

# Blood and Transplant

Information for hospitals served  
by NHS Blood and Transplant

# Matters

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## Next Edition

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### Issue 51 will feature articles on:

- Living Donor Kidney Transplantation in General and Non-Directed in particular.
  - Pathology at the time of Organ Donation.
    - The ATTOM Study.
  - NIHR Grant, Where are we now?
    - Patient's Story.

If you would like to comment on any of the articles in this edition of **Blood and Transplant Matters**  
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# EDITORIAL

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I hope that the last edition of Blood and Transplant Matters was well received and welcome to Issue 50. As I write this editorial, we have just had the first fall of snow this Autumn and it seems a long time ago that Zika was causing potential problems for the Summer Olympics and Para- Olympics in Rio this Summer.

However, the threat of Zika still persists and Ines Ushiro-Lumb outlines the 'Worldwide Impact of the Zika Virus Spread'. Providing an overview of the disease, diagnostic challenges and impact on the safety of outcomes of human origin – including blood and organs.

Dale Gardiner shares with us the problems facing 'Organ Donation in Three Different Countries' and the approaches that others are taking to improve organ supply. Interestingly, to note, the similarities are as much as the differences.

Emanuel Di Angelantonio outlines the 'three inter-related goals' of a newly created 'Blood and Transplant Unit in Donor Health of Genomics'. Although, early days the proposed work sounds very exciting, relevant and necessary.

Optimising supply is only one side of the equation, the other being appropriate use. Jo Shorthouse and Katy Cowan provide practical help and resources to enable hospitals to reduce 'Use of O D Negative Red Cells' and outlines the efforts of NHS Blood and Transplant (NHSBT) to improve appropriate supply. We rely upon volunteer donors for our blood supply, so it is very interesting to read the results of focus group work looking at donor opinion. Rachel Hale presents some data regarding donor opinion on blood donation, existing arrangements for collection and distribution as well as culturing red blood cells. If culturing red cells seems futuristic, Thomas Moreau described the successful First Steps for 'Laboratory Manufacture of Platelets for Transfusion'.

We have included another Patient Story, to remind us all why all the work is so necessary.

Finally, there is an interesting summary of a number of 'Cochrane Systematic review studies – and subsequent updates – that outlines the impact of those studies'.

There is a link to a survey in this edition, I would be grateful if as many as possible could complete the survey, we will use the feedback to improve the publication.

As always, there are both CPD questions based on the articles with answers appearing in the next edition – and some interesting cases with suggested answers, which I hope are both interesting and informing.

Have a good read. Any comments should be sent to myself or my hard working Editorial Assistant Lynne Hodkin at [blood&transplantmatters@nhsbt.nhs.uk](mailto:blood&transplantmatters@nhsbt.nhs.uk).

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# A Snapshot of the Worldwide Impact of the Zika Virus Spread

## Introduction

The Zika virus epidemic continues in the Americas and the Caribbean, with ongoing transmission in approximately 60 countries and territories globally and an expected rise in number of cases in the Asia Pacific region. The risk of local vector-borne transmission in Europe is also being monitored and remains low. Zika virus (ZIKV) does not occur naturally in the UK and as of November 2016, 170 proven and 81 probable travel-associated cases have been diagnosed since 2015.

## Transmission

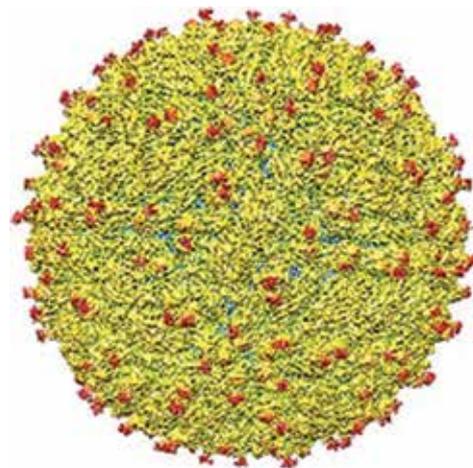
Human infections are primarily transmitted by *Aedes aegypti* mosquitoes, which also transmits dengue and chikungunya and is found throughout much of the Americas. Materno-foetal and sexual transmission is also known to occur. Although possible, no cases of transmission through transplantation of cells, tissues or organs have been reported to date; but transmission through blood products has been reported.

## Spectrum of Disease

The incubation period is approximately 3–12 days, with circa 80% of asymptomatic cases. When symptoms occur, they are mild, self-limiting, and may include pruritic maculopapular rash, conjunctivitis, joint pains and fever. Other co-circulating arboviruses such as dengue (DENV) and chikungunya (CHIKV) present in a similar way, making clinical diagnosis difficult. Severe thrombocytopenia has been reported as an uncommon complication of ZIKV, with suggestions that it may be immune-mediated. Guillain-Barre Syndrome (GBS) can occur, and the para-infectious or post-infectious mechanisms in ZIKV-infected individuals is being studied.

## Congenital Zika Syndrome

Zika virus is now recognised as the causative agent of congenital Zika Syndrome. The rate of symptomatic infection in mothers of babies with congenital Zika is around 65%, suggesting that the risk of foetal abnormalities is higher in symptomatic maternal Zika infection. Severe cases are associated with maternal infection during the first and early second trimester of gestation, when radial glial cells, the progenitor cells that give rise to neurons and other proliferating brain cells, are affected by ZIKV. Infection and loss of these cells lead to a process called brain disruption sequence, causing the striking appearance of affected babies. Neurological abnormalities are also seen in babies without microcephaly at birth hence the prognosis for these infants and the exact correlation with timing of maternal Zika infection require further investigation.



*A representation of the surface of the Zika Virus with protruding envelope glycoproteins (red) shown. Credit Kuhn and Rossmann, Purdue University.*

## Treatment and Prophylaxis

There is currently no drug approved to treat ZIKV infection. Candidate lead compounds for anti-ZIKV drug development have been identified through a drug repurposing screening program, with identification of two classes of antiviral and neuroprotective, with the latter being capable of protecting neural cells from ZIKV-induced cell death. At least five vaccine candidates are in pre-clinical or clinical trial stages of development.

## Diagnostic Challenges

The short duration of detectable viraemia makes laboratory diagnosis difficult. Antibody testing (IgM and IgG) has limitations and remains suboptimal, due to strong cross-reactivity with other flaviviruses, especially dengue virus. As regards to blood and other human substances, there is no place for serology in current donor screening algorithms. Work is in progress to develop and implement ZIKV Nucleic Acid Tests (NAT) for blood screening as well as NAT assays for simultaneous detection of ZIKV, DENV, and CHIKV, where required. Several diagnostic assays have received Emergency Use Authorization (EUA) by the US Food and Drug Administration (FDA), including two systems for blood donor testing which have yet to receive CE approval.

The World Health Organisation (WHO) is currently working on the provision of international reference material for ZIKV Ribonucleic acid (RNA) and antibodies, to enable comparative studies and improved diagnosis. As WHO Collaborating Centres for Blood Products and in vitro Diagnostic Devices, Paul-Ehrlich-Institut (PEI, Germany) was tasked to produce the molecular standard and the National Institute of Biological Standards and Control (NIBSC, England) to produce the antibody standard. To this

end, we in NHSBT developed a protocol to enable collection under concession, of serum from individuals who recovered from proven Zika infection after returning to England. This work is ongoing and thanks to the altruistic nature of several such individuals, NHS Blood and Transplant has been able to provide material for the production of the first international standard for worldwide use.

### **Impact on Virological Safety of Substances of Human Origin**

There is potential risk of transmission of ZIKV by blood, tissue, cells and organs, with special concern over severe outcomes in at risk recipients such as pregnant women. Probable cases of transfusion-acquired infection have been reported in Brazil, including an asymptomatic course in a stem cell transplant recipient (Barjas-Castro *et al*, 2016; Motta *et al* 2016).

