Rare blood donors: a personal approach

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The National Blood Group Reference Laboratory (NBGRL) in Israel was established in Jerusalem in 1971 and transferred to Magen David Adom (MDA), National Blood Services in 1995. This laboratory was the inspiration of the first author of this article for over 30 years. The realization of this vision was made possible by the cooperation of colleagues and laboratory workers in blood transfusion services throughout the country. The aim of the service was to provide diagnostic help in resolving immunohematologic problems found in the blood banks and clinics in Israel. In the beginning, only a part-time technician performed the work and testing was done using very limited reagents. The service was expanded by personal visits to all of the 22 blood banks in Israel to explain the aim of this new service and to educate them about the importance of resolving each and every case. One major issue was the cost involved in referring problems but it was decided at the outset that these would be covered by the government to ensure that a workup would be performed for all referred cases. The expansion of the service could not have been achieved without the help of the SCARF program. This voluntary service enabled us to identify the first rare donors in Israel, resolve complex cases, and find compatible blood for our patients. To illustrate the importance of the NBGRL in Israel and the rapid resolution of cases referred, several individual stories are described. The purpose of this review is to show the importance of the NBGRL in identifying rare blood groups and in providing and coordinating services and the importance of keeping in close contact with the rare donors to encourage and promote their donations, which may save lives. ***Immunohematology* 2006; 22:64–68.**

Key Words: rare blood donors, NBGRL, SCARF, personal approach

The Gerbich (Ge) Story

Two of the earliest samples that we received from SCARF were from a donor whose RBCs were Ge:–2,3 (Yus phenotype) with anti-Ge2 in the serum and a donor whose RBCs were Ge:–2,–3 (Gerbich phenotype) with anti-Ge2,3 in the serum.

In 1976, a sample from a Jewish blood donor (ZY) born in Iraq, whose ABO blood group could not be resolved, was referred from Magen David Adom (MDA) National Blood Services. This donor had never been transfused and no antibodies had been detected in his serum in previous donations. His RBCs typed as group A, D+ and the serologic workup demonstrated the presence of an antibody in his serum directed at a high-incidence antigen. The RBCs of the donor were subsequently shown to be Ge:–2,3 (Yus phenotype) and his serum contained anti-Ge2. These findings were proved using reagents provided by SCARF. They were confirmed at that time by overseas laboratories including that of the Medical Research Council Blood Group Unit (MRC BGU) in London, then directed by Dr. Ruth Sanger. The family of this donor was examined and it was found that the donor was married to a first cousin whose RBCs were shown to be Ge:2,3,4. However, three of his children were found to be Ge:–2,3 like him. The propositus was employed as a mounted policeman in Jerusalem and was frequently seen riding on his white horse by the staff of the laboratory where the diagnosis of his rare blood was established. Because of the potential injury involved in his work, it was decided to relocate him within the service to a more sedentary position. However, the donor later decided that he wished to return to his post working with the horses in spite of the risks involved. He and one of his sons became regular donors and their units were frozen in MDA for future use. When this son moved to live in the United States, he continued to donate blood there.

In subsequent years, 20 other cases of donors with anti-Ge2 were seen in our laboratory (Table 1); most of them were found in Jews who emigrated from Ethiopia and in Israeli Arabs. In the Ethiopian Jews in Israel, the Yus phenotype (Ge:–2,3,4) was found and the frequency of RBCs with the Ge:–2,3 phenotype may reach 0.015 to 0.1 percent.[1,2] Only two cases of donors with Gerbich phenotype Ge:–2,–3,4 were found, in one family who emigrated from Iraq.

We have not succeeded in convincing the other Gerbich negative individuals to become regular donors despite numerous letters, telephone calls, and even an invitation to the rare blood meeting, which we will describe later.

