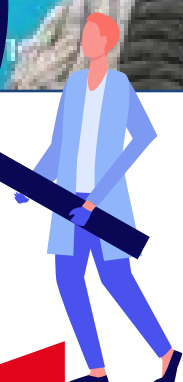




O⁺ B⁻ O⁻
 B⁺ B AB A⁺
 A⁻
LOB
 EFS Social Lab



EFS SOCIAL LAB PAPERS

N° 1, March 2021

DONATION OF BLOOD WITH A RARE PHENOTYPE OR PHENOTYPE OF INTEREST: A MAJOR CHALLENGE FOR EFS

Thin thank : Jacques Chiaroni (author) • Bruno Danic (co-author) • Bertrand Pelletier* • Corine Nicoué • Grégory March



INTERVIEW WITH JACQUES CHIARONI,
 Director of EFS
 Paca-Corse



3 questions to one of the two authors of the report, Professor Jacques Chiaroni

The work carried out by the EFS Social Lab is primarily intended for EFS to use internally to improve the donor experience. Why was it important to also give it external visibility through these EFS Social Lab Papers?

Prof. Jacques Chiaroni: *First of all, our work is visible externally not only through the EFS Social Lab Papers but also through scientific publications in international peer-reviewed journals, which are essential to position EFS in its research mission in terms of the scientific community. As far as the EFS Social Lab Papers are concerned, they have three objectives in my opinion. Firstly, by publicising our research work in the field of human and social sciences, this publication illustrates the fact that EFS is listening to societal trends that may impact blood donation today and tomorrow. Secondly, it responds to the need for transparency and communication with our partners and supervisory bodies, by shedding light on how EFS operates. This is based on scientific rigour, factual information and evaluation in the*

The EFS Social Lab draws on knowledge in the field of human and social sciences to devise action plans for improving the donor experience at Établissement français du sang (EFS, French Blood Establishment) sites. The EFS Social Lab Papers outline the results of its studies.

This first edition focuses on donors with a rare blood group o phenotype of interest - a priority target for EFS. Certain blood groups are very rare in the French population - a fact that is not widely known. It is therefore essential to have donors from these groups in order to transfuse patients with a rare blood group.

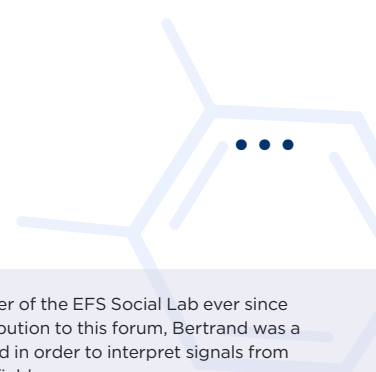
1. CONTEXT: A PRIORITY MISSION FOR EFS

EFS must make blood products available across France, ensuring that **each patient can receive a product compatible with their blood group**. During a transfusion, blood group compatibility is essential for patient safety. Otherwise, the transfusion will be ineffective or may even prove fatal in some cases.

different systems. The ABO system is the most widely known (with groups A / B / O / AB), but the diversity of blood groups is far greater, and a more detailed phenotype (combination of antigens) must be taken into account in the case of certain blood transfusions.

Blood groups are distinguished by molecules present on the surface of red blood cells, namely antigens. To date, **367 antigens have been identified in 41**

*This first issue is dedicated to Dr Bertrand Pelletier, an ardent supporter of the EFS Social Lab ever since its inception, who passed away on 15 February. In addition to his contribution to this forum, Bertrand was a figurehead for transfusion and EFS. He always kept an ear to the ground in order to interpret signals from society so as to help EFS progress, particularly in the social marketing field.





WHAT ARE THE DIFFERENCES BETWEEN RARE BLOOD GROUPS AND PHENOTYPES OF INTEREST?

Some blood groups are rare: these "rare bloods" are found in fewer than 4 per 1,000 inhabitants. Other groups are termed "**phenotypes of interest**" because they are found in lower numbers in blood donors compared to recipients - hence this can pose a problem for EFS in ensuring self-sufficiency for these groups. **More than 250 different rare blood groups are listed and it is estimated that over 700,000 individuals in France have a rare blood group.**

EFS is currently struggling to guarantee an adequate supply of certain rare blood groups in France. Some supplies have diminished altogether, and it has sometimes been necessary to import blood from other countries.