Whereas donor deferral on the basis of travel history and diagnosis is possible in non-endemic areas, blood donor selection guidance given by WHO for endemic areas relies on education, self-deferral and post donation notification of symptoms with quarantine of donations. Given the high percentage of asymptomatic infection and shelf-life of blood components, these mitigation strategies suffer from limitations. Other alternatives such as pathogen reduction technologies for plasma and platelets and NAT screening are not economically viable in the majority of currently affected countries. For up to date UK donor selection guidance, please refer to [www.transfusionguidelines.org.uk](http://www.transfusionguidelines.org.uk).

The precise influence of immunosuppression on Zika infection is currently unknown. There is scanty evidence of possible viral dissemination and fatal outcomes in immunocompromised individuals but an exact causative role of ZIKV has not been proven. A small case series from Brazil described four solid organ recipients with ZIKV, who

did not exhibit conjunctivitis, exanthema, or neurological symptoms but had thrombocytopaenia and eventually recovered (Nogueira *et al*, 2016). However, the possibility of rare yet severe outcome remains, and clinicians should be aware of potential risks in immunocompromised patients. In the absence of autochthonous ZIKV infection and inability to provide validated, timely screening, advice from various organisations and expert groups in non-endemic areas is that awareness, diligent history taking and individual specialist risk assessment remain as the mainstay of risk mitigation for transplant recipients. We have produced some guidance for Organ Donation and Transplantation (ODT) and as knowledge in this area is constantly evolving, interested readers are advised to consult the information available through the ODT microsite [www.odt.nhs.uk](http://www.odt.nhs.uk).

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## **A Tale of Three Countries in Organ Donation**

I was lucky enough to be invited to speak on deceased organ donation in three countries over October. I want to share with you not what I said but what I heard.

### **India**

As part of my visit I attended the 9th Annual Transplant Coordinator's Conference which was being hosted within the larger Indian Society of Organ Transplantation meeting. There I heard some of the challenges Indian organ donation is facing.

Though India is seeing rapid economic development, public health expenditure is around 1.4% of GDP

(7.6% UK). As a result, 90% of transplants are in the private sector and the opportunity to receive a transplanted organ is limited by the ability to afford one. To counter this inequity, I learnt that some charities and hospitals have resorted to crowdfunding, with one charity seeking to ensure that any child who needs a liver transplant can receive one, regardless of ability to pay.

India, through predominantly living kidney donation, carries out more kidney transplants per year than the UK (6000 vs UK 3300). This is still far short of the need. Since Indian law only allows living kidney donation to a relative, one of the unique responsibilities of transplant

coordinators is to scrutinise applications and ensure that the two individuals are related. This is not always easy to verify and I saw some interesting photoshopped wedding pictures. One response has been to consider the need for DNA testing (if individuals are claiming to be blood relatives) but this is costly and adds further financial burden.

The deceased organ donation rate in India is only 0.5 donors per million population (UK 21.0). When speaking to a hospital in Jaipur I was impressed by the enthusiasm the whole hospital, including senior managers, had to improve deceased donation. One of the barriers I heard was that diagnosing and confirming death using neurological criteria (brain death) is not common in India; this is despite a tragic estimated 150,000 road deaths per year. I was able to support the first National Deceased Donation Clinical Simulation Workshop in Delhi which was dedicated to teaching brain death: why diagnose, how to diagnose and how to explain the diagnosis to families. This meeting was hosted by the relatively recently established National Organ and Tissue Transplant Organisation (NOTTO) and the MOHAN Foundation, (Multi Organ Harvesting Aid Network), a charity established in 1997 to promote appropriate organ donation from deceased donors.

NHS Blood and Transplant has a Memorandum of Understanding with the MOHAN Foundation in order to promote collaboration and share learning. One key early success has been the launch of a free downloadable App, just search for 'donor optimisation' in the Apple or Android store.

### Singapore

Singapore is an example country where the introduction of presumed consent legislation has not resulted in sustained increases in deceased organ donation. Currently Singapore has a deceased organ donation rate of around 6.5 donors per million population. Efforts are currently focussed on engaging with intensive care clinicians to promote a culture change in the way deceased donation is considered. This is certainly the same area the UK has focussed on over the last eight years. Changing the predominant health care professional view that donation is something inflicted upon patients and families to instead, deceased donation is a fundamental component of good end of life care.

It is this message, rather than the legislation per se that is being promoted in Singapore. A great example is the short film 'If Tomorrow Never Comes – A short film by SingHealth Transplant' which is available on YouTube and now being shown to hospital staff in Singapore. It's a wonderful film that encourages Singaporeans (and all of us) to speak to our families about our end of life donation wishes. For health care professionals it opens a window onto the value individuals may have felt regarding deceased donation, and perhaps expressed to their family, months or even years before the tragic event that has led the patient to be now under our care.

I am positive that this message of hope will resonate as strongly in Singapore as it has in the UK.

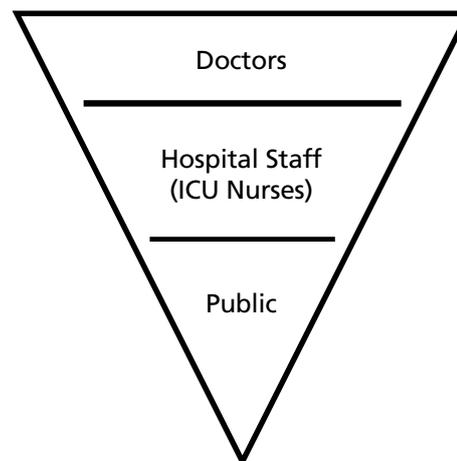
### China

Chinese deceased organ donation has been mired in controversy for many years for their use of executed prisoner organs. Under the leadership of Dr Jiefu Huang and Dr Haibo Wang, and with the full support of the Chinese government, China has forbidden this practice since January 2015. This has led to deceased donation rising and China is now achieving voluntary deceased donation rates of just under three donors per million population. While this does not sound very much compared to other countries, with a population of 1.3 billion people this is equating to nearly 4000 deceased donors per year (UK 1364).

The conference I attended in Beijing was not only a high level political meeting that celebrated the change in Chinese organ donation policy but, with the international experts present, became a true masterclass in deceased organ donation practice. It was fascinating to hear the Spanish and Croatian models (both around 40 donors per million population) extolled so elegantly. Likewise, experts from Canada, Australia, South Korea and the USA explained their models and it was an honour to present the UK donation success story.

Once again a remarkably similar message was expressed by all speakers. Credit goes to Howard Nathan (CEO of Philadelphia-based Gift of Life Donor Program, USA; 44 donors per million population) who managed to summarise everything I had learnt from three countries in one slide. Deceased donation is not primarily a transplant issue but an intensive care issue. Figure 1 is how Howard Nathan approaches the education and promotion of deceased organ donation.

**Figure 1:** Educate and Promote Organ Donation



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## New Research Centre to Underpin the Safety and Efficiency of Blood Donation

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The Blood and Transplant Research Unit (BTRU) in Donor Health and Genomics was launched by the University of Cambridge and NHS Blood and Transplant (NHSBT) in October 2015. Its mission is to conduct long-term research of major international importance in order to underpin the safety and efficiency of blood donation, for NHSBT and other blood services worldwide. The BTRU, which includes the Wellcome Trust Sanger Institute and the University of Oxford as key partners, has been funded by a four million award from the National Institute for Health Research (NIHR) following an open national competition.

The BTRU has three inter-related goals:

- To create knowledge and tools relevant to ensuring the sustainability of the blood supply.
- To train a new cadre of interdisciplinary researchers capable of sustainable research into donor health.
- To serve as a national and international research hub for donor health and genomics.