Table 1. The Gerbich negative phenotype in Israel

Number	Reason for referral	Sex	Country birth/origin	Gerbich groups	Gerbich antibodies
1a	Blood donor	M	Iraq	Ge:–2,3	anti-Ge2
1b	Family screening	M	Israel	Ge:–2,3	No antibody
1c	Family screening	F	Israel	Ge:–2,3	No antibody
1d	Family screening	F	Israel	Ge:–2,3	No antibody
2	Pregnancy	F	Ethiopia	Ge:–2,3	anti-Ge2
3	Pregnancy	F	Ethiopia	Ge:–2,3	anti-Ge2
4	Blood donor	M	Ethiopia	Ge:–2,3	anti-Ge2
5a	Pregnancy	F	Ethiopia	Ge:–2,3	anti-Ge2
5b	Family screening	F	Ethiopia	Ge:–2,3	anti-Ge2
6a	Pretransfusion	F	Iraq	Ge:–2,–3,4	anti-Ge2
6b	Family screening	F	Iraq	Ge:–2,–3,4	No antibody
7	Pretransfusion	F	Ashkenazi	Ge:–2,3	anti-Ge2
8	Donor screening	F	Ethiopia	Ge:–2,3	No antibody
9	Pregnancy	F	Ethiopia	Ge:–2,3	anti-Ge2
10	Pretransfusion	F	Iran	Ge:–2,3	anti-Ge2
11	Pregnancy	F	Ethiopia	Ge:–2,3	anti-Ge2
12a	Pretransfusion	F	Israeli Arab	Ge:–2,3	anti-Ge2
12b	Family screening	F	Israeli Arab	Ge:–2,3	anti-Ge2
13	Blood donor	M	Israeli Arab	Ge:–2,3	anti-Ge2
14	Blood donor	M	Israeli Arab	Ge:–2,3	anti-Ge2
15a	Pregnancy	F	Ethiopia	Ge:–2,3,4	anti-Ge2
15b	Family and pregnancy	F	Ethiopia	Ge:–2,3,4	anti-Ge2
16a	Pretransfusion	M	Israeli Arab	Ge:–2,3	anti-Ge2
16b	Family screening	M	Israeli Arab	Ge:-2	No antibody
17	Dialysis	F	Ethiopia	Ge:–2,3	anti-Ge2
18	Pretransfusion	M	Israeli Arab	Ge:–2,3	anti-Ge2
19a	Pregnancy	F	Israeli Arab	Ge:–2,3	anti-Ge2
19b	Family	F	Israeli Arab	Ge:–2,3	No antibody
19c	Family	F	Israeli Arab	Ge:–2,3	anti-Ge2
19d	Family	M	Israeli Arab	Ge:–2,3	anti-Ge2
20	Blood donor	M	Israeli Arab	Ge:–2,3	anti-Ge2

The JMH Story

Over the years, the National Blood Group Reference Laboratory (NBGRL) in Israel has identified five samples of blood that appeared to be JMH–. Two of these samples were subsequently found to be JMH variants (Table 2).

In 1980, a woman (MR) was admitted for surgery. An antibody directed at a high-incidence antigen was identified in her serum and no compatible blood units were found for transfusion. Additional testing at the NBGRL showed that this antibody did not react with enzyme (ficin)-treated RBCs. The identity of this antibody could not be established in our service. The RBCs of the patient reacted with anti-JMH. Samples of blood from this woman were sent to several overseas laboratories and an immediate reply was received from the former Gamma Biologicals, Inc., Consultation and Education Services (headed by Marilyn and John Moulds), notifying us that the antibody maker had a JMH variant phenotype. The RBCs of MR reacted with known anti-JMH but her serum did not react with known JMH– RBCs. Family screening identified a brother of the same ABO group and of the same JMH variant, so he could have been a potential donor if blood had been required for the surgery. This Jewish family immigrated to Israel from Poland. JMH variant antibodies are not considered to be clinically significant.[3]

Some time after this JMH variant (which was called MR)[4] was found, an additional JMH variant was examined in a patient who had a terminal illness. This variant was identified as being the same variant as that found on the RBCs of MR. This patient was also a Polish Jewish immigrant.

Many years later Dr. Axel Seltsam described the molecular background that underlies the molecular basis of the JMH variants.[5]

Table 2. The JMH variants in Israel

Number	Reason for referral	Sex	Country birth/origin	JMH groups	JMH antibodies
1a	Pretransfusion	F	Poland	JMH variant	Anti-JMH variant (MR)
1b	Family screening	M	Poland	JMH variant	Anti-JMH variant (MR)
2	Pretransfusion	M	Poland	JMH variant	Anti-JMH variant (MR)

