (3); Yt(a–) (1); and K₀ (1). Three incompatible transfusion cases were reported: two patients with anti-Js⁶ and one patient with anti-Yt⁶. For those cases, only hydration and transfusion of small volumes were performed, with good survival of transfused RBCs. For the patients with anti-Js⁶, a monocyte monolayer assay (MMA) was performed and the reactivity was less than 5 percent.

Table 1. Rare units shipped between 2012 and 2014 in Brazil

<table>
<thead>
<tr>
<th>Phenotype</th>
<th>Number of units shipped</th>
</tr>
</thead>
<tbody>
<tr>
<td>k⁻</td>
<td>11</td>
</tr>
<tr>
<td>D(b–)</td>
<td>5</td>
</tr>
<tr>
<td>S–s–U–</td>
<td>3</td>
</tr>
<tr>
<td>hr³⁻</td>
<td>3</td>
</tr>
<tr>
<td>Vel⁻</td>
<td>2</td>
</tr>
<tr>
<td>GE⁻²</td>
<td>2</td>
</tr>
<tr>
<td>Lan⁻</td>
<td>1</td>
</tr>
<tr>
<td>Co(a–)</td>
<td>1</td>
</tr>
<tr>
<td>Oₐ (Bombay)</td>
<td>1</td>
</tr>
<tr>
<td>RH⁻:–17</td>
<td>1</td>
</tr>
<tr>
<td>Rhnull</td>
<td>1</td>
</tr>
<tr>
<td>hr³⁻</td>
<td>1</td>
</tr>
<tr>
<td>r°r°</td>
<td>1</td>
</tr>
<tr>
<td>Lu(b–)</td>
<td>1</td>
</tr>
</tbody>
</table>

The profile of blood donors has changed in Brazil over the past 20 years, from remunerated to non-remunerated donors, and then from replacement to community donors. To ensure an adequate rare blood supply, it is crucial to recruit suitable blood donors. Recruitment campaigns and programs that educate such donors about the importance of blood donation have been developed. As incentives and motivation for the rare donors, the local and regional programs are organizing meetings with educational lectures and breakfast meetings. Recognition of the donors with letters, cards, and certificates or in the digital media is also being used as incentives.

Although the Brazilian national rare donor program is at an early stage and much work still needs to be done, we believe that soon we can have the program established.

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The rare donor program at the Hospital Sírio Libanês began in 1990, with the encouragement of Delores Mallory, John Moulds, and Marcela Contreras, because at that time no such strategy was available in Brazil. In addition, an important contribution of rare sera was supplied by the international Serum, Cells and Rare Fluids (SCARF) program. Although managed by local funds and having a modest capacity for screening rare donors, all inventory units are available for any transfusion service either from Brazil or overseas.

Since the inception of our rare donor program, 84,426 donors have been screened by serologic methods for several antigens, rendering a total of 161 rare donors, according to different blood group systems (Table 1). Furthermore, since 2012, we have found 36 new rare donors who currently actively contribute with regular donations whenever needed.

Table 1 depicts our results through December 2014. In addition to testing all 84,426 donor samples for the main Rh antigens (D, C, c, E, e), we also tested for the presence of Goa (RH30) in 20,344 donors to potentially find DIVa donors. A total of 186 rare units (26 from 2012–2014) were made available to 75 Brazilian patients, not only in our hospital, but in 13 additional hospitals or blood services facilities across the country. In addition, because storage of rare units in the frozen state is not widely available in Brazil, Hospital Sírio Libanês served as a facilitator for storage, thawing, and shipping of 34 rare units that included k– (N = 1), K0 (N = 2), Kp(b–) (N = 7), Yt(a–) (N = 10), Vel– (N = 12), and Di(b–) (N = 2), which were supplied either by national or international agencies (American Red Cross, New York Blood Center, Canadian Red Cross, and Osaka Red Cross) to seven blood services in the country during this period. There were two requests not filled during this period (one for a U– patient and one for an Rhnull patient).

We have not yet identified any Rhnull donors; this phenotype is recognized as the rarest in the world. Nevertheless, we understand that identifying such a donor, where high rates of failure are expected, can only be accomplished by an ongoing Rh antigen screening of all new donors, which we carry out in our service.

We were aware of one incompatible transfusion case: the serum from a previously transfused patient was sent to our laboratory for investigation and anti-Di was identified. This patient was subsequently transfused with two Di(b–) units through our rare donor program with no further hemolysis.

Table 1. Phenotypes of rare blood donors identified at the Hospital Sírio Libanês as of 2014

<table>
<thead>
<tr>
<th>Phenotype</th>
<th>Tested donors*</th>
<th>Total</th>
<th>2012–2014†</th>
</tr>
</thead>
<tbody>
<tr>
<td>k–</td>
<td>84,656</td>
<td>118</td>
<td>24</td>
</tr>
<tr>
<td>Di(b–)</td>
<td>40,551</td>
<td>13</td>
<td>4</td>
</tr>
<tr>
<td>rir’</td>
<td>84,426</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>rir”r”</td>
<td>84,426</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Kp(b–)</td>
<td>50,232</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>R, R’</td>
<td>84,426</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>rir’r’</td>
<td>84,426</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Vel–</td>
<td>9,477</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Kx– (McLeod)</td>
<td>50,232</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>O, (Bombay)</td>
<td>84,426</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>K0</td>
<td>50,232</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>U–</td>
<td>17,163</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>PP1P–</td>
<td>23,050</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Jk(a–b–)</td>
<td>32,915</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>161</td>
<td></td>
<td>36</td>
</tr>
</tbody>
</table>

*Since 1990.
†New donors added to our rolls between January 2012 and December 2014.

We have very strong support from voluntary non-remunerated donors in our service. We provide no special incentives for either rare donors already in the program or for those who are enrolling through screening procedures. In other words, although rare donors are quite unique, they receive the same care provided to any regular voluntary donor. So far, we have not perceived any untoward effect by applying this policy.

In summary, a rare donor program requires perseverance, patience, and long-term commitment, given that one cannot predict when rare blood will be needed. Being part of a global program under the aegis of several agencies (International Society of Blood Transfusion, AABB, American Red Cross, EFS [Etablissement Français du Sang], Canadian Red Cross, Japanese Red Cross, Sanquin, etc.) with active cooperation.
and mutual support increases the chances of finding a rare unit for a rare patient.

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Rare donor program: Canadian Blood Services

M. Goldman and L. St. Croix

In Canada, two blood services are responsible for the provision of all blood components: Héma-Québec for the province of Québec and Canadian Blood Services (CBS) for the rest of Canada. There is close collaboration between the two organizations to ensure the provision of rare blood units; units are shipped between the two blood services when necessary. This article will focus on the rare donor program at CBS. CBS has approximately 425,000 active donors (donors who have donated in the past 18 months) who donate approximately 900,000 red blood cell (RBC) units per year. Of these, approximately 2,000 donors have a rare donor code, and 800 RBC units are found in the frozen rare inventory. The inventory is managed nationally, with units being sent throughout the country wherever they are needed.