MIGRATION PROMOTES THE DIVERSIFICATION OF BLOOD GROUPS

The distribution of blood groups varies across the world. **One blood group may be common or exclusive in one part of the world and rare or even absent altogether in another part.**

Consequently, as a result of population movements, people may find themselves with a 'rare' blood type in their destination country compared to what would be

deemed a normal blood type in their country of origin. Thus, an O-negative European going to live in China would find it very difficult to get a blood transfusion, if required.

In the case of mainland France, people originating from or with ancestors originating from the African continent and its expansion into the Indian Ocean (Reunion, Mayotte, Comoros) are more likely to have a rare blood group or phenotype of interest for two reasons:

- ◆ There are more specific blood groups and variants in populations from these geographical areas than in others due to their higher level of genetic diversity. This is directly related to the fact that humans first appeared in this region around 250,000 years ago, thus allowing more time for diversity to accumulate in Africa. The rest of the planet was populated 'a mere' 70,000 years ago.
- ◆ There is a greater need for transfusions in these populations due to the presence of certain genetic conditions such as **sickle cell disease**, which is more widespread in Africa.

For historical reasons, **people from the African continent or of African descent account for a significant proportion of the recent immigration population** in France.

According to INSEE figures, there were 6.5 million immigrants (born abroad and living in France) in France in 2018 and 7.5

field of interactions with society. Finally, giving visibility to the work of the EFS Social Lab also allows EFS to participate in public debates on major society-related issues linked to bioethical issues and to the values of citizenship, solidarity and sustainable development, etc.

How was this report prepared? What pre-existing work did you rely on and what new studies did you carry out within the sub-working group?

Pr. J.C. : *The first step is to identify and prioritise an issue. This was quite obvious for "rare bloods and phenotypes of interest", which have been strategic issues for EFS for several years. However, these have never been explored in such detail and followed up with an action plan. We then identified the writers: Bruno Danic and myself, taking into account our previous work on the subject, particularly in the context of EFS 2035. Then we carried out a state-of-the-art analysis, based on numerous works as well as a literature review conducted by a Dutch researcher who reviewed over 2,500 publications concerning qualitative self-sufficiency and blood donation in migrant populations. We have drawn three main conclusions: the problem of rare blood types concerns all industrialised countries that experience population movements. Sociological and anthropological knowledge of the determinants of blood donation, i.e. its obstacles and incentives, provides a wealth of information but, on the other hand, there is a certain lack of experience in transforming this knowledge into practical actions that can be used in the field. This is why our paper proposes specific action plans that are made available to EFS professionals.*

You have a long-standing interest in rare blood types and phenotypes of interest, and have carried out numerous studies. What topic-specific issues are you particularly interested in?

Pr.J.C. : *As a young head of the blood group and issuing laboratory at the Marseilles*



Transfusion Centre, I came across difficulties in determining certain blood groups and therefore transfusing certain patients. On closer examination, I realised that all these complex blood groups were expressed in individuals of African ancestry. I therefore decided to focus on population genetics, which led me to complete my post-doctorate studies in this area at Stanford University. On my return to EFS Paca-Corse, I had the opportunity to build a team dedicated to blood group research. We focused our studies using three complementary approaches: a medical approach questioning the management of transfusion compatibility in patients with rare blood groups, a functional approach which seeks to provide a better understanding of the function of these molecules on the surface of red blood cells in normal and pathological situations, and a geographical approach which questions the preferential distribution of blood groups in human populations, its evolutionary forces and medical consequences, particularly in situations of population movement. This team is part of the ADES (Anthropology, Law, Ethics and Health) joint research unit involving the CNRS, Aix-Marseilles University and EFS, which I have been leading since January 2021. What interests me most is the ability to broach blood transfusion as a multidisciplinary science involving the biological, medical and cultural sectors.