The pp (Tj[a–]) Story

The first finding of a rare blood group in the NBGRL in Jerusalem, which proved to be the pp phenotype, was in 1972.[6] The blood was from a woman who had been hospitalized for bleeding after a miscarriage. The referring laboratory told us that the RBC typings of the patient tested as group B but the back tests "caused problems!" All RBCs (groups A, B, and O) were agglutinated and, within a short period, these RBCs hemolyzed in tube tests. We had never seen a blood specimen from a pp phenotype patient but this story sounded as though this was the problem. Fortunately, no immediate transfusion was required and the blood specimen was referred to the International Blood Group Reference Laboratory (IBGRL) in the United Kingdom for confirmation. Just before we received the answer to confirm these suspicions, the

patient was interviewed and she told the following story: She had previously been admitted to another hospital when she bled on a number of occasions in the first trimester of her pregnancies. She had only one live child. The previous hospital had told the patient that they were unable to find compatible blood for her and if she was readmitted and hemorrhaged she might die! On questioning the woman further, two important findings emerged. She had a sister living in Israel, who had the same obstetric history and who nearly died after a transfusion. She also told us that she had a cousin living in Israel who was said to have a rare blood type. We were able to follow up with this latter relative and we found that her blood had previously been referred to the MRC BGU, at that time directed by Rob Race, where her blood was found to be group AB, pp.[7] A small sample of serum from this patient had been stored in a freezer of the referring laboratory and the RBCs of our patient did not react with this serum! The following day we received the confirmation from the IBGRL in the United Kingdom and they arranged for two units of blood to be sent from Umea, Sweden, for our patient. These donors, who were twins, were found in a dance hall and they immediately donated their blood to be dispatched. A few years later, a Swedish newspaper heard this story and decided to bring the recipient and these donors together. The donors were flown to Jerusalem and the recipient arranged a party for them. The group met and communicated with the help of translators.

As soon as our patient was well enough, she began to donate her blood for freezing and she has donated regularly nearly every 3 months. Here was a great ending to a difficult problem. This lady told us, more than once, that after her blood group had been determined and she donated her blood for freezing, she could now go to bed and sleep easily without any worry of what might happen if she ever needed a transfusion.

Our second example of pp phenotype blood was found in a blood donor. He was group AB but unfortunately we were never able to follow up on this young man. It turned out that he had been adopted and did not want to know more relating to his rare blood group and we lost track of him.

The next family turned out to be very special.[8] This patient was being prepared for a cesarean section and no blood could be found for her. Her blood typed as group B, D+, pp. This was the same blood group as our first patient and it was agreed that some of the frozen units of our first patient would be available if needed. This new patient also had a history of numerous miscarriages and no live child.

Immediately, the family was investigated and two siblings were found to have RBCs of the pp phenotype. Her brother was group B and her sister was group O. The patient required transfusion, as she had a placenta accreta, and, after delivery of a healthy baby, had to have a hysterectomy. At that time she received one unit donated by her brother. The baby soon developed HDN and needed an exchange transfusion. The sister of the proposita was group O and her blood was used for the exchange transfusion for the baby.

The story relating to the sister was equally interesting.[9] This woman wanted to have a child but she was unable to continue her pregnancies past the first trimester: a classic story for a woman whose RBCs were of the pp phenotype. For a number of years, this woman called to inquire if any advances to help her have a child were known. The situation was critical for her and for her marriage, as both parents wanted to have children. One day, the patient called saying that she had heard on a midnight radio newscast that a woman in a hospital in Baltimore (who had a story similar to hers) had just delivered her first live child and she wanted to know if this advance could be applied to her situation. Dr. Paul Ness in Baltimore was immediately approached and, indeed, his patient had a similar blood group. With regular plasmapheresis as an inpatient, she was able to continue the pregnancy past the first trimester and she delivered a live child. The protocol used in Baltimore was performed on our patient at the Rambam Medical Center in Haifa, Israel. There were many problems but the patient finally delivered a live, healthy, full-term child who is now a young adult. The meaning of the name of the doctor who had engineered the treatment of the case in Baltimore, Dr. "Ness," in Hebrew translates as "miracle," and for our patient the birth of her child was indeed a miracle.

This story is special in that any transfusion problems in the family were overcome by the cooperation of the siblings. These three siblings have continued to donate their blood for storage in our frozen blood bank.

Over the following years we continued to see more cases of individuals who were of the special group pp. We noted that a great percentage of these patients were immigrants from North Africa, especially from Morocco, where the frequency of the pp phenotype reaches 1 in 55,663.[10]