Methods of Donor Screening, Recruitment, and Retention

Potential rare donors are found by several mechanisms. Close to 45,000 donors (approximately 10% of the active donor base), chosen based on ABO group, D type, and donation status, are phenotyped annually using an automated solid-phase platform, supplemented by manual testing. Implementation of the Immucor (Norcross, GA) NEO permits automated testing for the 11 common antigens (C, E, c, e, K, Fy^a, Fy^b, Jk^a, Jk^b, S, and s). When the typings have been performed on two separate donations, the phenotype will print on the donation label for all subsequent donations. Genotyping using an automated testing platform (Progenika-Grifols IDCore XT; San Marcos, TX) is done on samples with phenotypes of particular interest, such as group O, D− S− s−, or group O, D− Fy(a−b−), to identify rare donors. Genotyping is also being performed on samples from clinics with a high number of ethnically diverse donors and donors known to be missing a high-prevalence antigen originally typed using unlicensed serological reagents. Genotyping will be increasingly important to type donors of African origin, as there is an increasing need for RBC units to provide transfusion support for patients with sickle cell anemia. Identification of ethnically diverse donors for genotyping will be facilitated by the introduction of a voluntary question regarding donor ethnic origin in 2016. When an antibody to a high-prevalence antigen is identified in a prenatal patient, we attempt to recruit the individual to become a blood donor when she becomes eligible. We also attempt to obtain samples from family members of prenatal patients as well as patients with rare types identified by our diagnostic services laboratories. Testing of prenatal patients and family members of prenatal and diagnostic services patients has enabled us to find several rare donors whose phenotypes are not found on the automated genotyping platform, such as GE:−2,−3; Jr(a−); and Vel−.

We do not provide any incentives for rare donors. At the present time, these individuals are simply sent a letter explaining how rare their blood is. Often, they are contacted by phone to provide units for a given patient. We hope to develop more robust donor loyalty programs to retain these donors going forward.

Current Inventory, Imports, Exports, and Challenges

At the present time, we have 801 RBC units in our rare phenotype inventory (Table 1). On average, approximately 30 RBC units are deglycerolized every year. We currently have no Rhnull donors.

From 2011 through December 31, 2014, we imported 26 rare units from other countries and 9 rare units from Héma-Québec. Imported rare units included 7 K^0, 5 Jk(a−b−), 3 I−E−, 4 Co(a−), 2 Jr(a−), 2 Di(b−), 1 Rhnull, and 2 that were negative for multiple antigens. The American Rare Donor Program has graciously provided most of the international units imported, with the K^0 units coming from Japan and Finland, and the Rhnull unit coming from South Africa. Over the years, we have exported a small number of units including Bombay units to Australia and Kp(b−) Jk(b−) units to the United States.

We have had very few incompatible transfusion cases. In 2010, we were challenged by a patient who required AnWj− units. We provided units that were truly AnWj− or expressed the In(Lu) phenotype. These units came from our own donors, as well as from Héma-Québec and international donors. We were unable to find crossmatch-compatible units for a pregnant female with sickle cell anemia with multiple alloantibodies and other unidentified reactivity; this may have contributed to fetal loss. We are currently challenged to provide adequate transfusion support for patients with sickle cell anemia with
partial CE antigens and multiple antibodies requiring chronic transfusion support. We also have an inadequate number of Di(b−) donors; many Di(b−) individuals are part of the native Canadian population and live in remote areas.

Table 1. Frozen red cell inventory, Canadian Blood Services, March 2015 (N = 801)

<table>
<thead>
<tr>
<th>Phenotype</th>
<th>Number of units</th>
</tr>
</thead>
<tbody>
<tr>
<td>k−</td>
<td>147*</td>
</tr>
<tr>
<td>Fy(a−b−)</td>
<td>139†</td>
</tr>
<tr>
<td>Yt(a−)</td>
<td>137</td>
</tr>
<tr>
<td>Other</td>
<td>91</td>
</tr>
<tr>
<td>Vel−</td>
<td>46</td>
</tr>
<tr>
<td>Kp(b−)</td>
<td>38</td>
</tr>
<tr>
<td>Js(b−)</td>
<td>28</td>
</tr>
<tr>
<td>Co(a−)</td>
<td>26</td>
</tr>
<tr>
<td>O,… (Bombay)</td>
<td>24</td>
</tr>
<tr>
<td>I−</td>
<td>18</td>
</tr>
<tr>
<td>GE:−2,−3</td>
<td>17</td>
</tr>
<tr>
<td>U−</td>
<td>17</td>
</tr>
<tr>
<td>Jr(a−)</td>
<td>13</td>
</tr>
<tr>
<td>Lan−</td>
<td>11</td>
</tr>
<tr>
<td>Lu(a−b−)</td>
<td>9</td>
</tr>
<tr>
<td>SC:−1</td>
<td>8</td>
</tr>
<tr>
<td>Di(b−)</td>
<td>7</td>
</tr>
<tr>
<td>En(a−)</td>
<td>7</td>
</tr>
<tr>
<td>In(b−)</td>
<td>7</td>
</tr>
<tr>
<td>Jk(a−b−)</td>
<td>6</td>
</tr>
<tr>
<td>Gy(a−)</td>
<td>4</td>
</tr>
<tr>
<td>GE:−2,3</td>
<td>1</td>
</tr>
</tbody>
</table>

*Over 150 known donors; only units negative for several other antigens were frozen.
†Over 1500 known donors; only units negative for several other antigens were frozen.
‡Mainly rare phenotype combinations.

References


Mindy Goldman, MD (corresponding author), Medical Director, Donor and Clinical Services, Canadian Blood Services, 1800 Alta Vista Drive, Ottawa, ON, Canada, K1G 4J5, mindy.goldman@blood.ca; Lisa St. Croix, BSc, MLT, Business Continuity Program Developer, Supply Chain Operations Planning, London, ON, Canada.
Rare blood program in China

Z. Zhu, C. Wang, L. Ye, Q. Li, Z. Guo, J. Zhang, S. Han, and Q. Yang

In the past 5 years, nearly half of China’s regional blood centers have carried out a rare blood screening program aimed at elucidating the genetic characteristics of blood groups in the Chinese population and identifying high-prevalence antigen-negative blood donors. The Rare Blood Bank of China was established through serological screening and genetic testing, and currently more than 1300 rare blood donors have been identified. A total of 79 blood units of various rare blood types have been transfused in hospitals within the past 5 years.

In clinical transfusion, it is important to choose antigen-matched blood for patients to avoid alloimmunization. More than 300 blood group antigens are expressed on the human erythrocyte membrane; they are immunogens that can induce antibodies that can potentially cause adverse transfusion reactions. In addition to the challenge of matching for such a large number of antigens, the expression of these antigens differs among various populations, making it even more difficult to match donors to patients.

Screening Program for Rare Blood in China

Since 2003, screening donors for rare blood has been carried out as a routine process at the Institute of Transfusion of the Shanghai Blood Center. In 2007, a plan for establishing a national rare blood bank was included in the Blood Safety Program of Public Health special project by the Chinese Ministry of Health. Currently, there are 14 regional blood centers in China that carry out donor screening throughout the year and provide the obtained rare blood to the Shanghai Blood Center.

In screening for rare blood in China, we first test donor samples negative for high-prevalence antigens that are difficult to match in clinical transfusion practice but for whom patients have been identified, among which are samples with deleted or variant GPA, GPC, or Kell blood group glycoproteins. We use a urea method for screening for the Jk(a–b–) phenotype, as glycoproteins of the JK blood group system serve as a urea transport channel on the cell membrane of erythrocytes. In the meantime, specialized antisera, such as anti-Rh17, anti-Diβ, anti-Wrβ, and anti-Vel, are used to screen for antigens for which respective antibodies frequently cause clinical hemolytic transfusion reactions and hemolytic disease of the fetus and newborn (HDFN).

Because the resource of rare antisera is limited, the identification of rare blood donors is more dependent on molecular testing. Previously, tests were performed by detecting single mutations of blood genes, whereas we now use multiplex polymerase chain reaction (PCR) systems with mixed DNA pools.

