ANNUAL SHOT REPORT 2020

SHOT is affiliated to the Royal College of Pathologists
This report is produced by SHOT working with MHRA

MHRA

SHOT
Serious Hazards of Transfusion

Serious Hazards of Transfusion (SHOT)

Steering Group Chair	Professor Mark Bellamy
SHOT Medical Director	Dr Shruthi Narayan
Operations Manager	Ms Courtney Spinks
	Dr Jennifer Davies
Haemovigilance Data Manager	Ms Debbi Poles
Patient Blood Management Practitioner	Mrs Emma Milser
Clinical Incidents Specialist	Mr Simon Carter-Graham
Laboratory Incidents Specialist	Mrs Victoria Tuckley
National Coordinator for	Mr Joe Flannagan
Transfusion-Transmitted Infections (Public Health England)	Mrs Tali Yawitch

Working Expert Group (WEG) & Writing Group, on behalf of the SHOT Steering Group

Chair: Dr Shruthi Narayan
Dr Peter Baker, Professor Mark Bellamy, Dr Andrew Bentley, Dr Janet Birchall, Dr Paula Bolton-Maggs, Dr Catherine Booth, Dr Su Brailsford, Mr Simon Carter-Graham, Mrs Pamela Diamond, Mr Joe Flannagan, Mrs Heather Clarke, Dr Anicee Danaee, Dr Jennifer Davies, Dr Sharran Grey, Dr Heli Harvala, Dr Sarah Haynes, Dr Anne Kelly, Dr Tom Latham, Dr Puneet Malhotra, Dr Alistair McGrann, Mrs Emma Milser, Dr Helen New, Mrs Terrie Perry, Ms Debbi Poles, Dr Catherine Ralph, Dr Fiona Regan, Mr Chris Robbie, Dr Susan Robinson, Dr Megan Rowley, Dr Joseph Sharif, Mrs Diane Sidney, Miss Charlotte Silver, Ms Courtney Spinks, Ms Tracey Tomlinson, Mrs Victoria Tuckley, Dr Alison Watt, Mrs Tali Yawitch.

Steering Group (SG) during 2020

Chair: Professor Mark Bellamy

Dr Shubha Allard	British Society for Haematology Guidelines National Blood Transfusion Committee
Dr Lynne Anderson	Scottish National Blood Transfusion Committee
Mrs Anne Lockhart	Institute of Biomedical Science
Dr Paula Bolton-Maggs	Royal College of Pathologists
Dr Su Brailsford	Public Health England
Mr Graham Donald	Lay member
Dr Heidi Doughty	British Blood Transfusion Society
Dr Ruth Gottstein	Royal College of Paediatrics and Child Health
Dr Sheila MacLennan	Joint Professional Advisory Committee
Dr Gail Miflin	UK Forum
Major Andy Miles	Defence Medical Services
Dr Ranga Mothukuri	Royal College of Emergency Medicine
Dr Susan Robinson	British Society for Haematology
Dr Felicity Plaat	Royal College of Obstetricians and Gynaecologists
Dr Krishna Ramachandran	Royal College of Anaesthetists
Dr James Reid	Royal College of Physicians
Mr Chris Robbie	Medicines and Healthcare Products Regulatory Agency
Mrs Rashmi Rook	UK Transfusion Laboratory Collaborative
Ms Mervi Jokinen	Royal College of Midwives
Ms Ruth Burey	Royal College of Nursing
Ms Nina Vinall	Expertise in Patient Safety
Mr Suman Shrestha	Royal College of Nursing
Dr Charles Percy	British Society for Haematology

Honorary Steering Group Members

Dr Hannah Cohen	Founder Member and former Steering Group Chair
Dr Dafydd Thomas	Former Steering Group Chair
Dr Lorna Williamson	Founder Member
Dr John Barbara	Founder Member
Prof John Lumley	Founder Member
Dr Brian McClelland	Founder Member
Dr Derek Norfolk	Founder Member
Dr Clare Taylor	Former SHOT Medical Director
Dr Sue Knowles	Former Interim Medical Director of SHOT
Dr Dorothy Stainsby	Former National Medical Coordinator of SHOT
Dr Elizabeth Love	Former National Medical Coordinator of SHOT

NB. All members of the WEG are members of the Steering Group in their own right.

