NHS Blood and Transplant

Putting the Lab into CoILABoration. The challenges of investigating samples from patients with Sickle Cell Disorder

Dr Tom Bullock

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Consultant Clinical Scientist

Caring Expert Quality

Sickle Cell Disorder

NHS Blood and Transplant

- Sickle cell Disorder (SCD) is the fastest growing genetic blood disorder in the UK which mostly affects people of Black ethnicity.
- There are currently 17,500 people in the UK with SCD.
- Almost 300 babies are born in the UK with SCD each year
- People with sickle cell need regular blood transfusions – most often with the specific blood sub-type Ro.
- **However, NHS Blood and Transplant is only able to provide matched blood for just over half of hospital requests.**

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SCD and Blood Transfusion

- Automated red cell apheresis transfusions require between 8 to 10 units of red cells on average.
- Top-up transfusions may only need a couple of units of blood.
- Manual exchanges, which require around 3 to 8 units of red cells in an adult patient.
- Most patients will have an exchange transfusion every 4 to 8 weeks
- On average each patient may need around 100 red cell units every year.

Consequences……

Red blood cell alloimmunization in sickle cell disease: pathophysiology, risk factors, and transfusion management

Karina Yazdanbakhsh,[1] Russell E. Ware,[2] and France Noizat-Pirenne[3,4]

- **Alloimmunisation**
  - In SCD, the published rate of alloimmunization ranges from 20% to 50%
  - Differences in antigen expression between the largely Caucasian donor population and African / Afro-Carribbean patient population (incl. variants!)
  - SCD patients in Uganda and Jamaica, where donors and patients are racially more homogeneous, have reported alloimmunization rates of only 6.1% and 2.6%, respectively

Alloimmunisation

- Not surprisingly, antibodies against these common antigens are most frequently identified in SCD patients:

Blood group system	Antibodies
Rh	Anti-C, -D, -E
Kell	Anti-K
MNS	Anti-M, -S
Duffy	Anti-Fy^a, -Fy3
Lewis	Anti-Le^a, -Le^b

- Matching for Rh (C,D,E) and K antigens reduces the rate of alloimmunisation in chronically transfused patients with SCD from 3% to 0.5% per unit and is the recommended approach in British Society for Haematology (BSH) Guidelines.

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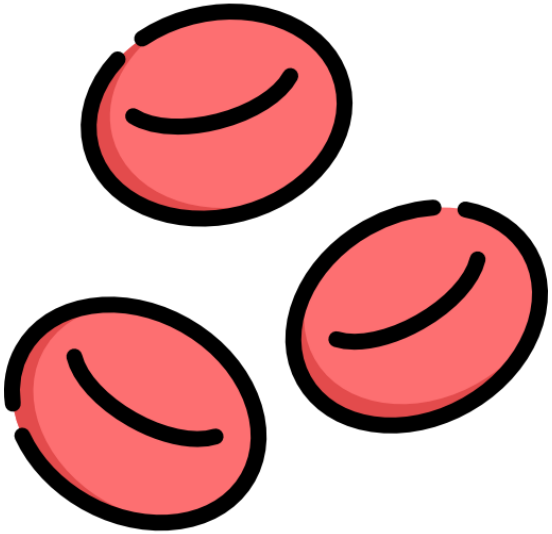
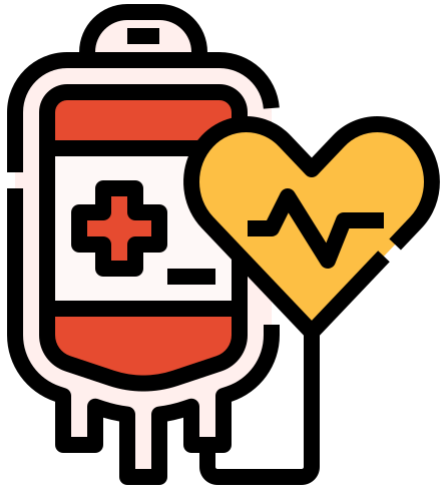
Red Cell Immunohaematology (RCI)

- RCI provides the following services:
  - Antibody identification
  - Crossmatching units for transfusion
  - Phenotyping
  - Investigation of transfusion reactions
  - Clinical advice