Our rare blood molecular screening program currently tests for 16 single nucleotide polymorphism sites including those associated with k–, s–, Co(a–), Yt(a–), and Fy(a–).

The DNA pool multiplex PCR screening method not only improves screening efficiency, but also largely reduces the cost. Furthermore, screening techniques utilizing blood-group gene chips also contribute to the acquisition of rare blood. We have carried out molecular testing on 450 donors in Shanghai using BloodChip reference chips (Grifols, Barcelona, Spain) and identified six donors with rare blood phenotypes, including s–, D(b–), and VS+.

Distribution Features of Rare Blood Groups in the Chinese Population

The prevalence of blood group antigens vary among different races and populations. The Chinese population mainly includes the Mongoloid (99.2%) and the Caucasian (0.8%). Han population is the main nationality in China, with 1.1 billion people, which accounts for 91.6 percent of the total Chinese population. Racially, the Northern Han belong to the Far Eastern race, whereas the Southern Han are a transitional race between the Southern Asian race and Far Eastern race.

Because the prevalence of the D– type is as low as 0.4 percent, challenges sometimes exist in supplying D– blood for clinical transfusion. According to the standard for blood product preparation and the guide for clinical blood transfusion in China, pre-transfusion examination includes the identification of the D type of both donors and recipients. Therefore, when blood transfusion services have excess D– blood, they will cryopreserve units with high-concentration glycerol and store them at −85°C. In China, all the regional blood centers have frozen D– blood units in their inventory. Large blood centers in Shanghai, Beijing, and
Guangzhou supply 2000 units of D– blood per year to clinics, approximately 40 percent of which are cryopreserved. Unlike those of European or African descent, the D– population in those of Asian descent (especially those from the Far East region) is of the Del phenotype. In China, the Del phenotype accounts for 20 percent of all D– people. So far, there is no evidence in our clinical practice of transfusion showing that Del individuals as donors cause alloimmunization to D, and thus we consider it safe to supply Del blood to the clinic as D– blood. Similarly, the results from an investigation on immune antibodies in pregnancy among Del women also support our view, in which none of the Del pregnant women in 118 cases developed anti-D.

Three Rhnull donors have been found in China, the blood from one of which has been provided to Rhnull patients. This Rhnull donor has normal RHD and RHCE, and the mutation of the RHAG may be causing the Rhnull phenotype.

Like the D– phenotype, Fy(a–) prevalence in the Chinese Han population is low (0.3%), and thus screening for Fy(a–) is also included in the screening program for rare donors in China. As Fy(a–) patients in China tend to produce anti-Fya in reaction to the corresponding antigen, there are more than 200 Fy(a–) donors in our rare donor records to meet the clinical requirements for Fy(a–) blood. Diego is somewhat a special blood group in people of Asian descent; both Di(a+) and Di(b–) phenotypes are of higher prevalence in this population than in others. Clinically, anti-Diα and anti-Diβ frequently result in transfusion reactions and HDFN; therefore, it is of great importance to screen for Di(b–) donors for Di(b–) patients.

Table 1. Rare blood donors in China as of 2015

<table>
<thead>
<tr>
<th>Phenotype</th>
<th>Number of donors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fy(a–)</td>
<td>204</td>
</tr>
<tr>
<td>Lu(a–b–)</td>
<td>86</td>
</tr>
<tr>
<td>E–c–Jk(a–)</td>
<td>36</td>
</tr>
<tr>
<td>E–c–Jk(b–)</td>
<td>32</td>
</tr>
<tr>
<td>If(adult)</td>
<td>28</td>
</tr>
<tr>
<td>Jk(a–b–)</td>
<td>27</td>
</tr>
<tr>
<td>para-Bombay</td>
<td>6</td>
</tr>
<tr>
<td>s–</td>
<td>5</td>
</tr>
<tr>
<td>PP1P–</td>
<td>5</td>
</tr>
<tr>
<td>D–</td>
<td>3</td>
</tr>
<tr>
<td>Co(a–)</td>
<td>3</td>
</tr>
<tr>
<td>Rhnull</td>
<td>3</td>
</tr>
<tr>
<td>Rsr2(CCDEE)</td>
<td>2</td>
</tr>
<tr>
<td>Ks</td>
<td>2</td>
</tr>
<tr>
<td>Vel–</td>
<td>2</td>
</tr>
<tr>
<td>P⁺</td>
<td>2</td>
</tr>
<tr>
<td>rr⁺(CCdEE)</td>
<td>1</td>
</tr>
<tr>
<td>C⁺D–</td>
<td>1</td>
</tr>
<tr>
<td>RH–:51 (MAR–)</td>
<td>1</td>
</tr>
<tr>
<td>Lan–</td>
<td>1</td>
</tr>
<tr>
<td>Yt(a+)</td>
<td>1</td>
</tr>
<tr>
<td>Fy(a–)D–</td>
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</tr>
<tr>
<td>Wr(b–)</td>
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</tbody>
</table>

Creation of a National Rare Blood Bank in China

Five years of screening has resulted in 1.5 million donors being screened, mostly using serology. Molecular screening is used for specific purposes. There are already over 1300 rare blood donors identified in the National Rare Blood Bank. Their information has been registered in the rare blood database and is available to medical professionals across China via a Web site. The phenotypes of the currently available units in the rare blood bank are summarized in Table 1; these units are from blood transfusion services across the country. After rare donors identified by these blood transfusion services are verified by the Shanghai Blood Center, the organizations register the donor information in the database and are responsible for keeping in regular contact with the donor. The methods of contact include sending messages to those rare blood donors for special holidays and organizing various activities for them as members of the donors’ club.

Clinical Application of Rare Blood Transfusion

In the most recent 5 years, 79 units of different types of rare blood have been supplied for clinical transfusion via the National Rare Blood Bank of China, including D–, Rhnull, Jk(a–b–), and Fy(a–).

Inevitably, there is still a long way to go to find the ideal balance between the rare blood supply from our bank and the demands from the clinics. Currently, every year, 20 percent to 30 percent of rare blood transfusion requests cannot be met. In 2015, there were two patients for whom we were unable to find the necessary type of rare blood: a 64-year-old female Di(b–) patient who needed transfusion because of anemia, and her serum contained anti-Diβ, which may have been due to pregnancy; the other was a patient with sickle cell disease who was Fy(a–b–) with autoantibody. We transfused the Di(b–) patient with Di(a+b+) blood. The patient did not have severe adverse reactions during the transfusion, and the patient’s hemoglobin improved after transfusion. Fortunately, the Fy(a–b–) patient improved without transfusion, was released from the hospital after 4 weeks, and returned to the United States to continue treatment.
Moreover, there are significant differences in regulations for blood product import and export in different countries, especially in infectious disease testing rules. Besides regular tests for human immunodeficiency virus, hepatitis B virus, and hepatitis C virus, tests for human T-lymphotropic virus, variant Creutzfeldt-Jakob disease, cytomegalovirus, and parvovirus B19 in donor blood are also mandatory in some countries. To some extent, the different requirements for infectious disease testing limit the distribution of rare blood to different countries.

References

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E-mail information to immuno@redcross.org or fax to (215) 451-2538
The Finnish Red Cross Blood Service serves as a national blood service and a reference laboratory for pre-transfusion testing. All challenging antibody identification cases and donor phenotyping and genotyping in Finland are thus carried out in our laboratory. This optimizes rare donor program management in Finland and helps in designing the transfusion strategy for patients with a rare blood type.