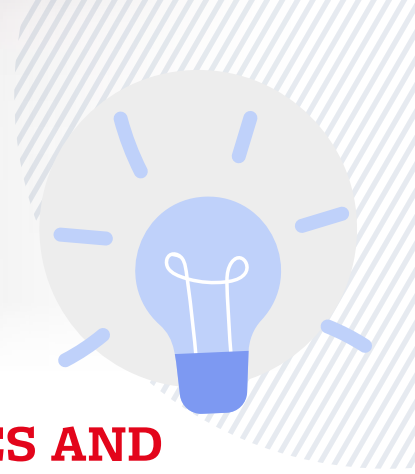
million people with at least one immigrant parent. Of these 14 million people, 6.3 million are of African origin or have a parent from Africa (4.3 million from North Africa and 2 million from sub-Saharan Africa).

Some French regions, mainly Paris and PACA (Provence, Alps and the French Riviera), have a higher population of migrants and their descendants. Since the origin of migration can also vary from one region to the next, **some rare groups are more numerous in certain parts of France than in others.** Within a region, the diversity of blood donors must therefore reflect the diversity of the population in order to ensure that every potential patient has access to compatible blood transfusion. This task is further compounded by the fact that, for epidemiological reasons, there can be no blood collections in French Guyana and Mayotte, where there are more rare phenotypes and patients with sickle cell disease.

EFS NEEDS DONORS OF AFRICAN DESCENT TO TREAT SICKLE CELL PATIENTS IN PARTICULAR

Hence, **in order to ensure that all blood groups are self-sufficient, the population of African descent must be a priority target for EFS.** This is particularly relevant since the need for transfusions for sickle cell patients is increasing over time, given the increase in the number of patients and their life expectancy. There are currently 30,000 people with sickle cell disease in France, 50% of whom live in the Paris region, 20% in the French Overseas Departments and Territories and 30% in the rest of mainland France. It is the most common genetic disease identified by neonatal screening, with 356 newborns testing positive for sickle cell disease in mainland France in 2016.





2. HOW EFS CURRENTLY ACCOMMODATES AND SUPPORTS DONORS WITH RARE BLOOD GROUPS AND PHENOTYPES OF INTEREST

HOW IS AN INDIVIDUAL WITH A RARE BLOOD GROUP IDENTIFIED?

The definitive diagnosis of a rare blood group is given by the French National Reference Centre for Blood Groups (Centre National de Référence pour les Groupes Sanguins, CNRGS). The patient in question is then registered with the rare blood group registry.

Individuals with rare blood groups are identified in different ways:

➔ **In blood donors:** rare blood is not automatically detected when identifying donor blood groups. Nevertheless, some situations or evidence lead(s) to more in-depth research to establish whether the donor has a rare blood group or phenotype of interest:

- ◆ The EFS teams may request extended tests during collection or when conducting laboratory tests based on clinical or biological information;
- ◆ Difficulties in interpreting the blood group may also lead to more in-depth analyses;
- ◆ EFS sometimes conducts large-scale detection campaigns with donor blood samples in order to specifically identify certain blood groups.

➔ **In patients:** when certain difficulties arise in interpreting blood groups during a **laboratory blood test**. In this case, the sample is sent to an EFS laboratory which will carry out extended testing.

➔ **In the siblings of an individual with a rare blood group:** the probability of having a rare blood group is 25% among family members where a rare blood group has already been identified. Consequently, all siblings are routinely tested when a rare blood group is detected by the CNRGS. This is designed to anticipate problems that could arise if such individuals required a blood transfusion.

HOW IS AN INDIVIDUAL WITH A RARE BLOOD GROUP INFORMED?

Following diagnosis by the CNRGS, the results and a covering letter are sent to the donor. Awareness of blood donation is heightened by the EFS "rare blood" officer, generally in a telephone conversation. During this discussion, the individual is informed of the difficulties they could experience if they required a blood transfusion. They are also made more aware of blood donation. The rare blood officer also asks the person about their siblings, who are advised to go for rare phenotype screening.