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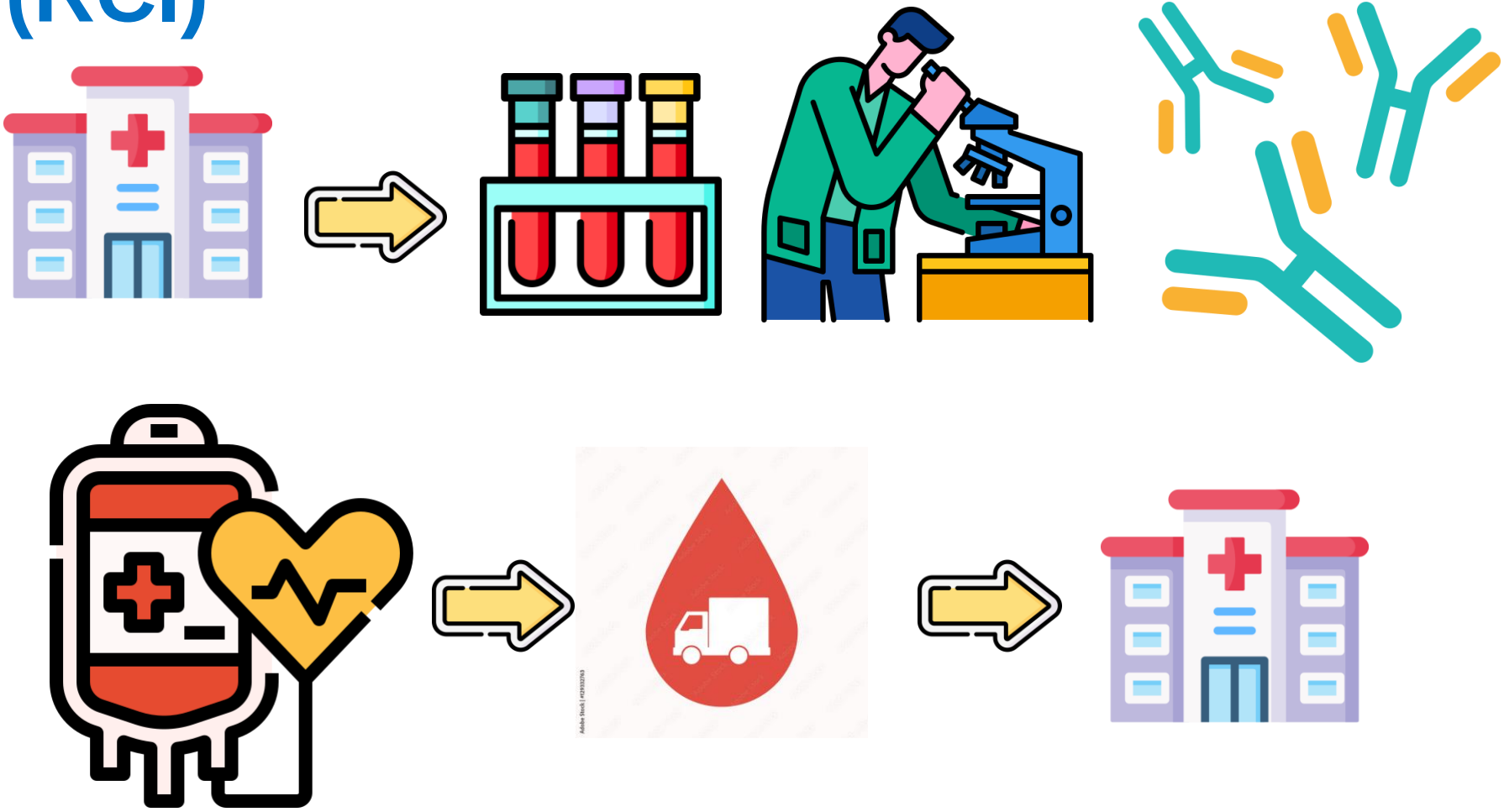
Red Cell Immunohaematology (RCI)