The Finnish rare donor program has operated for over 30 years. A blood type is considered rare if its prevalence is 1 in 1000 or less, with the most common rare phenotypes in Finland being LW(a–), Jk(a−b−), and Pk. Because of the problematic availability of rare blood, we implemented a program for freezing red blood cells (RBCs) in Finland with the Haemonetics (Braintree, MA) ACP 215 processing system in April 2010. The system is closed, therefore enabling an extended shelf life of the units after thawing compared with an open system. Based on our validation results, the units are safe for use for 7 days after thawing.

At present, we have around 130 donors aged 18–65 years with rare blood types in the donor registry, of which about 70 are active donors with donations in the past 2 years (Table 1). During 2012–2014, 12 new rare donors were added to our database. Blood types that are globally rare but more common in Finland, such as Jk(a−b−) and LW(a−), are represented in our donor database and in the stock of frozen RBC units and are also available internationally. In 2012–2014, 57 thawed and deglycerolized units were distributed domestically and 24 deglycerolized and 13 fresh units were distributed internationally. With the exception of Vel−, hr−, and O

(Bombay) blood types, we have been able to meet the need for rare blood in Finland using Finnish donors.

There has been only one international request that could not be fulfilled and that was for Rhnull. We have had one Rhnull donor (possible regulator type) with no antibodies. Unfortunately, that donor is no longer eligible for donation.

A patient with anti-LW\(^a\) received nine crossmatch-compatible D− LW(a+) RBC units during a liver transplantation. The transfusion of LW(a+) blood was unavoidable because the time of the liver transplantation was not possible to foresee, and we could not predict the amount of bleeding during the operation. According to the laboratory results, there were no signs of hemolysis after the surgery.

Small incentives are provided to all donors occasionally, but there are no extra incentives for rare donors. The rare donors are informed about the special importance of their donations and about the cryopreservation of RBCs, which makes the time point of a donation more flexible and convenient for the donor than donations made only on special request.

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<table>
<thead>
<tr>
<th>Phenotype</th>
<th>Number of donors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jk(a−b−)</td>
<td>24</td>
</tr>
<tr>
<td>LW(a−b+)</td>
<td>19</td>
</tr>
<tr>
<td>k−</td>
<td>11</td>
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<tr>
<td>Co(a−)</td>
<td>6</td>
</tr>
<tr>
<td>Lu(b−)</td>
<td>5</td>
</tr>
<tr>
<td>Pk</td>
<td>4</td>
</tr>
<tr>
<td>Vel−</td>
<td>3</td>
</tr>
<tr>
<td>p</td>
<td>1</td>
</tr>
</tbody>
</table>

Table 1. Rare donors in the Finnish Red Cross Blood Service who donated in 2013–2014.
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The French national rare blood program

T. Peyrard

French regulations stipulate that a blood type is regarded as rare if its prevalence is 4 in 1000 or less (i.e., ≤1 in 250) in the general population.1,2 The National Rare Blood Donor Database was implemented in France in the late 1960s to ensure the transfusion and obstetric safety of patients with rare blood phenotypes.3,4 The national rare blood bank was later set up in the early 1980s.5 Potential rare blood donors from the national database are highly encouraged to donate blood on a routine basis for the national rare blood bank. This facility, located in the city of Créteil (a few kilometers from Paris), is co-managed by the National Immunohematology Reference Laboratory (National Reference Center for Blood Groups [CNRGS], Department of the National Institute of Blood Transfusion, Paris, France) and the French National Blood Service (Etablissement Français du Sang, Ile de France, Ivry/Seine, France). Confirmation of the rare blood type, registration of new people with a rare blood type in the national database, choice of red blood cell (RBC) units to be frozen, and selection and delivery authorization of rare blood units are exclusively carried out by the national Immunohematology Reference Laboratory (IRL). To date, 12,929 individuals (patients and donors) are listed in the National Registry of People with a Rare Blood Phenotype or Genotype.

Rare blood units from the national rare blood bank are frozen according to the Cohn method, using glycerol in an ionic medium to achieve a final glycerol concentration of 40 percent (wt/vol), the so-called high-glycerol method. RBC units are subsequently stored at a mean temperature of –80°C. Since late 2005, the Haemonetics Automated Cell Processor (ACP) 215 closed-circuit instrument (Haemonetics, Braintree, MA) has been systematically used to glycerolize and deglycerolize RBC units, allowing for a 7-day shelf life for thawed units when stored at 2°C to 6°C in a saline-adenine-glucose-mannitol additive solution.6,7

The national rare blood bank currently includes 6,539 cryopreserved blood units, from 1,744 blood donors. This facility maintains two categories of rare blood units: (i) RBCs negative for a high-prevalence antigen (prevalence ≤1 in 250); and (ii) RBCs negative for multiple common antigens within the Rh system: r,r′, r,r″, r,r′, and R,R,. This prevalence threshold is not exclusively considered for defining a rare blood donor in our country, however. The whole phenotype is taken into account in order to assess the need for cryopreservation of the RBC unit with the intent of ensuring maximal efficiency of the rare blood bank. For example, and as of today, a donor with a rare k– phenotype will be eligible for RBC unit cryopreservation only if the blood type is group O, R,R, or R,R, or rr, with three homozygous expressions for Fy/a/Fy/b, Jk/a/Jk/b, and S/s, in order to fulfill the most common requests for multiply-alloimmunized patients or to prevent alloimmunization to the major RBC antigens.

Of note, RBCs negative for multiple common antigens within several different blood group systems are not currently considered for cryopreservation at the national rare blood bank. This practice is explained by the fact that all donors in France have been typed for Rh (C, E, c, e) and K for more than 20 years and around 20 percent of repeat blood donors are subject to extended phenotyping (Fy/a, Fy/b, Jk/a, Jk/b, M, N, S, and s).

Activity Report from January 2012 to December 2014

From 2012 to 2014, 797 rare donors gave blood, including 214 new donors. A total of 2113 RBC units were provided. In the same period of time, 167 patients were transfused, for a total of 854 RBC units and 441 transfusion episodes. This corresponds to an average of 285 RBC units per year (4.3 per 106 inhabitants per year). Of note, this value increased by 70 percent since the early 2000s.6 Among those 167 patients, 72 (43%) were of African/Caribbean descent, accounting for 314 (39.4%) of the delivered RBC units. Most of the patients of African/Caribbean descent suffered from sickle cell disease (70%). As a result, 30 percent of the requested rare cryopreserved units were transfused to patients with sickle cell disease from 2012 to 2014 in France.

The top 10 most requested rare phenotypes during that period were as follows: Fy(a−b−) (38%), k– (15%), r′r′ (12%), Lu(b−) (5.4%), S−s−U− (4.1%), S−s−U−var (3.5%), r′r′ (2.3%), Yt(a−) (1.8%), GE:−2,3 (1.6%), and Vel− (1.6%) (Fig. 1).

In this 3-year timeframe, 44 rare RBC units (5.2%) were shipped abroad (Table 1): Germany 26 (59%), Switzerland 6 (14%), Belgium 4 (9%), Sweden 3 (7%), Iceland 2 (4.5%), Monaco (4.5%), and United Kingdom 1 (2%).
To our knowledge, no unfilled rare blood request was reported in our country from 2012 to 2014.

Transfusion of Incompatible Blood

To the best of our knowledge, seven cases of transfusion with incompatible blood were reported from 2012 to 2014. The alloantibodies involved were as follows: anti-Lu\textsuperscript{b}, anti-U, anti-Co\textsuperscript{a} (2 cases), anti-Yt\textsuperscript{a} (2 cases), and anti-AnWj.