A key development that enabled creation of the BTRU was the establishment of the INTERVAL randomised trial, an academic-NHSBT collaboration that recruited approximately 50,000 whole blood donors between 2012 and 2014. The INTERVAL trial (due to report in 2017) aims to identify the optimum frequency of donation that ensures the well-being of donors as well as maintenance of the blood supply. As well as using traditional measures (for example, number of pints donated, self-reported well-being), this study is using innovative measures to help produce a more complete picture of the consequences of more-frequent versus less-frequent blood donation, such as online neuro-cognitive testing and objectively-measured physical activity using a wristworn device for a week.

Some of the efforts in the BTRU build heavily on the INTERVAL study. For example, INTERVAL has emerged as one of Europe's largest genomics studies, enabling us to gain major new insights into the regulation of iron metabolism and blood cell traits. All 50,000 participants have already had extensive genotyping done to profile hundreds of thousands of key markers across the genome. Our preliminary analyses have identified more than 1000 novel genetic risk factors for haematological traits, findings which could help to inform future strategies that aim to stratify donors on the basis of their capacity to give blood frequently. In collaboration with the Sanger Institute, we have commenced whole-genome sequencing (in other words, measuring all three billion genetic base pairs of each participant), which should open new opportunities to identify rare alleles.

Other major initiatives in the BTRU involve recruitment of additional blood donors into new research studies. For example, the ongoing COMPARE study is comparing several different methods (for example, copper sulphate test versus haematology analyser versus finger-prick HemoCue versus spectroscopy) to assess pre-donation haemoglobin levels in about 31,000 blood donors. The goal is to inform future screening strategy in NHSBT by identifying the method that best combines accuracy, cost-effectiveness, feasibility and acceptability in order to prevent inappropriate donations. As a further example, we are developing plans for a cluster-randomised trial to identify additional ways to prevent in-session fainting and vasovagal symptoms.

In developing and conducting its plans, the BTRU seeks extensive engagement with donors, NHSBT staff and leaders, and the academic transfusion medicine community. For example, we value and actively seek input from donors, patients, and other lay people who serve on various advisory committees that help shape the goals and activities of the BTRU. In close partnership with the NHSBT communications and external affairs teams, we are engaging with the public and donor community to raise awareness of our work. We host a regular scientific seminar series on donor health, open to all NHSBT staff, that has already featured several world-leading authorities as speakers, including those from Canada, Denmark, the Netherlands, and the USA.

In summary, we are excited that the establishment of the BTRU in Donor Health and Genomics has opened major new opportunities for fundamental and applied research with the potential to improve NHSBT and other blood services.

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## Demand for O D Negative Red Cells – How the Patient Blood Management Teams are Supporting the Challenge



### Background

Total red blood cell (RBC) usage is falling due to improved surgical techniques and the implementation of patient blood management (PBM) initiatives, including the use of alternatives to transfusion. However, O D Negative RBC usage remains constant, and in some regions, it is actually increasing. Stability of supply for universal components such as O D negative RBC remains a challenge for most blood services around the world and NHS Blood and Transplant (NHSBT) is working hard to ensure components are available when required. Approximately 8%<sup>1</sup> of the UK population is O D Negative, but current average demand is greater than 13% which means that focused effort is required for NHSBT to maintain stocks to meet demand.

The NHSBT PBM, service delivery and clinical teams have promoted appropriate use of O D negative RBC and reduction of wastage through a number of targeted initiatives. However, recent national and regional audit reports have indicated that in some areas practice is poor and further work is required to improve hospital stock management and to reduce inappropriate use if supply is to be sustained. Also in response, NHSBT has implemented initiatives to reduce the number of substitutions of other blood groups with O D negative RBC. Progress has been made in some areas, such as improved management of Ro units.

More effort is still needed – a collaborative approach between the National O D Negative Working Group, NHSBT and the hospitals is required.

### Actions Underway by the National O D Negative Working Group and NHSBT

Reducing O D Neg issues is now a key priority for NHSBT.

**Campaign:** The launch of a new National Campaign to encourage hospital staff to make a difference and **“Save One O D Neg a Week”**. Trusts are asked to identify “OD Neg Champions” and focus on making every O D Negative unit count.



**Resources:** O D Negative resources and the “OD Neg Toolkit”, provided by the O D negative Working Group and PBM Team are accessible via the Hospitals and Science website: [hospital.blood.co.uk](http://hospital.blood.co.uk)

Resources include the following:

- OD Negative presentation.
- OD Negative audit/survey results and recommendations.
- OD Negative infographics.
- Blood Stocks Management Scheme tools.
- OD Negative Factsheet.
- “Top Tips” for use of satellite fridges.
- Campaign information.
- National Blood Transfusion Committee Recommendations for Appropriate Use of O D Negative RBC.

**Donor Recruitment:** At NHSBT we have been taking a number of actions to pro-actively recruit new donors and to maintain and retain existing donors particularly of blood group O D Negative. Information is given to newly registered donors telling them how important certain blood groups are and what they are used for. New recruitment marketing initiatives have been created which provide newly registered donors with their blood group at the point of registration. This process is called “Know Your Type”. We are also making significant investment in our donor marketing websites and planning processes.

**Guidelines:** NHSBT clinicians are leading the development of new British Committee for Standards in Haematology guidelines on the clinical use of O D Negative RBC. These will be available early 2017.

**Substitutions:** Work is taking place within the NHSBT supply chain to define how the organisation can improve the supply of blood for patients with sickle cell disease. 70% of these patients have the Rh phenotype Ro and most require regular transfusions. Currently only approximately 45% of the 2000 units requested for these patients each month are fulfilled with Ro red cells, the rest being substituted with O D Negative. We are working towards recruiting and retaining more Ro donors and ensuring that units of blood are in the right location at the right time to maximise use for Ro patients.

### **Actions for Hospitals**

- Actively promote the “Save One O D Neg a Week” campaign within their Trust and reduce demand for this precious component.
- To identify an “OD Neg Champion” (primary target: laboratory staff) to focus on making every O D Negative unit count.
- Collect and monitor data on wastage of O D negative units.
- Collect and monitor data about why O D Negative units are issued to non-O D Negative patients.
- Review amount of stock held – can it be reduced?
- Educate relevant healthcare staff on the issues/challenges around O D Negative red cells so that they understand how important it is to preserve supply and avoid wastage.
- Download and use the educational resources supplied by NHSBT PBM teams to promote appropriate use.
- Feedback progress to the Hospital Transfusion Committees, Regional Transfusion Committees and NHSBT.
- Link with the regional NHSBT PBM Practitioner for help and support.



### **Conclusion**

Whilst many hospitals have already worked hard to manage O D Negative RBC and to reduce stock levels, inappropriate use and wastage, successive audits and surveys show that further work is required. NHSBT and the National O D Negative Working Group are committed to supporting hospitals to ensure improvements are seen and that there is a sustainable supply of O D negative RBC in the future for those patients for whom there is no alternative blood component.

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### **Reference:**

<sup>1</sup>Blood Group Distribution Survey – Blood Stocks Management Scheme 2009

[www.bloodstocks.co.uk/usefulresources/bloodgroupdistribution/index.asp](http://www.bloodstocks.co.uk/usefulresources/bloodgroupdistribution/index.asp)

# 'Extending the Gift?': Donor Perspectives on Laboratory Grown Red Blood Cells

## Introduction

While previous research has explored blood donor views and experiences of donation, little is known about what donors might think about culturing and scaling up production of donated red blood cells (RBCs) and whether, for example, they see this as an extension of the donor 'gift'. We are conducting a small qualitative study in collaboration with the Bristol Blood and Transplant Research Unit (BTRU) to investigate public and patient views of cultured red blood cells (cRBCs). This article reports the preliminary analysis of two focus group discussions with blood donors.