Requests for further information should be addressed to:

Non-infectious hazards

SHOT Office
Manchester Blood Centre
Plymouth Grove
Manchester
M13 9LL

Tel +44 (0) 161 423 4208
Website www.shotuk.org
Twitter @shothv1

Enquiries shot@nhsbt.nhs.uk

Email m.c.bellamy@leeds.ac.uk
shruthi.narayan@nhsbt.nhs.uk
jeni.davies@nhsbt.nhs.uk
emma.milser@nhsbt.nhs.uk
debbi.poles@nhsbt.nhs.uk
simon.carter-graham@nhsbt.nhs.uk
victoria.tuckley@nhsbt.nhs.uk
fahim.ahmed@nhsbt.nhs.uk

Infectious hazards

Tali Yawitch
Scientist (Epidemiology)
Public Health England Epidemiology Unit/NHSBT
61 Colindale Avenue
London NW9 5EQ

Tel +44 (0)20 8327 7602
Email tali.yawitch@phe.gov.uk

Disclaimer: The information in Annual SHOT Report case studies is provided to SHOT by reporters. All reports are anonymised, and SHOT relies on reporters submitting correct and accurate information. SHOT does not accept responsibility for any inaccuracies which may arise from incorrect information being submitted.

Copyright notice

Please cite this work as:

S Narayan (Ed) D Poles et al. on behalf of the Serious Hazards of Transfusion (SHOT) Steering Group. The 2020 Annual SHOT Report (2021).

This work was undertaken by SHOT. The work was funded by NHS Blood and Transplant, Northern Ireland Blood Transfusion Service, Scottish National Blood Transfusion Service and the Welsh Blood Service through the UK Forum.

Published July 2021

ISBN 978-1-9995968-3-5

Illustrations by Jenny Leonard https://jennyleonardart.com/
Design, vector illustration & production of the report by ARC www.e-arc.co.uk
Printed on paper from responsible sources.

print & plant

A collaborative initiative to restore forests around the globe.
For more information please visit: www.e-arc.co.uk/environment

Contents

Please see the beginning of each chapter for a glossary of abbreviations used

1 Foreword

At the time of writing, we are emerging from another period of COVID-19 lockdown and stringent societal restrictions. The vaccination program is well advanced, and so there is a sense of hope that we may well now be passed the worst, and able to return to some form of 'normality'. Whether this will be the case, or whether we are simply in the precursor phase of further waves and surges of the pandemic, is not yet clear. Certainly, the spectres of waning immunity and new viral variants mean that while we can have hope, we cannot have confidence in the future.

The death toll from COVID-19 has been severe, but the NHS has survived. It has survived though at a great cost. Much work delivering 'routine' healthcare has been set aside. And for those patients, their needs were not 'routine'; many have conditions which have progressed, tragically, in some cases, beyond effective treatment. Healthcare workers are exhausted, and many plan to leave their profession. We now face years of backlog. The pressures on the NHS are different now to those at the height of the pandemic, but they are not less. In many ways, they are far greater.

However, we are in a very different position now should we have to face a further wave, another surge, of COVID-19 infection, compared with a year ago. We have learned a huge amount about COVID-19 as a disease, and even more about how to manage a pandemic, both in society and in the health services. Much of what we have learned will outlast the pandemic and has wider applicability. For example, new needs have accelerated the development of technologies and skills and catapulted us into better and more agile practices. This has been particularly true in haemovigilance. Several members of the SHOT Steering Group have shared their personal reflections with me; there are many similarities and common experiences.

The most obvious among these is that meetings, teaching and training, and debriefing after errors, incidents and near misses, can be done very effectively by electronic means. Small group videoconferences have proved extremely effective at disseminating learning points and promoting inclusivity and have meant that the 'reach' of these activities is much greater. They can be more targeted and structured in a more bespoke way. Delivered in small groups, their impact has likely also improved.

But unto each yin, its yang: beside these positives, there have been some recurring negatives. Among these is the observation that the incidents reported to SHOT through the pandemic have been remarkably similar to those reported in previous years. This calls into question the effectiveness with which learning is disseminated to, and retained by, the healthcare teams at the sharp end of transfusion. One lay commentator has suggested that every healthcare organisation should have a senior person to act as a transfusion champion. Observing that healthcare professionals have 'extremely hierarchical structures', the commentator suggested that to be effective, the champion would need to be at the apex of the pyramid. It has also been suggested that the thrust of safety efforts should target those which continue to cause greatest harm, in particular, transfusion-associated circulatory overload. There are golden opportunities here for the wider implementation of information technology in transfusion prescribing, and the use of decision aids.

It seems unlikely that society will ever be quite the same again; nor will healthcare. The opportunities for using change to advance transfusion safety are plain to see. Let us seize the moment.