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Panreactivity

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FORM FRM783/2.2

Effective: 25/10/19

ID Panel Profile

CE
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IVD

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NHSBT REAGENTS Panel 1

Product	Lot No.	Product	Lot No.	Product	Lot No.
ID Panel in Alsevers	R144 3490	ID Panel Papainised in Alsevers	R154 3490	ID Panel in LISP	R146 3490
ID Panel in CellStab	R143 3490	ID Panel Papainised in CellStab	R153 3490	Expiry Date : 2021.10.21	
ID Panel in CellMedia	R163 3490	ID Panel Papainised in CellMedia	R173 3490		

Patient's Name D.O.B.		Ref. No.	Sample No.	Conclusion Tested by Date

Unless otherwise indicated, all cells are positive for Kp^b and Lu^b and negative for Wr^a and Co^b.

Instructions for use can be found at http://www.blood.co.uk/reagents

EC REP Quality First International OÜ,Laki 30,12915 Tallinn, Estonia

	Rh	C	D	E	c	e	C^w	M	N	S	s	P1	Lu^a	K	k	Kp^a	Le^a	Le^b	Fy^a	Fy^b	Jk^a	Jk^b	Other
1	$R_1^WR_1$	+	+	0	0	+	+	0	+	0	+	4	0	0	+	0	+	0	+	0	+	0	
2	R_1R_1	+	+	0	0	+	0	+	0	+	0	3	0	+	+	0	+	0	0	+	0	+	
3	R_2R_2	0	+	+	+	0	0	0	+	0	+	0	0	0	+	0	0	+	+	0	0	+	
4	r'r	+	0	0	+	+	0	+	0	+	0	4	0	0	+	0	+	0	+	0	+	0	
5	r''r	0	0	+	+	+	0	+	0	+	0	3	0	0	+	0	+	0	0	+	+	0	
6	rr	0	0	0	+	+	0	+	+	0	+	3	0	+	0	0	0	+	+	0	+	0	
7	rr	0	0	0	+	+	0	0	+	0	+	0	0	+	+	0	0	+	0	+	0	+	
8	rr	0	0	0	+	+	0	+	0	0	+	3	0	0	+	+	+	0	0	+	0	+	
9	rr	0	0	0	+	+	0	+	0	0	+	1	+	0	+	0	0	+	0	+	0	+	
10	rr	0	0	0	+	+	0	0	+	+	0	4	0	0	+	0	0	0	0	+	+	0	

Reagent							DAT Profile	Anti-IgG	IgA	IgM	C3c	C3d	Ctrl
Lot No.							Result						

(Template Version 01/04)

Cross-Referenced in Primary Document: SOP883

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Panreactivity

Toolkit

NHS Blood and Transplant

Temperature

Techniques

DAT

Reagents

Genotyping

Pre-warming

Warm washing

Alloadsorption

Titration

Autoadsorption

Clinical History

Solving Cases, Saving Lives

Explore RCI and gain unique expertise that can change lives and build a brilliant career.