INDIVIDUALS WITH RARE BLOOD GROUPS AND BLOOD DONATION

Rare blood donors may come forward to donate blood following a call from the CNRGS in response to a specific shortage in National Blood Bank stocks of rare phenotype blood, or further to a call from EFS in preparation for elective surgery to be performed on a patient with a rare blood type, for example. They can, of course, also attend donor centres of their own volition.

EFS RESEARCH INTO RARE BLOOD

EFS is currently conducting several research projects on rare blood, both in a laboratory context (for example to enhance the safety of transfusions or to facilitate them) and in human and social sciences, notably to understand the motivations and obstacles in terms of blood donation in individuals with a rare blood type.

3. RARE BLOOD AND PHENOTYPES OF INTEREST: WHAT CAN HUMAN AND SOCIAL SCIENCES TEACH US?

Several human and social science studies conducted by EFS and other research organisations in France and abroad have focused on the subject of rare blood. For the reasons outlined above, most studies focus on individuals of sub-Saharan African descent, who represent the priority target for identifying those with a rare blood group. A review of the scientific literature was supplemented by the findings of a qualitative survey carried out by Viavoice at the request of EFS in Paris and Marseilles, during which 35 people of African ancestry were interviewed.



INCENTIVES AND OBSTACLES IN CERTAIN SOCIO-CULTURAL GROUPS: THE SOCIO-ANTHROPOLOGICAL APPROACH

The following concepts emerge from these different studies.

The concept of rarity is perceived as extremely positive

Among donors who have already been identified, it generates pride, as evidenced with other non-rare blood groups. This pride is also seen in universal donor groups (O-negative blood) or in people with specific antibodies (e.g. anti-tetanus), or even in plasma and platelet donors (due to the smaller number of donors and the longer time needed for these donations compared to blood donation).

Thus, the confirmation of a rare blood group may give the individual in question further incentive to donate. Those interviewed in the qualitative study conducted by EFS did not express any fear of racial repercussions in terms of the difference in blood characteristics. However, **the latter may well be used for stigmatisation purposes**. Malicious comments are sometimes posted on social

networks and on certain websites, exploiting the increase in these needs for xenophobic propaganda purposes.

The revelation of rarity can lead to anxiety.

Although EFS correspondence seem to be appreciated, the technical nature of the information concerning the analytical results and the lack of explanations provided could result in withdrawal and even rejection. The factors that increase this anxiety expressed by rare blood donors in the qualitative study are, in particular, the unfamiliarity with the sender of the correspondence (CNRGS), the notion of genetic transmission and the risk for descendants and siblings, the advice to inform their GP and to carry all of these documents around with them (thereby linking rarity to danger and difference) coupled with the fear of not being able to have a transfusion if required.

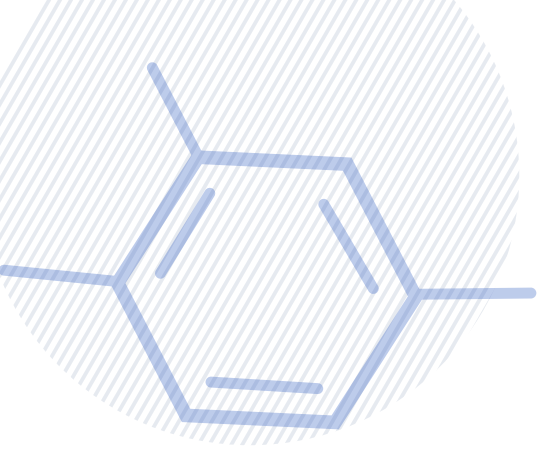
Today, rare blood donors are not always received in a specific manner at EFS collection sites. According to collection staff, **the explanations given may be perceived as inadequate or even as causing anxiety for some donors**. This may be due to limited knowledge of the specificity of rare blood groups, and/or to the absence of pedagogical language that would avoid tactlessness or lack of precision in the explanations.