Professor Mark Bellamy, Past President, Intensive Care Society; Professor of Critical Care, The Leeds Teaching Hospitals NHS Trust, and Chair of the SHOT Steering Group.

2 Participation in United Kingdom (UK) Haemovigilance

Authors: Debbi Poles and Chris Robbie

Key SHOT messages

- Complete and accurate reporting to SHOT and the MHRA is essential to ensure good quality haemovigilance
- Approximately 7% of reports were submitted under an incorrect category and required re-submission under a different category, which indicates that further guidance and clarification are needed
- Reporters are encouraged to review their participation benchmarking data on an annual basis, to ensure all appropriate reporting is captured

Abbreviations used in this chapter

ADU	Avoidable, delayed and under/overtransfusion	**MHRA**	Medicines and Healthcare products Regulatory Agency
ANTID	Anti-D immunoglobulin errors	**NHS**	National Health Service
BSQR	Blood Safety and Quality Regulations	**NM**	Near miss
CCP	COVID-19 convalescent plasma	**RBRP**	Right blood right patient
FFP	Fresh frozen plasma	**SABRE**	Serious adverse blood reactions and events
IBCT-SRNM	Incorrect blood component transfused-specific requirements not met	**SD**	Solvent detergent-treated
MB	Methylene-blue treated	**UK**	United Kingdom

Introduction

In the calendar year 2020, a total of 4063 reports were received by SHOT. It is encouraging to see that haemovigilance reporting has continued throughout a very difficult year. Reporting numbers only dipped slightly, with 185 fewer reports received compared to 2019 (n=4248), 4.4% less.

Whilst there was a small drop in submitted cases during the most pressured months of the pandemic, there has not been a dramatic reduction in reporting during this time which is a testament to our dedicated reporters. December 2020 saw a large increase in submitted reports, and this is likely due to a backlog of reports being submitted before the end of the reporting year.

The date a report is submitted is not always within the same month that the event occurred, Figure 2.1 compares the number of reports submitted in each month, with the number of reports that actually occurred in that month. This shows that there were fewer incidents that took place during April 2020 which was at the height of the first wave of the pandemic. This is plotted against the number of components issued during each month, which also dipped dramatically during April 2020. The number of incidents by date of event appears to follow the pattern of issue data in general.