Zarqa Ali, RCI reading tube testing results over a lightbox

Ben Bowden, RCI prepping patient samples for a genotyping investigation

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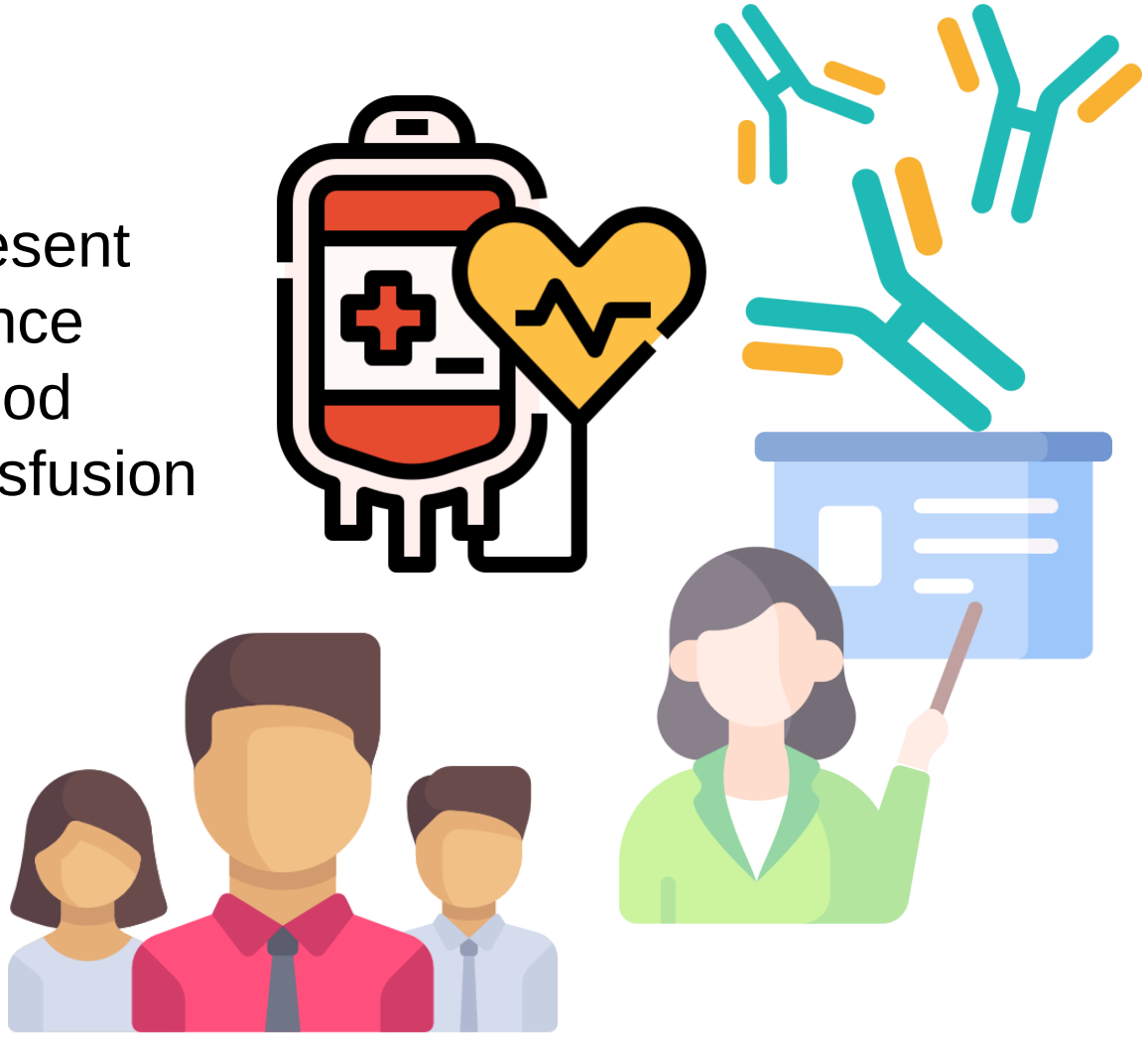
Red Cell Immunohaematology (RCI)

- Clinical advice
  - Antibody(ies) present
  - Clinical significance
  - Availability of blood
  - Planning for transfusion
  - Teaching
- Regional HGP MDT
- National HGP MDT



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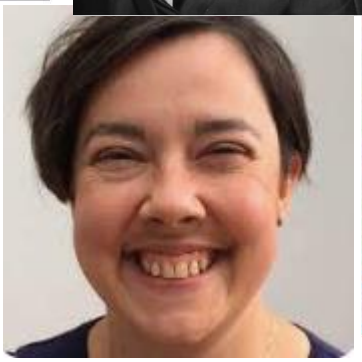

Toolkit

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Temperature

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Clinical History

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International Blood Group Reference Laboratory

- Molecular Diagnostics (MD) laboratory

Standard Genotyping	(RhD, C, c, E, e, K/k, $Fy^{a/b}$, $Jk^{a/b}$, M/N, S/s, U-, U^{var})
Extended Genotyping (haemoglobinopathy array) - This genotyping test array is particularly suited for haemoglobinopathy patients	RhD, C, c, E, e, (including common RhD, C and e variants),V, VS, hrB, hrS , K/k, $Kp^{a/b}$, $Js^{a/b}$,$Do^{a/b}$, $Fy^{a/b}$, $Jk^{a/b}$, M/N, S/s, U-, U^{var}