Motivation and factors promoting blood donation

Some of the factors motivating individuals in the socio-cultural study groups to donate blood are similar to those of other blood donors. Thus, the key factors in donating blood are a feeling of being useful, the values of solidarity, general interest and a desire to help people without meeting them. An optimistic vision of the world and of oneself, linked to social integration in this respect, also promotes blood donation: blood donors claim they are more "at ease with their lives and in society" and say they are happy or even fortunate. Studies in France have shown that participation in blood donation increases with each generation of immigrant families, reaching a participation rate comparable to the French average by the third generation.

The confidence placed in EFS also promotes blood donation. Even if EFS and its functioning are still not that well known (notably what happens to the blood bags once they have been collected), the institution is seen as a serious organisation, promoting health and safety whilst respecting ethical principles compared to the transfusion system in other countries.





frequented by younger people.

- ◆ **Associations** linked to countries of origin, the **media** in these countries, messages on social networks and "community" **influencers** can also be used to promote donation.

The obstacles to blood donation

Among potential donors from these socio-cultural groups, **deferral** may be an even greater obstacle to returning to donation than in the general population, particularly due to the following:

- ◆ **Cultural relationships to time** pose a problem insofar as an inability to donate when the decision is made makes it even more difficult to return to donation ("if we have to come back another time, we invariably never will").

- ◆ **Deferral can be felt as stigmatising and discriminatory**, particularly when it is linked to a trip to an individual's country of origin or to the country where their family lives.

- ◆ A misunderstanding may arise between the donor and the person announcing the deferral if **they do not refer to the same cultural framework** during their conversation, particularly in the way they understand health or illness.

- ◆ Another obstacle specific to **sickle cell disease** exists due to the **triple stigma attached to this decision**: the disease,

ethnicity and female gender (in Africa, women are often stigmatised because of this disease, since they are considered responsible for its transmission). In addition to being a biological fact, sickle cell anaemia is also a social phenomenon created by social stakeholders. This should be borne in mind in messages heightening awareness of sickle cell anaemia.

- ◆ **The influence of the transfusion model in the country of origin**: populations that have immigrated may, without any further information, cling to the idea that the transfusion model of the country of origin is universal, such as replacement donation, which is still very much in evidence in Africa (close relations are invited to donate blood to compensate the patient's needs). In other countries, such as Vietnam, for instance, compensated donation is practised (if you are a blood donor you do not pay for a transfusion as a patient, and you are entitled to routine biological tests) or even paid donation (platelet aphaeresis donation). Other people may fear that their blood is being marketed or that donation is not sufficiently secure.

- ◆ **A varying degree of racial discrimination in everyday life or in experiences involving the health care system**: this can foster a fear that donated blood will not be accepted or used. In addition, a negative experience of the world of health, or even of donation, can lead to difficult empathy towards the recipient if this experience is seen as racial discrimination (whether real or supposed).

There are other specific or greater incentives for immigrants or individuals of African descent:

- ◆ **The civil act** of donating blood is a marker of belonging to the society in which they live;

- ◆ **The recognition** given to the donor following their donation and specific recognition for rare blood donors in particular;

- ◆ **Information on the structure of the blood donation system**, which may, for instance, provide reassurance about the ethical values of EFS;

- ◆ **Screening for transmissible diseases**, which is more ambivalent, could be an incentive, but it could also prove to be an obstacle (fear of detecting a disease);

- ◆ **Families can be introduced to donation**, particularly when a relative is affected by diseases warranting transfusions such as sickle cell anaemia (but this could also represent an obstacle for some people as blood may be associated with death);

- ◆ The role played by a **community linked to ethnic origin**: an Australian study and an American study have shown that blood donation could be perceived as promoting links within such communities;

- ◆ **Festivities** organised in some communities, e.g. of Comorian origin, are also ideal forums for raising awareness of blood donation, but they are seldom





◆ A reception process in collection centres that does not pay sufficient attention to **diversity**: respect for dietary rites (cultural or religious) is crucial. In addition, communication materials that do not include ethnic minorities to adequate extent, the absence of blood donor clinics in the donors' usual environment, and the idea that the staff and volunteer donor organisations do not reflect the diversity of the population, can give the impression that the blood donor clinic is only for one part of the population. This can also contribute to a lack of empathy towards patients in need of transfusion.