For the AnWj– patient (group A, E–c–, K–) with a strong anti-AnWj (antibody titer >2048), multiple transfusions with In(Lu) rare blood units were uneventfully carried out (no AnWj– donor available in France). A major decrease of the stock of ABO/Rh-compatible In(Lu) RBC units occurred. As we were informed that the patient was under palliative care, the possibility of the so-called “in vivo crossmatch” procedure (transfusion of 50 mL incompatible blood, with close clinical and biological monitoring)\textsuperscript{8,9} was collectively considered. A prophylactic treatment was given 8 hours prior to the transfusion, based on a bolus of corticosteroids (equivalent to 100 mg of hydrocortisone) and intravenous immunoglobulin infusion (1 g/kg).\textsuperscript{10} A blood sample drawn after infusion of 50 mL incompatible blood showed mild hemolysis of plasma and a weakly positive direct antiglobulin test. Transfusion with AnWj+ RBCs was decided to be cautiously carried on. Severe fever and rigors occurred at the end of the blood bag infusion, however, and the clinicians decided to immediately stop the transfusion. The few subsequent transfusions in this patient were as previously performed with In(Lu) RBCs, until the end of his life.

Anti-Lu\textsuperscript{b} was responsible for a poor hemoglobin increase and a moderate febrile non-hemolytic transfusion reaction.

Table 1. International requests supported by the French national rare blood program from 2012 to 2014

<table>
<thead>
<tr>
<th>Country</th>
<th>Rare phenotype</th>
<th>ABO/Rh/K</th>
<th>Alloantibodies</th>
<th>Number of RBC units provided</th>
</tr>
</thead>
<tbody>
<tr>
<td>Belgium</td>
<td>Yt(a–)</td>
<td>O, D–C–E–c+c+e+; K–</td>
<td>Anti-Yt\textsuperscript{a}, anti-Lu\textsuperscript{b}</td>
<td>2</td>
</tr>
<tr>
<td>Belgium</td>
<td>Sec– (R\textsuperscript{h}R\textsuperscript{r}, RH:–46)</td>
<td>O, E–c–; K–</td>
<td>Anti-Sec, anti-E</td>
<td>2</td>
</tr>
<tr>
<td>Germany</td>
<td>Fy(a–b–)</td>
<td>O, D+C–E–c+c+e+; K–</td>
<td>Anti-Fy3, anti-C, anti-E, anti-s, anti-P1</td>
<td>3</td>
</tr>
<tr>
<td>Germany</td>
<td>S–s–U–</td>
<td>O, D+C–E–c+c+e+; K–</td>
<td>Anti-U</td>
<td>1</td>
</tr>
<tr>
<td>Germany</td>
<td>S–s–U–</td>
<td>B, D+C–E–c+c+e+; K–</td>
<td>Anti-U</td>
<td>11</td>
</tr>
<tr>
<td>Germany</td>
<td>rr’</td>
<td>O, D+C+E–c+c+e+; K–</td>
<td>Anti-D, anti-c, anti-S</td>
<td>8</td>
</tr>
<tr>
<td>Iceland</td>
<td>D – –</td>
<td>O, D+C–E–c+c+e+; K–</td>
<td>Anti-Hr\textsubscript{c}</td>
<td>2</td>
</tr>
<tr>
<td>Monaco</td>
<td>Fy(a–b–)</td>
<td>A, D+C–E–c+c+e+; K–</td>
<td>Anti-Fy3, anti-A1, anti-E, anti-C, anti-Fy\textsuperscript{a}, anti-Jk\textsuperscript{a}, anti-Lu\textsuperscript{b}, antibody to a high-prevalence antigen of undetermined specificity</td>
<td>2 autologous units for elective surgery (no possibility to cryopreserve RBC units in Monaco)</td>
</tr>
<tr>
<td>Sweden</td>
<td>S–s–U–</td>
<td>A, D+C–E–c+c+e+; K–</td>
<td>Anti-U</td>
<td>2</td>
</tr>
<tr>
<td>Sweden</td>
<td>S–s–U–</td>
<td>A, D+C–E–c+c+e+; K–</td>
<td>Anti-U, anti-D</td>
<td>1</td>
</tr>
<tr>
<td>Switzerland</td>
<td>GE–2,3</td>
<td>O, D+C–E–c+c+e+; K–</td>
<td>Anti-Ge2</td>
<td>2</td>
</tr>
<tr>
<td>Switzerland</td>
<td>P\textsuperscript{1}</td>
<td>A, D+C+E–c+c+e+</td>
<td>Anti-P</td>
<td>3</td>
</tr>
<tr>
<td>Switzerland</td>
<td>O\textsubscript{h} (Bombay)</td>
<td>O\textsubscript{h}, D+C+E–c+c+e+; K–</td>
<td>Anti-H</td>
<td>1</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>D – –</td>
<td>O, D+C–E–c+c–e–; K–</td>
<td>Anti-Hr\textsubscript{c}</td>
<td>1</td>
</tr>
</tbody>
</table>

RBC = red blood cell.
Incompatible transfusion was uneventful for anti-Yt\textsuperscript{a} and rather unexpectedly for anti-U. The two cases of anti-Co\textsuperscript{a} incompatibility were said to be of undetermined outcome.

**Incentive Measures for Rare Blood Donors**

New rare blood donors receive a specific card with mention of their rare phenotype and an explanatory accompanying letter. Their siblings are also encouraged to be tested for the same identified rare specificity. Those documents are sent to the regional medical referee of the French National Blood Service and are further forwarded to the donor. For the most exceptional blood types, the medical referee usually contacts the donors by phone to make them aware of the great importance of giving blood on a regular basis. When a decrease in the inventory of a given rare specificity occurs, the national IRL contacts the regional medical referee to ask for new blood donations. At the end of 2014, a season’s greetings card was sent to the most loyal rare blood donors.

**Rh\textsubscript{null} Donors**

The French national rare donor database contains only one Rh\textsubscript{null} active donor, group A (Rh\textsubscript{null} of the so-called regulator type, with compound heterozygous mutations in the RHAG gene). This donor lives in Lausanne, Switzerland. No rare blood bank exists in that country. In addition, the different rules for blood donor testing between Switzerland and France (testing for anti-HTLV-I/II and anti-HBc are mandatory in France) makes the importation of rare blood in our country even more difficult. As a result, this donor, very aware of the rarity and usefulness of his very special blood, kindly travels to the French–Swiss border to donate in France.\textsuperscript{11} As of today, eight RBC units from this donor are cryopreserved at the national rare blood bank.

**Acknowledgments**

The author warmly thanks the whole staff of the CNRGS (National Institute of Blood Transfusion, Paris, France) and the National Rare Blood Bank (French National Blood Service, Créteil, France) for their high commitment to the French national rare blood program.

**References**


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National rare donor program in Iran

M. Moghaddam

Iranian Blood Transfusion Organization (IBTO) is the sole organization providing blood services to hospitals and other medical centers throughout Iran, with a network of over 220 blood centers in 31 provinces. As a reference center, the immunohematology laboratory of the IBTO has been responsible for identifying and providing compatible blood for patients with rare blood types and for multiply transfused patients such as those with thalassemia who have developed several clinically important antibodies.

Prior to 2009, IBTO used traditional non-systematic services when managing rare blood for these patients. However, to provide better service to donors and patients, IBTO decided to expand the operation of identifying rare blood donors and storing units of blood by developing the Iranian Rare Donor Program. This program expanded the management of rare blood to a systematic approach whereby the organization was prepared for any critical time when the request for rare blood was received for a patient with a difficult blood type.