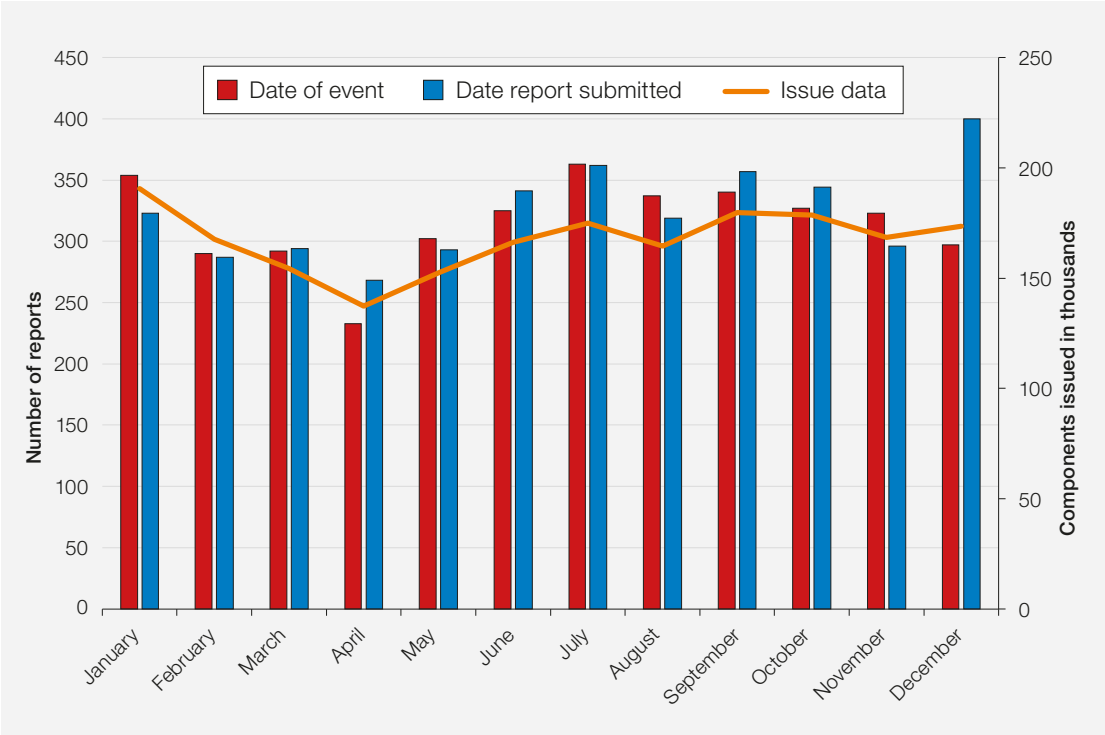


Figure 2.1: SHOT reporting by month during 2020

Not all reports submitted are SHOT-reportable or are included in the analysis for this Annual SHOT Report. Figure 2.2 details the fate of all submitted reports during 2020. Of the 735 withdrawn reports, 110 were submitted from the four Blood Services, which are MHRA-reportable only. Any patient impact that resulted from an error in the Blood Service would be reported to SHOT by the hospital concerned. The remaining withdrawn cases are those that were either reported in error or were determined to be not SHOT-reportable. Some of these would still have been included by the MHRA as they would be reportable under the BSQR. The 395 incomplete reports are those that were awaiting completion by the reporters at the time the 2020 data were downloaded. Reasons for non-completion could be that they are awaiting the outcome of investigations or were reported later in the year. Once complete, these reports will be reviewed for inclusion in the 2021 Annual SHOT Report. Reports relating to anti-D immunisation are counted separately, as they form part of a separate study, and are not within the usual SHOT reporting categories.

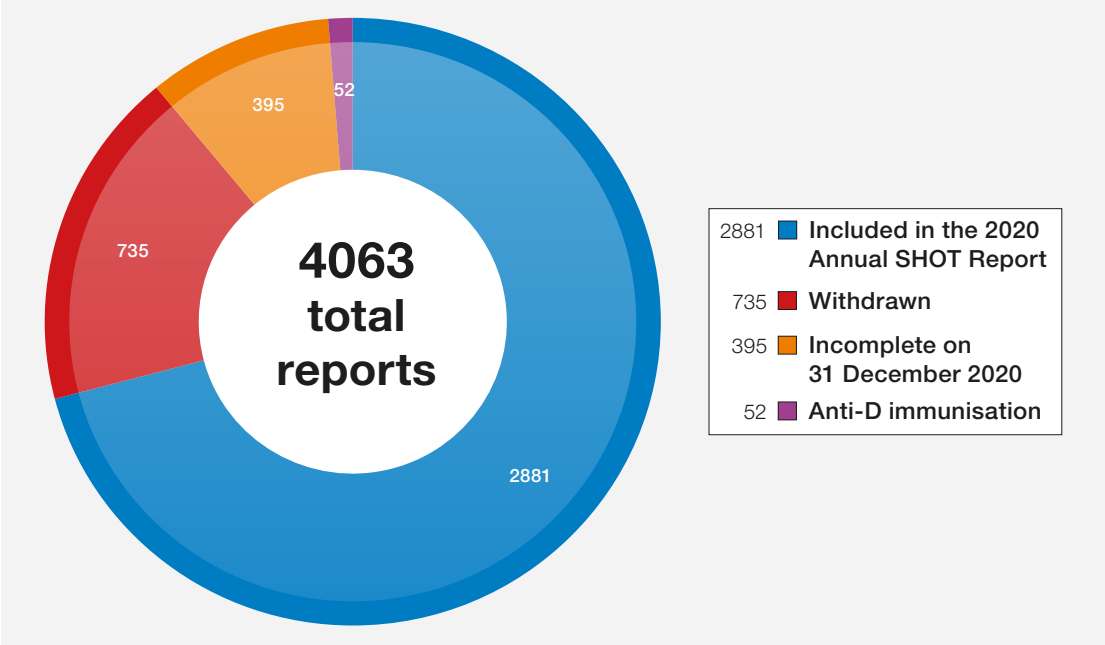


Figure 2.2: Status of reports submitted to SHOT in the calendar year 2020

Reporting organisations in 2020

All but two UK NHS Trusts/Health Boards submitted reports during 2020. Both these were specialist centres and possibly low users of blood components.