NHS
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Genotyping

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INTERNATIONAL BLOOD GROUP REFERENCE LABORATORY

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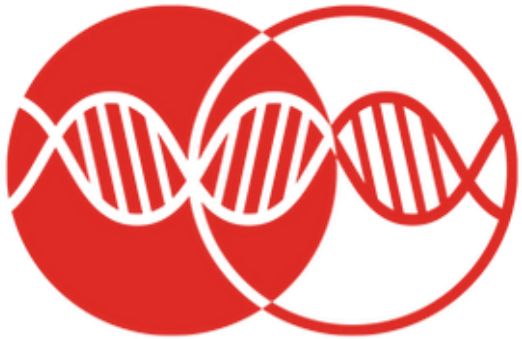
Home / Services / Molecular Diagnostics / NHS England programme for Haemoglobinopathy blood group genotyping

NHS England funded programme for blood group genotyping

Improving blood matching for people living with anaemias



Haem Match

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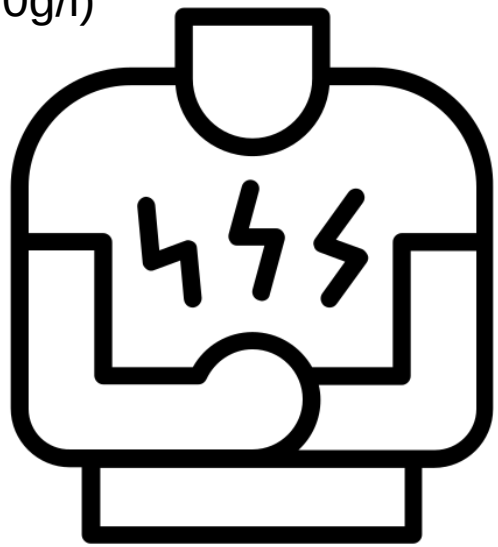
Recent case

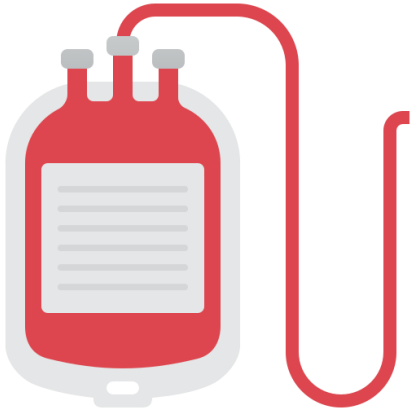
- Patient with SCD
- Gp B ccDDEe (R2r) K-
- Previously identified antibodies
  - Anti-C
  - Anti-S
  - Anti-Jka
  - Anti-Fy3
- Hb is currently 30g/l. Was 56g/l yesterday (normally 60-70g/l)
- Hip surgery 3 weeks ago
- Wound haematoma
- Infection
- Surgical exploration planned
- History of previous hyperhaemolysis / DHTR
- Patient is in severe pain
- Concerned that they are in sickle crisis



Recent case

NHS Blood and Transplant

- Search for Gp B D pos C- K- S- Fy(a-b-) Jk(a-)
    - 2 units nationally (Colindale and Tooting)
- Search for Gp B D neg C- K- S- Fy(a-b-) Jk(a-)
    - 2 more units (Filton and Basildon)
- Search for Gp O Ro K- S- F(a-b-) Jk(a-)
    - 1 unit (Colindale)
- 6 units in NFBB that match extended type
- Haematology team did not transfuse and gave eculizumab. Hb nadir 22g/lthen reticulocyte function improved and pt. Hb recovered without transfusion



Where do we get rare blood?

NHS Blood and Transplant

There are a number of sources of rare blood. They are usually searched in a specific order of preference, based upon whether rare blood is available from one source or not, in addition to these other factors;

- The number of units
- Urgency of the request
- Specification of units

The sources of rare blood include the following, and are generally searched in this order of preference:

1. Fresh Stock
2. Call in donors
3. National Frozen Blood Bank (NFBB)
4. International Rare Donor Panels (IRDP)

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Where?

1. Any ‘wet units’ available in NHSBT’s general stock:

- This is a search of all current stock available within all of NHSBT’s manufacturing centres or stock holding units.
- This is the first place that is searched when rare blood is required.
- Sometimes combinations of antigen negative units can be found at various places around the country and can be brought to one centre to be crossmatched with the patient at the regional RCI reference laboratory and then subsequently issued to the hospital.