History

The first initiative toward developing the Iranian Rare Donor Program was triggered through a collaborative program called the Joint Program Review and Planning Mission (JPRM 2008–2009) between the World Health Organization (WHO) and IBTO with a goal to increase blood safety in Iran. Available resources were studied and the absence of processes and deficiencies in provided services were identified and analyzed.

We also contacted international organizations that were already experienced in rare donor activities. In this endeavor, contact was initiated between IBTO and the International Blood Group Reference Laboratory (IBGRL-WHO) in Bristol, UK, to learn from their experience and to receive their support. IBTO was interested in a longstanding collaboration with IBGRL-WHO.

Dr. G. Woodfield (past chair of the International Society of Blood Transfusion [ISBT] Working Party on Rare Donors) was kind enough to accept IBTO’s invitation to travel to Tehran in 2010 to share his scientific knowledge and technical expertise through a series of lectures in a 2-week workshop.

Responsible heads of the IBTO’s special serology laboratories attended the workshop. They were selected to be the future technical specialists who would participate in the national rare donor program. The goal was to review the approaches that would help in the establishment of a systematic and successful national rare donor program.

Other issues that needed close attention were designing the complete structure of the rare donor program, finding the correct approach to screening blood donors to identify rare red blood cell (RBC) phenotypes for the program’s data registry, and deciding on the number of donors to be screened in a specific period of time.

National Rare Donor Database

To meet the requests of patients with rare blood types, IBTO decided to regularly screen blood donor samples received randomly from selected blood centers in 31 provinces at the Immunohematology Reference Laboratory in Tehran for rare blood types. Populations from these provinces are ethnically and geographically diverse. Today, more than 35,000 blood samples have been phenotyped serologically. The initial antigens screened are in the Rh (C, c, E, e), Kell (K, k), Duffy (Fyα, Fyβ), Kidd (Jkα, Jkβ), and MNS (S, s) systems. All blood samples are selected from group O blood donors.

The National Rare Donor Database currently consists of information from approximately 1000 active rare donors divided into two groups; this process was adopted from a review article published in Immunohematology.1 Group I (rare donors) are defined as those negative for multiple common antigens (428 new donors added in 2012–2014) and Group II (very rare donors) are defined as those negative for a high-prevalence antigen (72 new donors added in 2012–2014). The inventory of very rare units currently consists of about 170 frozen RBC units stored at −80°C (Table 1). The national database also includes two Rhnull donors and two K0 donors. Their molecular backgrounds have yet to be identified.

Where Are We Now?

In 2015, the Iranian Rare Donor Program is a well-established service in IBTO. Between 2012 and 2014, a total of 93 rare units were shipped domestically to medical centers in the country, with 2 requests not filled. One request was for a
The second request was for a 28-year-old male thalassemia intermediate patient with antibody of unknown specificity. There were also three incompatible transfusion cases. All three patients were suffering from beta thalassemia intermediate disorder. One patient was identified as having warm autoimmune hemolytic anemia. Because blood transfusion was not helpful and due to extramedullary hematopoiesis, intravenous steroids and radiotherapy were started with good outcome. The other two patients were identified with multiple antibodies including anti-E, -c, -M, -Jk\(^a\), and an antibody of unknown specificity. The patient with anti-M and -Jk\(^a\) experienced a severe hemolytic transfusion reaction and died due to the transfusion of multiple incompatible RBC units.

In general, the practice in Iran has been to use oral promethazine, diphenhydramine, and hydrocortisone as prophylaxis prior to RBC transfusion to a patient with a history of transfusion reactions rather than referring the patient’s sample to an immunohematology reference laboratory to identify the antibody and provide antigen-negative blood. With the establishment of the Iranian Rare Donor Program, we hope to see this practice eliminated.

26-year-old labor and delivery patient from Ilam province with an antibody against an unknown high-prevalence antigen. The second request was for a 28-year-old male thalassemia intermediate patient with antibody of unknown specificity.

There were also three incompatible transfusion cases. All three patients were suffering from beta thalassemia intermediate disorder. One patient was identified as having warm autoimmune hemolytic anemia. Because blood transfusion was not helpful and due to extramedullary hematopoiesis, intravenous steroids and radiotherapy were started with good outcome. The other two patients were identified with multiple antibodies including anti-E, -c, -M, -Jk\(^a\), and an antibody of unknown specificity. The patient with anti-M and -Jk\(^a\) experienced a severe hemolytic transfusion reaction and died due to the transfusion of multiple incompatible RBC units.

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### Table 1. Identified donors and current inventory of very rare blood in Iran as of 2014

<table>
<thead>
<tr>
<th>Phenotype</th>
<th>Number of donors</th>
<th>Frozen RBC units stored at –80°C*</th>
</tr>
</thead>
<tbody>
<tr>
<td>O(s) (Bombay)</td>
<td>32/10/26</td>
<td></td>
</tr>
<tr>
<td>Fy(a–b–)</td>
<td>14/22/12</td>
<td></td>
</tr>
<tr>
<td>Lu(a–b–)</td>
<td>3/5/10</td>
<td></td>
</tr>
<tr>
<td>r'</td>
<td>1/9/10</td>
<td></td>
</tr>
<tr>
<td>k–</td>
<td>4/5/9</td>
<td></td>
</tr>
<tr>
<td>D–</td>
<td>3/3/8</td>
<td></td>
</tr>
<tr>
<td>R,R1</td>
<td>7/10/5</td>
<td></td>
</tr>
<tr>
<td>r'r''</td>
<td>2/0/3</td>
<td></td>
</tr>
<tr>
<td>Kp(b–)</td>
<td>1/0/2</td>
<td></td>
</tr>
<tr>
<td>R,R2</td>
<td>1/2/2</td>
<td></td>
</tr>
<tr>
<td>R,R2'</td>
<td>0/2/1</td>
<td></td>
</tr>
<tr>
<td>K(_a)</td>
<td>0/2/1</td>
<td></td>
</tr>
<tr>
<td>Rh(_null)</td>
<td>0/2/0</td>
<td></td>
</tr>
</tbody>
</table>

* RBC = red blood cell.

### Encouraging Rare Donors

Personal appreciation, educational materials, and occasionally gift cards of no more than a $20 value, to compensate for donor time off from work or transportation expenses, are offered as incentives to encourage awareness and willingness among donors to collaborate with the program.

Every year, January 11th is celebrated as National Rare Donor Day in Iran for rare donor recognition and is attended by officials from the Ministry of Health and IBTO’s higher management; the activities are covered by the national media. After joining the ISBT Working Party on Rare Donors in 2010, our goal has been for Iran to be one of the active members of the committee. It is currently the only country from the Eastern Mediterranean Region in the Working Party. For the first time in September 2014, IBTO organized an international meeting on rare donors supported by the ISBT Academy. International speakers and participants from Europe, Asia, New Zealand, Africa, and the Middle East attended the meeting.

IBTO is potentially ready to fill orders and ship rare units for international requests, particularly to meet requests from neighboring countries.