## Methods

We have conducted seven focus groups: Two with people affected by blood disorders (and one interview), two with members of the public, one with mothers of young babies and two with blood donors. These donors (n=12) were recruited by NHSBT staff at donation sessions and by telephone.

Most of the donors were aged over 50 (n=9), with three between 18-24. There were five men and seven women. All identified as White. Three had been involved in other aspects of blood services, in other words the INTERVAL study, platelet or umbilical cord blood donor, or professionally; so more research would be needed to get a wider representation of the donor population. Some participants in our other focus groups were also found to be blood donors but this data is not reported here.

## Results

### What Donors Think About Blood Donation

The donors agreed that blood donation is 'essential' to the NHS because, in a donor's words, an "ocean" of blood is needed; they saw blood as a valuable resource, 'every drop counts', and showed concern that not enough people (particularly from some ethnic groups) were being recruited to keep up with demand. However, they were against recruiting more donors by paying for blood. While advocating that everybody who is medically able to, should donate, they proposed that paying for blood would recruit the 'wrong type of donor', for example drug addicts who need money for drugs and had a greater risk of passing on diseases. The donors gave a variety of reasons for donating, not all of which were altruistic; for example, some saw it as payback for NHS treatment and others liked the feeling of being a good person that it gave them.

### What Donors Think About the Existing Arrangements for Collection and Distribution of Blood

The donors expressed trust in the NHS organisations running the UK blood donation services; for example, that their donations would not be wasted if possible or that they were disposed of appropriately (rather than sold on, in what a participant called a 'red market'). They also articulated trust that the donation was collected safely and properly screened and cross-matched; which they proposed meant that both donors and recipients are protected from contamination, recipients are not exposed to allergic reactions and that donors had a free health check. However, donors testified that collection services could be advertised and run more effectively; for example, so that donors are not turned away because of insufficient capacity to accept more donations.

### What Donors Think About cRBCs

Despite a lack of knowledge among them about the development of this technology, there was a consensus that in principle the growing of RBCs in the laboratory is a good idea for people with blood disorders and rare blood groups, because of perceived blood shortages particularly for these groups. Some also proposed that cRBCs could fill the gap in general blood supplies. Conversely, participants expressed concerns about the cost, quality control, replication mistakes, scaling up of production, contamination of cRBCs, becoming reliant on this source and fears that inaccurate media reports could persuade some donors that they were no longer needed.

The NHS was identified as being the trusted manufacturer of cRBCs and there were several concerns about the involvement of commercial companies in producing RBCs, in other words unethical research conduct and putting the maximisation of profits before patient safety and access to treatment. However, participants conceded that pharma can provide financial resources for research and expertise.

The donors conceptualised cRBCs as being different to non-cultured RBCs in various ways: more sterile; kosher; genetically modified to include beneficial elements; lacking in elements that non-cultured blood has. However, there were also concerns that there might be negative components/contaminants in cRBCs that scientists are currently unaware of, particularly from stem cells. Some donors also perceived cRBCs as not coming from a person, which they proposed could be a positive feature for some people and negative for others.

## Conclusion

The focus groups highlighted donor trust in NHS blood services and this extended to NHS manufacture of RBCs. This contrasted with concerns about non-NHS blood services, in other words commercial and non-UK; this is consistent with other social research on blood donation.

The donors conceptualised cRBCs as different from non-cultured blood in a variety of ways, some positive and some negative. These donors had not received information about cRBCs but had some awareness of stem cell technologies and the ethical sensitivities relating to use of embryonic (and fetal) stem cells. They showed concern that some donors could be dissuaded from donating if they wrongly understood their donations to be no longer needed; perhaps from inaccurate media reports. Also, despite initial positivity about the development of this technology, they articulated numerous concerns about the cost, availability and safety of cRBCs. Some had confidence that the technology would be carefully tested and regulated if delivered by the NHS.

As for 'extending the gift', while they did not use this phrase, donors reported that they would be happy for their blood to be used to grow RBCs, and several were

enthusiastic about the possibility of their RBCs being immortalised in cell lines; some saw this as validation of the quality of their donation. However, this could lead to a hierarchy of donors, with some feeling rejected and this could threaten their donor identity. This in turn could have a negative effect on the recruitment and retention of donors, the availability of donated blood and damage social relations between public, donors and blood collection services.

So while there is cautious optimism about the development of these technologies among the participants, donors in general may have concerns that need to be addressed if cRBCs are to be socially acceptable and trusted in the same way as non-cultured donated blood, collected and distributed by the NHS, currently is in the UK.

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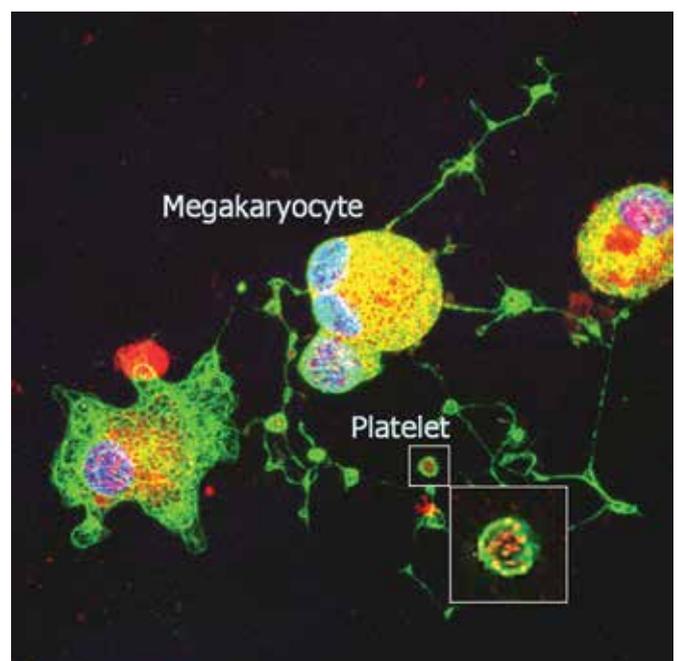
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## First Steps in Process for the Manufacture of Stem Cell Derived Platelets for Transfusion

<http://www.nature.com/ncomms/2016/160407/ncomms11208/full/ncomms11208.html>

Researchers from NHS Blood and Transplant and the University of Cambridge have developed an innovative method of producing megakaryocytes (the precursors of platelets) and platelets themselves from human pluripotent stem cells in the laboratory. The study, published in Nature Communications, was supported by a grant from the National Institute for Health Research and the Leukaemia and Lymphoma Society.

Platelets, whose primary function is to stop haemorrhage by forming a clot at the site of an injury to a blood vessel, are the second most abundant circulating cells in the blood stream after red blood cells (about two million in a drop) and are produced by megakaryocytes in the bone marrow.