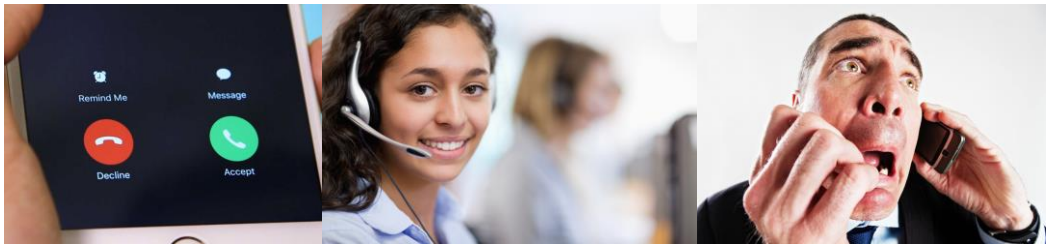
Where?

2. Call in rare phenotype donors to donate:

- There are existing donors that NHSBT is aware of who have a rare type. Calling in these donors is only really an option if there is time to call the donor in to be bled and the donation tested before the scheduled date of transfusion.

- Additionally the donor has to satisfy the NHSBT donation criteria in order to be fit to donate, so that the process of donation is safe for the donor and the donated blood is safe for the patient.

- Often, if one unit of blood is required then two donors have to be called in as a number of factors could mean that the donation is unable to be taken.



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Where?

Problems?

- Donor does not attend
- Donor has recent medical history (illness / vaccination) that excludes them from donation.
- Donor does not pass fitness to donate Hb threshold test
- Donor does not pass travel or lifestyle screening questions

In very rare cases the donor may be a member of the patient's family, who also shares the rare type through genetic inheritance and is compatible with the patient.

Alternatively it may be the patient themselves, through autologous donation, where the patient donates some of their own red cells prior to the operation in order to be given back to them, if required.

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Where?

3. The National Frozen Blood Bank (NFBB)

- NFBB holds small stocks of frozen rare blood of specific phenotypes which can be thawed, on request for certain patients with corresponding antibodies where compatible blood is not available from the first two sources.

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Where?

- There is an 6-8h processing time for 1 unit of frozen blood, with each additional unit taking 4-6h, so a two unit request could take up to 8-10h to thaw and process.
- Travel time and crossmatching in the regional RCI lab have to be factored into the request.
- Therefore frozen blood is not suitable for very urgent requests for immediate transfusion.
- Frozen units may not always be a viable option due to the shorter shelf life of a thawed unit (72h)
- Large orders of units are typically not supported by the NFBB, as this would deplete stocks too quickly. Large orders are normally sustained by appropriate transfusion planning and calling in of rare donors.



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Where?

4. The International Rare Donor Panel (IRDP)

The International Rare Donor Panel (IRDP) was conceived under a joint World Health Organisation (WHO) and ISBT initiative in 1965 to facilitate the rapid location and exchange of rare blood between countries.

The panel currently contains details of rare donors from 27 contributing countries and also frozen unit inventories from frozen blood banks around the world. The compilation and maintenance of the IRDP is carried out by the Red Cell Reference department of the IBGRL in Bristol, UK.

ISBT International Society of Blood Transfusion

International Rare Donor Panel

The IRDP database can only be accessed by authorised users.

Access the database

Where?

NHS Blood and Transplant

4. The International Rare Donor Panel

This is maintained by the International Blood Group Reference Laboratory (IBGRL) Red Cell Reference Lab.

At IBGRL:

- Compile and maintain information on rare donors from 27 countries
- Keep up to date data on contributors, donors and contact personnel
- Make information available to other blood centres/clinicians via internet
- Assist with search requests when required

Spanish Society of Blood Transfusion and Cellular Therapy (SETS)

Canadian Blood Services

Swiss Transfusion SRC

New Zealand Blood Service

South African National Blood Service (SANBS)

Sanquin (The Netherlands)