### References


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The Israeli rare donor blood program

V. Yahalom, L. Finkel, E. Shinar, and O. Asher

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(b–), 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-Ytα (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 unfilled 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

<table>
<thead>
<tr>
<th>Phenotype</th>
<th>Number of donors</th>
<th>Number of frozen units</th>
<th>Number of units requested</th>
<th>Number of units supplied</th>
</tr>
</thead>
<tbody>
<tr>
<td>k–</td>
<td>79</td>
<td>204</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>Fy(a–b–)</td>
<td>57</td>
<td>148</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Kp(b–)</td>
<td>53</td>
<td>240</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Yt(a–)</td>
<td>51</td>
<td>108</td>
<td>104</td>
<td>84</td>
</tr>
<tr>
<td>Lu(b–)</td>
<td>49</td>
<td>145</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>GE:–2,3</td>
<td>21</td>
<td>42</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>p</td>
<td>12</td>
<td>47</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Group O, D–e–</td>
<td>8</td>
<td>17</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Dr(a–)</td>
<td>7</td>
<td>18</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>AnWj–</td>
<td>7</td>
<td>10</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Group O, D–c–</td>
<td>6</td>
<td>11</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>P2k*</td>
<td>6</td>
<td>10</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Vel–</td>
<td>6*</td>
<td>13</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>K:–22</td>
<td>3</td>
<td>6</td>
<td>0</td>
<td>0</td>
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<tr>
<td>JMH–</td>
<td>3</td>
<td>24</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>P1k</td>
<td>3</td>
<td>5</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Lan–</td>
<td>3</td>
<td>5</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>ABTI–</td>
<td>3</td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Jsf(b–)</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Inab–</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>RAPH:–1</td>
<td>2</td>
<td>8</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
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<td>H–</td>
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<td>3</td>
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<tr>
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<td>136</td>
<td>111</td>
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</table>

*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-Ytα, 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\(^4\), 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\(^4\) 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.\(^3\)

**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−, Pk−, 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.

Acknowledgments

Special thanks go to Dr. Cyril Levene for his vision and dedication, which enabled the establishment of the Israeli NBGRL. We appreciate the assistance of many colleagues along the years, especially at the IBGRL-UK, New York Blood Center-USA, and Bloodcentralen Skane University Hospital, Sweden. We also want to acknowledge our rare blood donors and the staff of the NBGRL for their expertise and efforts. We thank Dr. Martin Ellis for reviewing the manuscript.

References


Vered Yahalom, MD (corresponding author), Medical Director, National Blood Group Reference Laboratory, Magen David Adom–National Blood Services, Tel Hashomer, Ramat Gan, 52621, Israel, veredy@mda.org.il; Lilach Finkel, BSc, Laboratory Technician; Eilat Shinar, MD, Director; and Orna Asher, PhD, Director, National Blood Group Reference Laboratory, Magen David Adom–National Blood Services, Tel Hashomer, Ramat Gan, Israel.
NIH Annual Symposium Announcements

September 21, 2016
6th Annual Red Cell Genotyping Symposium. 2016: Clinical Steps. The Department of Transfusion Medicine, Clinical Center, National Institutes of Health (NIH), and the BloodCenter of Wisconsin are co-hosting this symposium on the NIH campus in Bethesda, Maryland. For information, registration fee, and advance registration, contact Phyllis Kirchner, BloodCenter of Wisconsin, P.O. Box 2178, Milwaukee, WI 53021-2178; e-mail: phyllis.kirchner@bcw.edu; or visit our Web site: www.bcw.edu/rcg2016

September 22, 2016
35th Annual Immunohematology and Blood Transfusion Symposium. The Department of Transfusion Medicine, Clinical Center, National Institutes of Health (NIH), and the American Red Cross are co-hosting this symposium on the NIH campus in Bethesda, Maryland. There is no registration fee, but advance registration is encouraged. Contact Karen Byrne, NIH/CC/DTM, Bldg. 10/Rm. 1C711, 10 Center Drive, MSC 1184, Bethesda, MD 20892-1184; e-mail: kbyrne@cc.nih.gov; or visit our Web site: http://www.cc.nih.gov/dtm/research/symposium.html
The Johns Hopkins Hospital Specialist in Blood Bank Technology Program

The Johns Hopkins Hospital was founded in 1889. It is located in Baltimore, Maryland, on the original founding site, just 45 minutes from Washington, DC. There are approximately 1,000 inpatient beds and another 1,200 outpatient visits daily; nearly 600,000 patients are treated each year.

The Johns Hopkins Hospital Transfusion Medicine Division is one of the busiest in the country and can provide opportunities to perform tasks that represent the entire spectrum of Immunohematology and Transfusion Medicine practice. It provides comprehensive support to all routine and specialized areas of care for surgery, oncology, cardiac, obstetrics, neonatal and pediatric, solid organ and bone marrow transplant, therapeutic apheresis, and patients with hematological disorders to name a few. Our intradepartment Immunohematology Reference Laboratory provides resolution of complex serologic problems, transfusion management, platelet antibody, and molecular genotype testing.

The Johns Hopkins Hospital Specialist in Blood Bank Technology Program is an onsite work-study, graduate-level training program for certified Medical Technologists, Medical Laboratory Scientists, and Technologists in Blood Banking with at least 2 years of full-time Blood Bank experience.

The variety of patients, the size, and the general intellectual environment of the hospital provide excellent opportunities for training in Blood Banking. It is a challenging program that will prepare competent and knowledgeable graduates who will be able to effectively apply practical and theoretical skills in a variety of employment settings. The Johns Hopkins Hospital Specialist in Blood Bank Technology Program is accredited by the Commission on Accreditation of Allied Health Education Programs (CAAHEP). Please visit our website at http://pathology.jhu.edu/department/divisions/transfusion/sbb.cfm for additional information.

Contact: Lorraine N. Blagg, MA, MLS(ASCP)CMSBB
Program Director
E-mail: lblagg1@jhmi.edu
Phone: (410) 502-9584

The Johns Hopkins Hospital
Department of Pathology
Division of Transfusion Medicine
Sheikh Zayed Tower, Room 3100
1800 Orleans Street
Baltimore, Maryland 21287

Phone (410) 955-6580
Fax (410) 955-0618
Web site: http://pathology.jhu.edu/department/divisions/transfusion/index.cfm
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Rush University is fully accredited by the Higher Learning Commission (HLC) of the North Central Association of Colleges and Schools and the SBB Certificate Program is accredited by the Commission on Accreditation of Allied Health Education Programs (CAAHEP).

Applications for the SBB/MS Program can be submitted online at the following website: http://www.rushu.rush.edu/admiss/hlthadm.html

Contact: Yolanda Sanchez, MS, MLS(ASCP)CM, SBB, Director, by e-mail at Yolanda_Sanchez@rush.edu or by phone at 312-942-2402 or Denise Harmening, PhD, MT(ASCP), Director of Curriculum by e-mail at Denise_Harmening@rush.edu
Applications are invited from medical or science graduates for the Master of Science (MSc) degree in Transfusion and Transplantation Sciences at the University of Bristol. The course starts in October 2016 and will last for 1 year. A part-time option lasting 2 or 3 years is also available. There may also be opportunities to continue studies for PhD or MD following the MSc. The syllabus is organized jointly by The Bristol Institute for Transfusion Sciences and the University of Bristol, Department of Pathology and Microbiology. It includes:

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- Practical techniques in transfusion and transplantation
- Principles of study design and biostatistics
- An original research project

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For further details and application forms please contact:

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Paul O’Gorman Lifeline Centre
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# Becoming a Specialist in Blood Banking (SBB)

## What is a certified Specialist in Blood Banking (SBB)?
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- This person will have advanced knowledge, skills, and abilities in the field of transfusion medicine and blood banking.