The Anti-Vel Story

The first example of anti-Vel, sent to us in 1976, was in the serum of a pregnant woman who had been admitted to a local hospital for delivery. The hospital was unable to find compatible blood for her before the delivery. The specimen arrived in the NBGRL on a Friday and the urgency for an answer meant that the staff had to stay on to find a solution. We were doubtful that we could solve this case but in the middle of the night we found one last rare RBC sample from SCARF in our collection that lacked the high-incidence antigen Vel. To our surprise, this RBC sample was compatible with the serum of this patient. At that time, there was no blood in Israel and no known blood donors whose RBCs were Vel–. As this woman was near term, the decision was made with the blood bank director and the gynecologists to take an autologous unit from the patient and, after a few days, to take a second unit before her delivery. Near the end of the first donation the patient did not feel well and we positioned her in the Trendelenburg position, only to find that this did not really help her. We realized almost immediately that, in this position, the uterus was pressing on her chest, restricting her air entry, and so we reversed the position. At once the patient felt well and the phlebotomy of the blood unit was completed successfully.[11]

Through the WHO International Rare Donor Panel in the United Kingdom, we contacted the Red Cross Blood Bank in Toronto, Canada, and arranged to have two units of this rare blood shipped to Israel. Fortunately, the woman delivered a healthy baby and she only received her own predonated blood units. One first cousin was found to be Vel– in the family investigation.

Three additional examples of anti-Vel have been seen over the years and hemolysis was seen with enzyme (ficin)-treated RBCs in all of them.

The Cartwright (Yt) Story

The following summary of the Yt blood group shows how the NBGRL must look out for findings that could have bearing on the distribution of any particular blood group and consider the value of investigating them in the population.

Anti-Yt^a was first detected in the NBGRL in Jerusalem in 1974. Over the subsequent 12-year period, 14 people who had anti-Yt^a in their serum were found among 4470 referrals. This frequency of 1 in 320 was considered much higher than would have been expected. To investigate the Yt^a and Yt^b frequencies in Israel, anti-Yt^a and anti-Yt^b reagents were required. Anti-Yt^a was available but we needed a supply of anti-Yt^b. A sample of anti-Yt^b was offered by Marilyn and John Moulds, which enabled the testing of the Yt groups of Israeli Jews, Arabs, and Druze. These tests showed a high frequency of the *Yt^b* allele, which explained the relatively high frequency of samples with anti-Yt^a in our population. The *Yt^b* allelic frequencies ranged between 0.1005 and 0.1522 in the Jewish communities and were 0.1294 and 0.1429 in the Arab and Druze communities, respectively.[12,13] These are the highest *Yt^b* allelic frequencies observed so far in any population tested,[4] which explains why anti-Yt^a is the most frequently detected antibody directed at a high-incidence antigen in the NBGRL.

In retrospect, it is interesting that the late Dr. Lyndall Molthan (in a written communication) had written that she considered anti-Yt^a as "The Jewish Connection"!

First Rare Blood Donor Meeting

For many years, we considered setting up a meeting of our rare blood donors with the staff of the NBGRL; this finally took place in April 2002. A special program was prepared and invitations sent out. The venue was the MDA National Blood Services and the attendance far exceeded our expectations, showing us that our rare donors understood the importance of this gathering. Each person was registered and received a badge and a folder of detailed information about their blood group. Also included was a request to give permission to be listed on the International Rare Donor Panel managed by the IBGRL in the United Kingdom, to which 43 donors agreed. The meeting began with refreshments to enable the mingling of donors and staff. The more formal program included lectures and active participation of a number of individual rare donors to talk about their personal stories and problems. Throughout the whole meeting our donor room remained open for the rare blood donors and their families to donate. Thirty-two rare donors donated blood and 15 samples were drawn from family members for testing.[14]

Today, we have 566 registered rare blood donors, some unique in the world, and more than 1200 frozen units of rare blood are stored in high glycerol solution in freezers at –80°C.

Our beginnings were modest. The service was started in one small room with one physician and one

laboratory worker employed for half of a day. We began with minimal reagents, test tubes, and racks; a simple centrifuge; a refrigerator; and one freezer. It did not take us long to realize how many rare blood groups came to light. This is certainly due to the ingathering of the exiles to Israel from a multitude of different ethnic backgrounds. Clearly, there has been a necessity for additional help for the NBGRL in Israel. This help has always been willingly extended by SCARF and by many colleagues and laboratories all over the world; they examine referred samples of blood and give their advice. If we tried to list and thank all we would surely leave some out, but we do want to mention and thank Marilyn and John Moulds from the former Gamma Biologicals, Inc.; the then MRC BGU in London directed by the late Rob Race and Ruth Sanger and by Patricia Tippett; and the WHO IBGRL in the United Kingdom, managed by Carolyn Giles and later by Joyce Poole and Marion Reid from the New York Blood Center. Their help has proved invaluable to us, to the patients, and to the field of immunohematology in general.

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