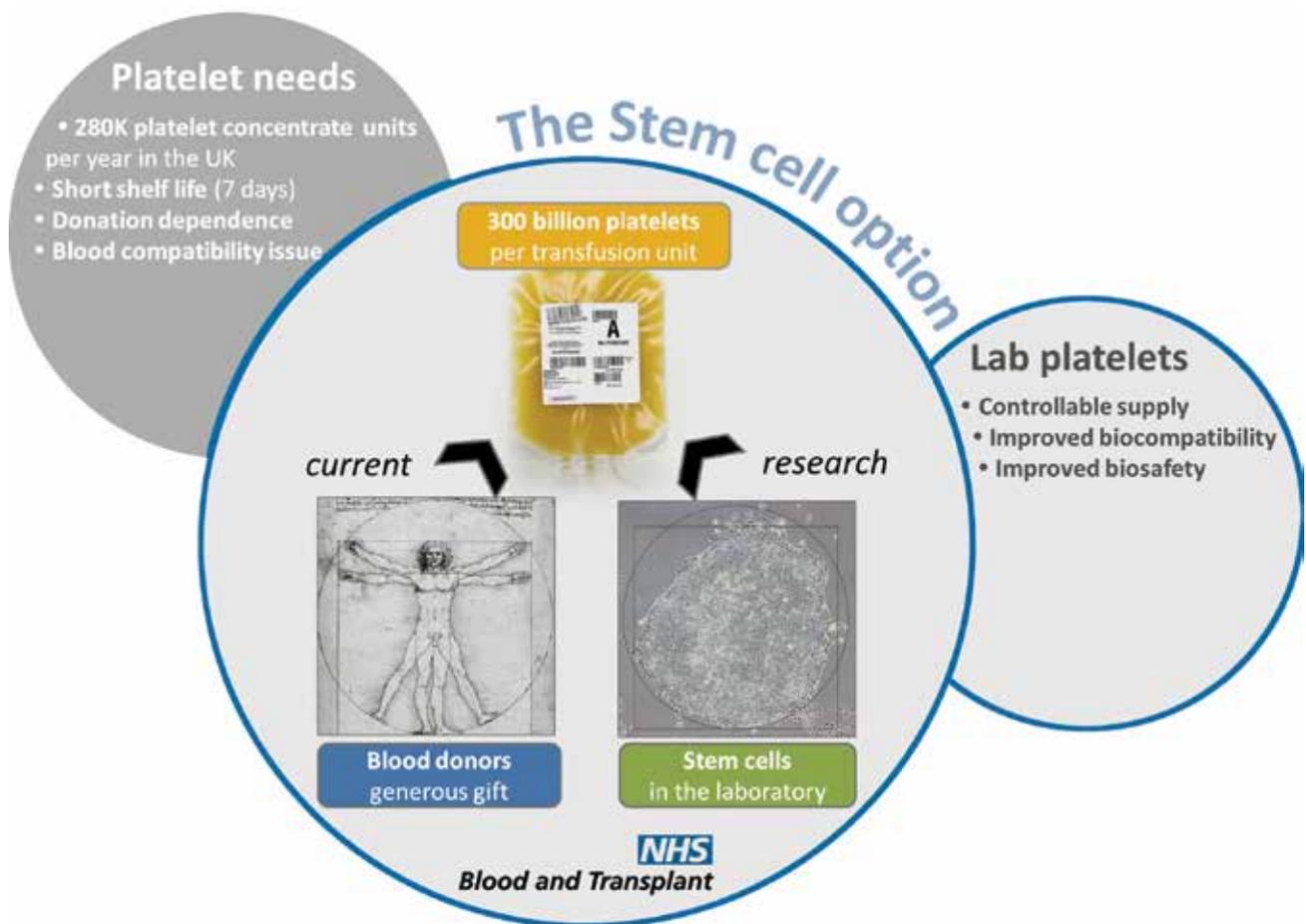
*Microscope Picture of a Megakaryocyte Releasing Platelets in Vitro*

Platelet transfusions are needed by patients with life threatening bleeding due to trauma or surgery. Regular transfusions are also needed by people who are undergoing treatment for cancer or leukaemia and by individuals with severe blood disorders who aren't able to make enough platelets in their bone marrow. Altogether, with the increase in high-dose cancer therapies, advanced surgical procedures and the ageing population 280,000 platelet units have been transfused in 2015 in the United Kingdom.

Currently, prophylactic and therapeutic bleeding treatment essentially relies on transfusion of ABO and Rhesus-D matched platelet concentrates collected from whole blood donations or specifically by apheresis. However, patients who require multiple transfusions may develop antibodies to platelets that have different tissue types – coded by the so-called HLA type-I antigens – to their own. This means that the patient's antibodies will recognise and destroy any non-compatible transfused

platelets before they have a chance to work by stopping or preventing bleeding. That is known as platelet transfusion refractoriness which is a complication for regularly transfused individuals and multiparous women who then require the special provision of HLA type-I matched platelet units sourced from a small pool of genotyped recallable donors. The platelet matching can be even more difficult when the patient is from a Black or Asian background and has a type which is underrepresented in the donor population. Altogether, the dependence on donations combined with the limited shelf life of platelet concentrates (seven days) represents a notable logistical, financial and biosafety challenge for the NHSBT and health organisations worldwide.

Making megakaryocytes and platelets in the laboratory from renewable stem cells embodies a potential revolution for the field of transfusion medicine and has been a long standing challenge.



*Illustration of the Stem Cell Option for Platelet Production for Transfusion*

Indeed, the relative inefficacy of methods developed so far has hampered the perspectives of reaching the sheer number of platelets needed to make a single unit for transfusion, in other words 300 billion platelets. In these perspectives, the Cambridge Research Team has

explored a novel strategy and found a way to “rewire” the stem cells to make them become megakaryocytes more efficiently. The team of researchers has discovered that the megakaryocyte identity could be conferred to stem cells by artificially switching on a combination of three key genes

and lead to the production of over hundred thousand pure megakaryocytes per single stem cell. In addition, while the acquisition of the megakaryocyte identity is driven cell-internally by these three genes, the cell culture requirements are minimal and more amenable to translation to clinical

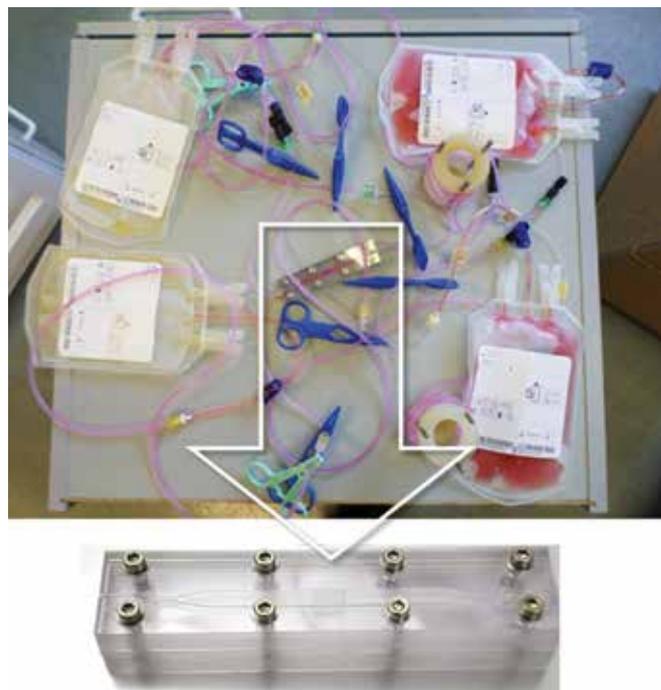


*Formation of Blood Clot including Stem Cell Platelets produced in the Laboratory (in green)*

While this research represents a critical step towards the in vitro production of platelets by allowing large scale production of the precursor cells – the megakaryocytes – with unprecedented efficiency, the next challenge is to improve the in vitro culture systems for subsequent platelet generation. Cedric Ghevaert's team is leading concurrent research on customised bio-reactors recreating the natural bone marrow environment from which platelets are released in the body. These are showing high potential for the scaling-up of platelet manufacture and combined with the megakaryocyte forward programming method could ultimately achieve the human transfusion goal for ex-vivo stem cell derived platelets.

The success of this research team in producing megakaryocytes in the laboratory has paved the way for this ultimate aim. Prospects for manufactured stem cell derived platelets are many as they could provide customised advanced transfusion products that would potentially be suitable for all patients regardless of their blood type, carry no risk of transmitting infection and could be more effective than platelets collected from blood. It will however be many years before a process for the large scale production of clinical grade platelets is developed and donated platelets, either as part of a blood donation or by dedicated platelet donation by apheresis using a machine collection process, will still be needed by patients for the foreseeable future.

processes. This breakthrough method called “forward programming” has the potential to produce several platelet transfusion units from as few as one million starting stem cells and could in the future lead to the controllable manufacturing of platelets for human transfusion.