## Individuals who have an SBB certification serve in many areas of transfusion medicine:
- Serve as regulatory, technical, procedural, and research advisors
- Perform and direct administrative functions
- Develop, validate, implement, and perform laboratory procedures
- Analyze quality issues preparing and implementing corrective actions to prevent and document issues
- Design and present educational programs
- Provide technical and scientific training in transfusion medicine
- Conduct research in transfusion medicine

## Who are SBBs?
- Supervisors of Transfusion Services
- Managers of Blood Centers
- LIS Coordinators
- Educators
- Supervisors of Reference Laboratories
- Research Scientists
- Consumer Safety Officers
- Reference Lab Specialists
- Quality Assurance Officers
- Technical Representatives
- Reference Lab Specialists
- Why become an SBB?
- Professional growth
- Job placement
- Job satisfaction
- Career advancement

## How does one become an SBB?
- Attend a CAAHEP-accredited SBB Technology program OR
- Sit for the examination based on criteria established by ASCP for education and experience.

**However:** In recent years, a greater percentage of individuals who graduate from CAAHEP-accredited programs pass the SBB exam.

**Conclusion:** The BEST route for obtaining an SBB certification is . . . to attend a CAAHEP-accredited Specialist in Blood Bank Technology Program.

Additional information can be found by visiting the following Web sites: www.ascp.org, www.caahep.org, and www.aabb.org

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<tr>
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<th>Contact Name</th>
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<th>E-mail Contact</th>
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<td>American Red Cross, Southern California Region</td>
<td>Catherine Hernandez</td>
<td>909-859-7496</td>
<td><a href="mailto:Catherine.Hernandez@redcross.org">Catherine.Hernandez@redcross.org</a></td>
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<td>614-253-2740 ext. 2270</td>
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8. Figures

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   a. Introduction — Purpose and rationale for study, including pertinent background references
   b. Case Report (if indicated by study) — Clinical and/or hematologic data and background serology/molecular
   c. Materials and Methods — Selection and number of subjects, samples, items, etc. studied and description of appropriate controls, procedures, methods, equipment, reagents, etc. Equipment and reagents should be identified in parentheses by model or lot and manufacturer’s name, city, and state. Do not use patient’s names or hospital numbers.
   d. Results — Presentation of concise and sequential results, referring to pertinent tables and/or figures, if applicable
   e. Discussion — Implication and limitations of the study, links to other studies; if appropriate, link conclusions to purpose of study as stated in introduction
5. Acknowledgments: Acknowledge those who have made substantial contributions to the study, including secretarial assistance; list any grants.
6. References
   a. In text, use superscript, Arabic numbers.
   b. Number references consecutively in the order they occur in the text.
7. Tables
   a. Head each with a brief title; capitalize the first letter of first word (e.g., Table 1. Results of…) use no punctuation at the end of the title.
   b. Use short headings for each column needed and capitalize first letter of first word. Omit vertical lines.
   c. Place explanation in footnotes (sequence: *, †, ‡, §, ¶, **, ††).
8. Figures
   a. Figures can be submitted either by e-mail or as photographs (5 × 7” glossy).
   b. Place caption for a figure on a separate page (e.g. Fig. 1 Results of…), ending with a period. If figure is submitted as a glossy, place first author’s name and figure number on back of each glossy submitted.
   c. When plotting points on a figure, use the following symbols if possible:
      ◦ ● ○ △ ▲ ▼.
9. Author information
   a. List first name, middle initial, last name, highest degree, position held, institution and department, and complete address (including ZIP code) for all authors. List country when applicable. Provide e-mail addresses of all authors.

III. EDUCATIONAL FORUM
A. All submitted manuscripts should be approximately 2000 to 2500 words with pertinent references. Submissions may include:
   1. An immunohematologic case that illustrates a sound investigative approach with clinical correlation, reflecting appropriate collaboration to sharpen problem solving skills
   2. Annotated conference proceedings
B. Preparation of manuscript
   1. Title page
      a. Capitalize first word of title.
      b. Initials and last name of each author (no degrees; all CAPs)
   2. Text
      a. Case should be written as progressive disclosure and may include the following headings, as appropriate
      i. Clinical Case Presentation: Clinical information and differential diagnosis
      ii. Immunohematologic Evaluation and Results: Serology and molecular testing
      iii. Interpretation: Include interpretation of laboratory results, correlating with clinical findings
      iv. Recommended Therapy: Include both transfusion and nontransfusion-based therapies
      v. Discussion: Brief review of literature with unique features of this case
      vi. Reference: Limited to those directly pertinent
      vii. Author information (see II.B.9.)
      viii. Tables (see II.B.7.)

IV. LETTER TO THE EDITOR
A. Preparation
   1. Heading (To the Editor)
   2. Title (first word capitalized)
   3. Text (written in letter [paragraph] format)
   4. Author(s) (type flush right; for first author: name, degree, institution, address [including city, state, Zip code and country]; for other authors: name, degree, institution, city and state)
   5. References (limited to ten)
   6. Table or figure (limited to one)

Send all manuscripts by e-mail to immuno@redcross.org
A. For describing an allele which has not been described in a peer-reviewed publication and for which an allele name or provisional allele name has been assigned by the ISBT Working Party on Blood Group Allele Terminology (http://www.isbtweb.org/working-parties/red-cell-immunogenetics-and-blood-group-terminology/blood-group-terminology/blood-group-allele-terminology/)

B. Preparation
1. Title: Allele Name (Allele Detail)
   ex. RHCE*01.01 (RHCE*ce48C)
2. Author Names (initials and last name of each (no degrees, ALL CAPS)

C. Text
1. Case Report
   i. Clinical and immunohematologic data
   ii. Race/ethnicity and country of origin of proband, if known
2. Materials and Methods
   Description of appropriate controls, procedures, methods, equipment, reagents, etc. Equipment and reagents should be identified in parentheses by model or lot and manufacturer’s name, city, and state. Do not use patient names or hospital numbers.
3. Results
   Complete the Table Below:
<table>
<thead>
<tr>
<th>Phenytype</th>
<th>Allele Name</th>
<th>Nucleotide(s)</th>
<th>Exon(s)</th>
<th>Amino Acid(s)</th>
<th>Allele Detail</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>e weak</td>
<td>RHCE*01.01</td>
<td>48G&gt;C</td>
<td>1</td>
<td>Trp16Cys</td>
<td>RHCE*ce48C</td>
<td>1</td>
</tr>
</tbody>
</table>
   Column 1: Describe the immunohematologic phenotype (ex. weak or negative for an antigen).
   Column 2: List the allele name or provisional allele name.
   Column 3: List the nucleotide number and the change, using the reference sequence (see ISBT Blood Group Allele Terminology Pages for reference sequence ID).
   Column 4: List the exons where changes in nucleotide sequence were detected.
   Column 5: List the amino acids that are predicted to be changed, using the three-letter amino acid code.
   Column 6: List the non-consensus nucleotides after the gene name and asterisk.
   Column 7: If this allele was described in a meeting abstract, please assign a reference number and list in the Reference section.

4. Additional Information
   i. Indicate whether the variant is listed in the dbSNP database (http://www.ncbi.nlm.nih.gov/snp/); if so, provide rs number and any population frequency information, if available.
   ii. Indicate whether the authors performed any population screening and if so, what the allele and genotype frequencies were.
   iii. Indicate whether the authors developed a genotyping assay to screen for this variant and if so, describe in detail here.
   iv. Indicate whether this variant was found associated with other variants already reported (ex. RHCE*ce48C,1025T is often linked to RHD*DIVa-2)

D. Acknowledgments

E. References

F. Author Information
   List first name, middle initial, last name, highest degree, position held, institution and department, and complete address (including ZIP code) for all authors. List country when applicable.
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