◆ Finally, **language** barriers may result in a refusal to donate. An inadequate command of the French language is already a factor in social exclusion. It should not become an additional factor in exclusion from donation. Moreover, blood donation described in a person's mother tongue is reassuring and removes any element of mystery even if French is understood. It can be difficult to take language into account in practice, but consideration could be given to the use of a sworn interpreter on an ad-hoc basis.

◆ **Fear of the procedure and its repercussions**: fear of the needle, discomfort, transmission of infectious diseases, concern about blood regeneration and loss of energy or even an adverse effect on health post-donation seem to be more prevalent in this element of the population according to the studies.

◆ **Religion** is not an obstacle to blood donation and religious representatives are often very active in this field. Whatever the religion, with the exception of Jehovah Witnesses, religious principles seem to promote blood donation. However, this is open to potential misinterpretation by some believers.

◆ Looking at obstacles, we should also refer to the regulatory criteria for donor selection, which often lead to a higher refusal rate, and the haemoglobin level, in particular, the physiological threshold of which is lower in populations of sub-Saharan African descent than in those of Western European ancestry, as reported in numerous studies.

EVALUATION OF METHODS FOR ACTIONS/INITIATIVES TO ENCOURAGE BLOOD DONATION

Several studies have been carried out in certain population groups where people with a rare blood group are over-represented. They have shown that activities aimed at raising awareness of the importance of blood donation lead in the short term to an increase in donors among the target population. However, the effect subsides in the longer term. These studies also highlight the importance of the cultural adaptation of messages and information leaflets, especially for recruitment.

Nevertheless, all of these studies have weaknesses, notably the failure to take into account confounding factors and the absence of a control population (no non-exposed population of the same type was studied). Finally, the studies are conducted over periods which are too short to measure significant impacts, particularly in terms of donor retention.



4. HOW TO BOOST THE RARE BLOOD GROUP AND BLOOD GROUP OF INTEREST SECTOR? ACTIONS RECOMMENDED BY THE EFS SOCIAL LAB

The EFS Social Lab proposes a 10-strong action plan based on 5 key themes to boost the collection of rare blood and phenotypes of interest. This action plan focuses on 5 key areas:

- 1 Optimising the existing system and defining a specific pathway for rare blood donors, while better informing donors and patients.**

It is important to focus discussions on the concepts of rarity, pointing out the desirable features of the phenotype in question. Clear messages should be delivered focusing on the absence of disease, reminding individuals of the importance to donate again for themselves and above all for others, highlighting the sibling and family links and, above all, answering all questions in real time.

- 2 Creating a network of rare blood officers including doctors from the blood drive in each EFS regional establishment (Établissement de transfusion sanguine, ETS).**

The EFS Social Lab recommends the compilation of an annual activity report for each region, taking stock of the actions undertaken to recruit donors with rare blood or a phenotype of interest, and evaluating these actions.

The network dynamics of the 'rare blood' officers, based on sharing information and feedback, will generate an annual national summary of activity reports, good practices to be adopted and scientific or benchmark news.

- 3 Systematically evaluating awareness and recruitment actions implemented.**
- 4 Creating a reference tool to help recruit rare blood donors** for blood drive managers to help them identify where to organise blood drives and raise awareness: use of demographic data, search for specific media, contacts, opinion leaders, adaptation of communication media/tools, management of the language barrier.
- 5 Training for EFS employees and partner volunteers in welcoming diversity.**

WHAT IS THE EFS SOCIAL LAB?



The EFS Social Lab is the French Blood Establishment's system for listening to society and donors. Its mission is to improve knowledge of donors, people likely to donate or to impart or share information on blood donation by drawing on human and social sciences, and conducting donor surveys. It recommends actions to be taken to expand the Innovadon programme, which seeks to create a new donor experience, build on donor retention and to recruit new donors.

To cite this publication: Jacques Chiaroni, Bruno Danic, Donation of blood with a rare phenotype or phenotype of interest: a major challenge for EFS, EFS Social Lab Papers, no 1, March 2021.