*Pilot Scale Laboratory Bioreactor for Improved Platelet Production in the Laboratory*

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## Case Study – Noah’s Story

Noah McIntosh suffered a cardiac arrest as a baby after a rare strain of Ecoli left him fighting for his life.

He spent several gruelling months in hospital suffering multiple complications from the illness, including kidney and heart failure.



*Noah asleep in Hospital as a baby.*

The infection damaged his kidneys and he is expected to need a transplant by the time he is a teenager.

Noah received six blood transfusions and the illness inspired his mum Alice Jeans from Blandford to donate blood for the first time in 2016.

Noah became ill in October 2014 when he appeared to have a tummy bug. He was about to leave Dorchester Hospital, when he suffered a Tonic-clonic seizure (also known as a Grand Mal), a type of seizure that affects the whole brain.

Mum Alice, a gymnastics instructor, said: “I went to pick him up, and his eyes rolled to the back of his head and his arms and legs went into spasm. It was horrendous.”

Noah was taken to the Paediatric Intensive Care Unit (PICU) at Southampton General Hospital. The infection caused Noah to develop Haemolytic Uraemic Syndrome (HUS), which is the premature death of red blood cells, and he received his first blood transfusion.

His infection was diagnosed as E Coli, and in particular the 055 strain. There was a cluster of cases in Dorset during 2014 and 2015 (for example <http://www.dailymail.co.uk/news/article-2853304/Mystery-source-E-coli-outbreak-two-young-children-intensive-care-restaurant-cleared-blame.html>). Alice was in contact with Public Health England, but no definite cause was established.

While at Southampton General, Noah’s heart rate soared to more than 180 beats per minute. He was rushed back into the PICU and doctors found he had fluid on his heart.

The fluid was making his heart work harder, causing a cardiac arrest. Noah’s heart was restarted after three minutes of Cardio Pulmonary Resuscitation. The doctors had to perform surgery to drain the fluid.

After a spell in intensive care, Noah went on to a general ward, but then his condition deteriorated again.

Alice said: “He wasn’t eating, his body went blue and white.”

He was diagnosed with oedema, a build up of watery fluids in the tissue, and spent several more days in intensive care.

Noah spent in total, around three and a half to four weeks in Intensive Care over three different spells, and was only discharged from hospital on December 19th, 2014.

During his treatment, Noah, who is A positive, had further blood transfusions to deal with the haemolytic uraemic syndrome.

His kidneys are currently functioning at around 60%. He has regular check ups to see how much protein is leaking into his urine. Alice has been told he is likely to need a kidney transplant when he reaches puberty, although timings can vary.



*Noah having fun in the playground 2016*

Alice, who is engaged to Noah's dad Stewart McIntosh, an operations controller, became a blood donor for the first time on Friday, June 10, 2016.

She said: "Without people donating blood Noah wouldn't be here today. I am eternally grateful.

"There was no question about me giving blood. I thought if those other people hadn't given blood it wouldn't have been there for Noah. If I can help somebody who is in the same position, that would be special.

"It was really quick too – I thought it would take longer."

**Alice Jeans**



Noah and Mum Alice

## Impact Story 1 – Recombinant Factor VIIa for the Prevention and Treatment of Bleeding in Patients without Haemophilia (publications: 2007, 2008, 2011, 2012)

**IMPACT: The risk of side effects were highlighted over multiple updates**

An expectation of a Cochrane review is that it will be updated at regular intervals. This process of adding new trial data into existing analyses can reveal interesting patterns in outcome data that would not be observed outside of such a setting. One example of this is our review of recombinant factor VIIa for the prevention (prophylactic) and treatment (therapeutic) of bleeding in patients without haemophilia. The benefits and risks of off-label use of recombinant factor VIIa in patients without haemophilia are contested. We therefore performed a systematic review to assess the effectiveness and safety of recombinant factor VIIa. At the latest update (2012), the systematic review contained 29 trials: 16 examined the prophylactic use of recombinant factor VIIa [n = 1361 participants] and 13 trials examined the therapeutic use of recombinant factor VIIa [n = 2929 participants]. There were mixed results in terms of the benefit (mortality, blood loss, use of red blood cell transfusion) of recombinant factor VIIa when compared to placebo (placebo was the comparator arm in all but one of the 29 trials), with the exception of the risk of arterial events. This risk has increased over the three versions of the review and lead to the following conclusion in the 2012 manuscript. "The effectiveness of recombinant FVIIa as a more general haemostatic drug, either prophylactically or therapeutically, remains unproven. The results indicate increased risk of arterial events in patients receiving recombinant FVIIa. The use of recombinant FVIIa outside its current licensed indications should be restricted to clinical trials".

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## Impact Story 2 – Is Fresh Frozen Plasma Clinically Effective? (publications between 2004 and 2012)

### **IMPACT: From review to providing the evidence base for new primary research**

In 2004 we undertook a systematic review of all published randomised controlled trials that examined the clinical effectiveness of Fresh Frozen Plasma (FFP). At the time, this was the first large review of the use of this intervention and the premise for the review was the steady growth in the use of FFP in many countries over the two decades preceding 2004. By 2004, in England, the usage of FFP (adult dose units) was about 300,000 units each year. This level of usage was surprising due to doubts about the effectiveness of plasma transfusion and the well recognized complications of FFP. The original systematic review identified a real lack of quality evidence to support the efficacy of FFP use. Subsequent updates to this review (now including over 80 randomised controlled trials) have not fundamentally changed this original finding. Rather, consistent patterns have emerged from the data suggesting very limited clinical effectiveness of FFP.

The original review fed into the British Committee for Standards in Haematology guidelines for FFP use which were updated in the same time period. The original review also informed the design and successful completion of a National Comparative Audit of FFP usage which identified the breadth of clinical usage of FFP in the UK. It also informed a series of clinical studies in critical care (ISOC). The original review and subsequent updates provided the impetus for two observational studies of haemostatic testing in patients admitted to adult critical care who are not bleeding but considered to be at greater risk of bleeding due to laboratory evidence of coagulopathy (ISOC-1 and ISOC-2) and have been widely referenced in most national guidelines for FFP use.

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## Impact Story 3 – Prophylactic Platelets in Haematological Malignancy. (initially published in 2004, this Cochrane review has been updated three times and is the focus of five separate publications 2004, 2005, 2010, 2011, 2012)

### **IMPACT: From review to clinical trial**

This was our first systematic review and explored the use of platelet transfusions for the prevention of thrombocytopenic bleeding (a prophylactic transfusion). The premise for this review was, whilst the ready availability of platelet concentrates had contributed to the development of intensive treatment regimens for haematological and other malignancies and there had been considerable advances in platelet transfusion therapy over the previous 30 years, there was still much debate about the use of prophylactic platelet transfusions for the prevention of thrombocytopenic bleeding.

The original review, published in 2004, identified eight small trials with a total of 752 patients. Three trials compared the use of platelets transfused prophylactically with platelets transfused therapeutically (when bleeding occurs); two trials compared giving prophylactic platelets at different doses and three trials compared different trigger levels for the giving of a prophylactic platelet transfusion. Across all trials there were no significant differences in the number of deaths, severe bleeding events, red blood cell transfusion requirements or remission rates between the comparison groups.

The original review concluded that there was no reason to change clinical practice based on the evidence available. However, the unresolved uncertainty about the practice of prophylactic transfusion therapy prompted one of the review authors to consider what further research could be undertaken to address the question about the use of prophylactic platelets. Working with other colleagues in NHS Blood and Transplant's Clinical Trials Unit a Trial of Prophylactic platelets' [TOPPS] in haematological malignancies was developed and conducted. The trial published in the New England Journal of Medicine in 2013 randomised 600 patients: 301 received no platelet prophylaxis and 299 received platelet prophylaxis. The results supported the need for the continued use of platelet prophylaxis in patients with a haematological malignancy for reducing bleeding as compared to no prophylaxis.