Australian Red Cross

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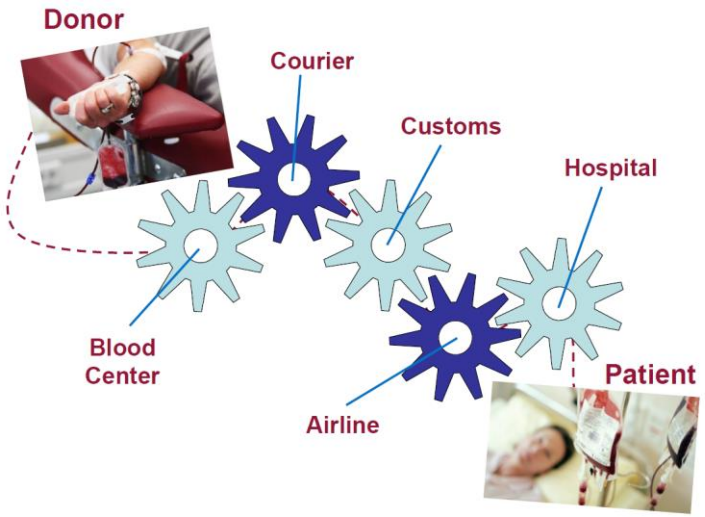
Where?

- Logistically, sourcing units from the IRDP can be challenging, with a number of obstacles to be overcome.
- It is not suited to urgent requests for transfusion.

The following need to be considered when sourcing units from the IRDP:

- Availability of courier companies with the capacity to handle temperature controlled products
- Packaging to ensure temperature lasts the distance
- Cancellation of flights - no control
- Government regulations
- Import/export duties / charges
- Different rules depending on country
- Significant delays can be encountered..



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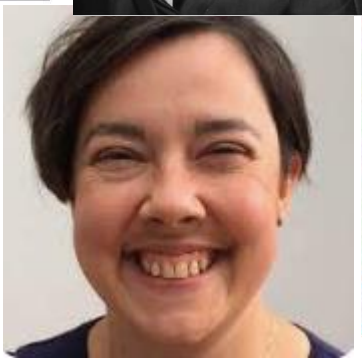


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FOR
SICKLE CELL

Donors

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R_o subtype

What is the Ro subtype?

The Ro subtype is a variation of the Rh positive blood type.

Ro individuals express:

cDe

Why is the Ro subtype important?

The Ro subtype is particularly important for two reasons:

- Demand is increasing by 10-15% each year
- Only 2% of regular donors have the Ro subtype
- Majority of donors White Caucasian
- Majority of Ro individuals are Black African / Afro-Caribbean heritage (10x more)

Sickle Cell Disorder

NHS Blood and Transplant

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- There are currently 17,500 people in the UK with SCD.
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- People with sickle cell need regular blood transfusions – most often with the specific blood sub-type Ro.
- **However, NHS Blood and Transplant is only able to provide matched blood for just over half of hospital requests.**

Targeted donor recruitment

- Recruitment of more Donors from more diverse backgrounds part of NHSBT strategy.

Grow and diversify our donor base

- Includes donors of not just RBCs but stem cells, organs and tissues.

Supply and Demand of Ro Blood 2023

NHS Blood and Transplant

Table 3: Requests from English hospitals for red cell units with the Ro phenotype and/or for transfusion to patients with sickle cell disorder, 2016/17 to 2022/23

	Red cell units requested, where the order specified:						
Financial year	Ro only (not intended for sickle cell disorder patients)	Both Ro and intended for sickle cell disorder patients	Intended for sickle cell disorder patients only (not Ro)	Total Ro units requested	% change from previous year	Total units requested for sickle cell disorder patients	% change from previous year
2016/17	16,842	30,374	25,278	47,216	-	55,652	-
2017/18	22,367	31,164	24,742	53,531	+13.4%	55,906	+0.5%
2018/19	25,106	35,542	27,009	60,648	+13.3%	62,551	+11.9%
2019/20	24,682	41,454	32,940	66,136	+9.0%	74,394	+18.9%
2020/21	23,655	42,696	33,784	66,351	+0.3%	76,480	+2.8%
2021/22	27,452	47,090	37,399	74,542	+12.3%	84,489	+10.5%
2022/23	27,910	47,614	38,966	75,524	+1.3%	86,580	+2.5%

Note: More than 99 per cent of all Ro requests also specified the K- phenotype.

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Zarqa ghtbox


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