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## Impact Story 4 – Stem Cells for Acute Myocardial Infarction (publications between 2008 and 2015)

### *IMPACT Reframing the Debate on (Stem) Cell Therapies for Heart Disease*

This Cochrane review was first published in 2008 and also published in the European Heart Journal (EHJ) in the same year. The second publication, in the EHJ, has now reached over 580 citations (SCOPUS index), contributed to raising the impact factor of the journal for three consecutive years, selected as one of the 'best published articles in the EHJ in 2008' and presented by invitation in one of the major clinical forums in cardiology (European Society of Cardiology conference) held in Stockholm in 2010.

Its update version in 2012 was rated one of the top five reviews in the Cochrane Library that year. The most recent version of the review (2015) identified 41 relevant RCTs (2,732 participants; 1,564 cell therapy treated versus 1,168 controls) where cell treatment were compared to no cells (placebo or control). The main findings were that cell treatment did not reduce the risk of mortality, re-infarction or re-hospitalisation for heart failure. Moreover, cell therapies had no effect on morbidity or heart function. This review is the first to use trial sequential analysis (TSA) to estimate the required information size (IS) of the relevant meta-analyses. This review was deemed underpowered to detect a relative risk reduction in mortality and re-hospitalisation for heart failure of 35% and that we would require recruiting at least 4,055 participants to draw robust conclusions about treatment effect in patients who have suffered a recent Myocardial Infarction.

The findings of this review have been taken into consideration by the Transnational Alliance for Cell-based regeneration Therapies In Cardiovascular Syndromes (TACTICS) group. This international group of experts (formed in May 2015) is reviewing cell therapy approaches for ischaemic heart disease and currently writing a series of position papers in the field.

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## Impact Story 5 – Donor Safety: Hypertension and Type II Diabetes (published in Vox Sanguinis in 2010)

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### **IMPACT: Support the Change in Blood Donation Guidelines**

To 2007, existing blood donors who developed one of two long term conditions: non-insulin dependent type 2 diabetes and treated hypertension were deemed ineligible by the UK blood services to donate blood out of concerns for any detriment to their or a potential recipient's health. Potential new donors were also not eligible to donate if they presented with either condition. However, such ineligibility to donate was considered a potential threat to the future sufficiency of the blood supply. As part of a wider project to re-evaluate which (if any) exclusion criteria for UK blood donors could be relaxed, we were commissioned in 2007 by a Specialist Advisory Group of the UK Blood Services, to conduct a systematic review on the evidence for the exclusion of donors with treated hypertension and non-insulin dependent type 2 diabetes controlled by oral hypoglycaemic drugs.

The review identified 16 relevant papers, but none directly addressed the review questions. However, all included papers that provided contributory data and the findings were consistent. No study found any evidence of increased risk to homologous (allogeneic) or autologous blood donors with treated hypertension or with raised baseline systolic blood pressure up to 200 mmHg. We found very few data relating to blood donation by diabetic subjects. This review supported changes to blood donor guidelines which were implemented by NHS Blood and Transplant in 2008.

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## CPD Questions

### Zika Virus

#### 1. Human Infections are Primarily Transmitted by:

- a) Anopheles Quadrimaculatus Mosquito.
- b) Aedes Aegypti Mosquito.
- c) Aedes Albopictus Mosquito.
- d) Aedes Aegypti Mosquito.

#### 2. In the United Kingdom (UK) the Zika Virus:

- a) Occurs naturally.
- b) Travel associated cases have been diagnosed.
- c) Cases have not been detected.
- d) Will not be a problem as human biting mosquitoes do not exist.

#### 3. Transmission by Blood Tissue, Cells and Organs:

- a) Has been proven.
- b) Cannot occur.
- c) Probable cases have been reported.
- d) Always results in symptomatic disease.

#### 4. A Tale of Three Countries

##### Organ Donation in India:

- a) Most transplants are in the Private Sector.
- b) Most transplants are in the Public Sector.
- c) Has a high deceased Organ Donation rate, when compared to the UK.
- d) Relies upon a high rate of diagnosing and confirming death, using neurological criteria.

#### 5. Organ Donation in Singapore:

- a) Has a high deceased Organ Donation rate when compared to the UK.
- b) Has pressured consent for deceased donation.
- c) Has seen sustained increase in deceased Organ Donation.
- d) Efforts are consequently focussed on engaging emergency case clinicians.

#### 6. Organ Donation in China:

- a) Still rely upon use of executed prisoner organs.
- b) Has voluntary deceased donation rates greater than the UK.
- c) Has voluntary descending donation rates less than the UK.
- d) Has deceased donation rate greater than Croatia.

#### 7. BTRU in Donor Health of Genomics:

- a) Is entirely funded by NHSBT.
- b) Is jointly funded by NHSBT and University of Cambridge.
- c) Is jointly funded by Wellcome Trust and University of Oxford.
- d) Is funded by the National Institute of Health Research Award.

#### 8.

- a) Will have completed all work with the publication of the INTERVAL Study in 2017.
- b) The INTERVAL Study was a key development that enabled the creation of this BTRU.
- c) The COMPARE Study will identify additional ways to present in-session fainting and vasovagal symptoms.
- d) The COMPARE Study will involve 50,000 whole blood donors.

#### 9. Supporting the Challenge

##### Approximately 8% of the UK population is O D Negative, current average demand is:

- a) 5%.
- b) 10%.
- c) 12%.
- d) More than 13%.

#### 10. Cultured Red Blood Cells were perceived by focus groups as:

- a) In principle a good idea.
- b) A cheap supply.
- c) Easy to scale up production.
- d) A further encouragement to donate.

**11. Manufacture of Stem Cell Derived Platelet for Transfusion:**

- a) Platelets are the third most abundant circulating cell in the blood stream.
- b) Platelets are produced by megakaryocytes circulating in the blood stream.
- c) There are about two million platelets in a drop of blood.
- d) Platelets primary function is to reduce clot formation.

**12.**

- a) Platelets in sufficient quantity for a single unit for transfusion have been achieved.
- b) Stem cells have to be 'rewired' to make them become megakaryocytes more efficiently.
- c) Efficient production of megakaryocytes from stem cells involve artificial switching on a combination of two key genes.
- d) The process of producing megakaryocytes from modified stem cells also requires substantial cell culture requirements.

**13. Impact Stories:**

**Systematic reviews and subsequent updates.**

- a) No effect upon clinical practice.
- b) Not provided useful evidence for guidelines.
- c) Always supported intervention.
- d) Provided evidence base for very primary research.

**14. Stem Cell Therapies for Heart Disease:**

- a) Systemic review have clearly supported the treatment.
- b) Systemic review have not been undertaken in this area.
- c) Systemic review have clearly shown no effect to the treatment.
- d) Systemic review was clearly underpowered to detect a relative risk reduction.

**14. Prophylactic Platelets in Haematological malignancy:**

**The first systematic review in this area**

- a) Identified scores of large trials.
- b) Involved many thousands of patients.
- c) Prompted a large clinical trial.
- d) Resulted in stopping use of platelet prophylaxis in such patients.

## Clinical Case Studies

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### Question 1

A 34 year old male with a history of mental health problems, is newly diagnosed with Thrombotic Thrombocytopenic Purpura (TTP). He is admitted to Intensive Therapy Unit (ITU) and referred for a plasma exchange.

- a) What plasma exchange protocol is recommended?
- b) He refuses treatment. How should this situation be managed?

### Question 2

A 65 year old man with a Lymphoproliferative disorder requires aortic valve surgery. He has pre-operative screening and is found to be O RhD Negative with DAT 4+ (C3d only) and a panreactive antibody, including against his own cells.

The patient's serum was further tested against I cells, i cells and his own cells at 37°C, 30°C, 20°C and 4°C with the following results:

I cells: 37°C Moderate reaction, 30°C strong reaction, 20°C strong reaction, 4°C strong reaction.

i cells: 37°C No reaction, 30°C no reaction, 20°C no reaction, 4°C weak reaction.

Own cells: 37°C weak reaction, 30°C moderate reaction, 20°C strong reaction, 4°C strong reaction.

The titration of the patient's serum using I cells performed at 20°C reached an end point of 16.

The titration of the patient's serum using i cells performed at 20°C was negative.

The titration of the patient's serum using his own cells performed at 20°C reached an end point of neat.

- a) Explain the results and their significance?
- b) What are the implications for the planned cardiac surgery and what options should be considered?
- c) What role, if any, would there be for plasma exchange?

### Answers to Clinical Cases

#### Question 1

- a) Minimum once daily plasma exchange with Octaplas or Fresh Frozen Plasma (FFP), initially 1.5 total plasma volume (TPV) for minimum three procedures, reducing to one TPV daily when stabilising and continuing until platelet count normal for at least two days. May increase to twice daily for severe or refractory cases.
- b) He requires formal assessment of capacity to consent. Under the Mental Capacity Act 2005, if a patient is assessed as not having capacity, treatment can be given without consent if deemed by the doctor to be necessary. The doctor should take into account as far as is reasonable and practicable the views of the patient's primary carer.

Note that in these cases treatment is given without consent rather than someone else consenting on behalf of the patient. Also, a court order is not required.

This patient was assessed by a psychiatrist as lacking capacity. The attending clinical team confirmed that treatment was necessary (in TTP, plasma exchange is urgently required because of the very high mortality rate in untreated cases). The case was discussed with his sister as his closest relative.

A line was placed with pre-procedure sedation as he was otherwise too agitated for a line to be placed safely. Plasma exchange proceeded after many delays. Ultimately the patient received full course of treatment and made a good recovery.

## Question 2

a) The anti-i is a cold antibody reactive only at 4°C so is not clinically significant. The anti-I is also a cold antibody, but is also moderately reactive at 37°C so clinically significant.

Anti-I is an auto-antibody associated with Cold Agglutinin Disease (CAD); there may be underlying mycoplasma infection or, as in this case, LPD.

This patient had evidence of compensated haemolysis with HB 130 and mild reticulocytosis and hyperbilirubinaemia.

b) Because I negative units are very rare, it would be difficult to find compatible units to cover surgery.

Cardiac surgery also usually involves cooling of the blood during bypass but in this case the antibody is strongly reactive at low temperatures so cooling has risk of stimulating haemolysis.

Options are:

1. Treat underlying LPD to attempt to reduce/eliminate the antibody.
2. Warm cardiac bypass and cardioplegia.
3. Provide I negative (ii) units.

c) Plasma exchange is a recognised second line treatment for patients with severe CAD and haemolytic anaemia. However, its role in preparation for surgery is not well established. There is no defined 'safe' level of antibody/agglutinin and it rebounds very quickly. There are also technical difficulties, because of red cell agglutination within the tubing.

In this case, options 1, 2 and 3 above were used but not plasma exchange.

1. The patient was treated with rituximab, which led to a reduction in the anti-I titres and the strength of reactivity at 37°C (now weak) but did not completely eliminate it.
2. The operation was undertaken using normothermic cardiopulmonary bypass and warm cardioplegia.
3. Two units of I negative (ii) red cells were supplied from the Frozen Blood Bank.

The operation was uneventful.

### **CPD Blood and Transplant Matters**

### **Answers Issue 49**

- |   |       |       |       |
|---|-------|-------|-------|
| 1. B  | 2. D  | 3. D  | 4. C  |
| 5. D  | 6. A  | 7. A  |       |
| 8. Matched pairs: AT BW; CZ DV; EX, FY & GU |       |       |       |
| 9. B  | 10. C | 11. A | 12. B |
| 13. D                                       | 14. C | 15. D |       |

# WE WOULD BE GRATEFUL IF YOU COULD COMPLETE A VERY SHORT READER QUESTIONNAIRE

The Questions Are Reproduced Below

You'll find the Questionnaire at <https://www.surveymonkey.com/r/MMJ5S3C>

Please complete by 31/03/17

## Blood & Transplant Matters Reader Questionnaire

### 1) What is your job role?

- Doctor
- Scientist
- Nurse
- Other – please state

### 2) Please specify what area you work within

- NHSBT
- NHS Trust
- Independent Organisation
- Other – please state

### 3) Please indicate your main area of interest

- Blood
- Organ Donation and Transplantation
- Tissues
- Other – please state

### 4) How would you rate Blood & Transplant Matters out of 10? (Please specify)

.....  
.....

### 5) Which sections of Blood & Transplant Matters do you prefer?

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- CPD Questionnaire
- Clinical Case Studies
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### 6) Do you read Blood and Transplant Matters?

- Fully
- Half
- Less than one third

If so why? .....

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### 7) Please indicate below how you think Blood and Transplant Matters could be improved

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- Printed Paper Copy
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### 9) Additional comments; please feel free to give further feedback below

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Thank you.

# Diary Dates

## 2017

### 01 February

#### Leadership in Transfusion

Location: Hilton Birmingham Metropole

For more information contact:

[www.bbts.org.uk](http://www.bbts.org.uk)

### 06 March

#### Manchester Blood Coagulation Course

Location: Hallmark Hotel Manchester Willowbank, Manchester

For more information contact:

[www.b-s-h.org.uk](http://www.b-s-h.org.uk)

### 10–12 March

#### FRCPATH 2 Mock Revision Course

Location: Education Centre, Kingston Hospital, London

For more information contact:

[www.b-s-h.org.uk](http://www.b-s-h.org.uk)

### 24–25 March

#### WMDA Spring Meeting

Location: Marseille France

For more information contact:

[www.wmda.info](http://www.wmda.info)

### 27–29 March

#### 57th BSH Annual Scientific Meeting

Location: Brighton

For more information contact:

[www.b-s-h.org.uk](http://www.b-s-h.org.uk)

### 4–6 May

#### Training Course on Haemopoietic Stem Cell Transplantation

Location: Saggart, Dublin, Ireland

For more information contact:

[www.esh.org/conferences/](http://www.esh.org/conferences/)

### 7 June

#### Clinical Laboratory Haemostasis 2017 UK NEQAS for Blood Coagulation Annual Scientific participants Meeting.

Location: Sheffield Hallam University, The Atrium Conference Centre, Sheffield

For more information contact:

[www.ukneqas.org.uk/](http://www.ukneqas.org.uk/)

### 14 June

#### World Blood Donor Day

For more information contact:

[www.who.int/worldblooddonorday](http://www.who.int/worldblooddonorday)

### 12 July

#### Annual SHOT Symposium

Location: Rothamsted Centre for Research and Enterprise, Harpenden, Hertfordshire

For more information contact:

[www.shotuk.org](http://www.shotuk.org)

### 8–9 September

#### ASH Meeting on Hematologic Malignancies

Location: Chicago, Fairmont Chicago, Millennium Park

For more information contact:

[www.hematology.org](http://www.hematology.org)

### 13–15 September

#### BBTS Annual Conference

Location: Glasgow

For more information contact:

[www.bbts.org.uk](http://www.bbts.org.uk)

### 16 September

#### World Marrow Donor Day

Location:

For more information contact:

[www.wmda.info](http://www.wmda.info)

### 7–10 October

#### AABB Annual Meeting

Location: San Diego, California

For more information contact:

[www.aabb.org/events](http://www.aabb.org/events)





*Blood and Transplant Matters is prepared  
and issued by NHS Blood and Transplant,  
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