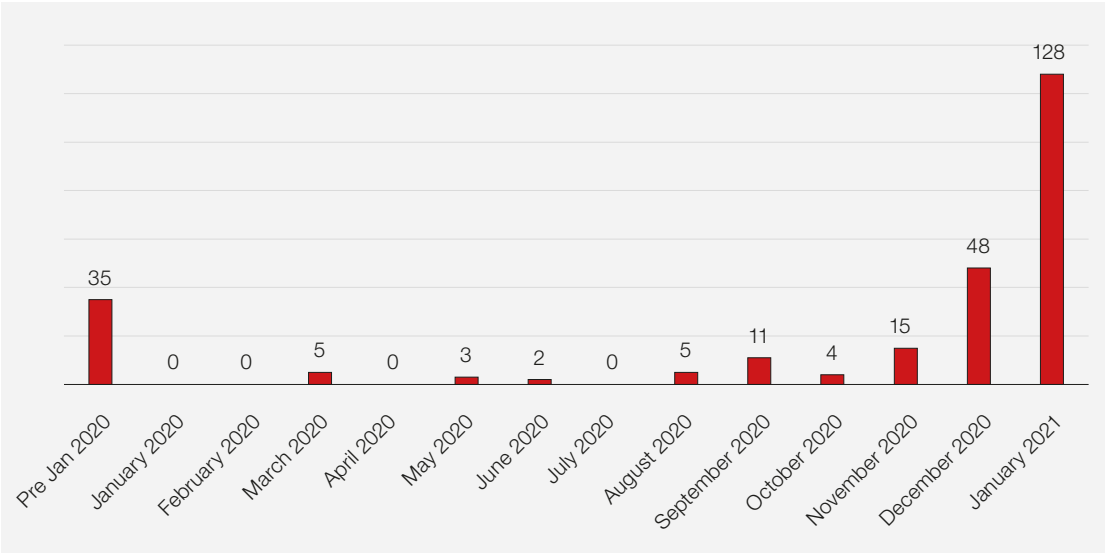
There were 15 non-NHS organisations that submitted reports in 2020, down from 26 that submitted reports during 2019. Analysis of the last 10 years of non-NHS reporting shows a downward trend since 2011 (75 reports), with 2020 seeing the lowest number of reports (22). This reduction could be due to the impact of the pandemic on private healthcare practices.

Figure 2.3: Ten years of reporting by non-NHS organisations 2011-2020

Analysis from SABRE

Figure 2.4 demonstrates excellent participation in the SHOT/SABRE haemovigilance schemes with most reporters reporting at least once within the previous few months. There are a small number of reporters who report less frequently. Most of those who have not reported at least once in the past 12 months are facilities without a transfusion laboratory or small NHS or private laboratories.

Figure 2.4: The last time a report was received on SABRE from an active SABRE account



SABRE participation data reflects accounts rather than Trusts/Health Boards whilst for SHOT, the individual accounts are amalgamated into the appropriate Trusts/Health Boards.

Blood component issue data 2020

Table 2.1 lists the total number of blood components issued from the UK Blood Services in 2020 and excludes CCP.

	Red cells	Platelets	FFP	SD-FFP	MB-FFP	Cryo	Totals
NHS Blood and Transplant	1,286,287	230,792	145,101	61,069	5,705	36,414	**1,765,368**
Northern Ireland Blood Transfusion Service	36,821	7,280	2,822	630	390	794	**48,737**
Scottish National Blood Transfusion Service	126,093	21,653	13,196	3,040	374	2,651	**167,007**
Welsh Blood Service	74,494	9,046	6,758	2,730	-	377	**93,405**
Totals	**1,523,695**	**268,771**	**167,877**	**67,469**	**6,469**	**40,236**	**2,074,517**

FFP=fresh frozen plasma; SD=solvent detergent-sterilised; MB=methylene blue-treated; Cryo=cryoprecipitate

SD-FFP data supplied by Octapharma

Paediatric/neonatal MB-FFP are expressed as single units; cryoprecipitate numbers are expressed as pools and single donations as issued; all other components are adult equivalent doses

Table 2.1: Total issues of blood components from the Blood Services of the UK in the calendar year 2020 (excluding CCP)

SHOT reporting by UK country

Figure 2.5 shows the total number of components issued and the number of reports analysed and included in the 2020 Annual SHOT Report per 10,000 components issued across all four UK countries.

The distribution of the number of submitted reports is proportionate to the number of components issued. This year the number of submitted reports that have been analysed and included in this SHOT Report are shown, this number excludes data relating to COVID-19 convalescent plasma (CCP).

The full table containing the breakdown of data from 2020 and previous years can be found in the supplementary information on the SHOT website (https://www.shotuk.org/shot-reports/report-summaryand-supplement-2020/).

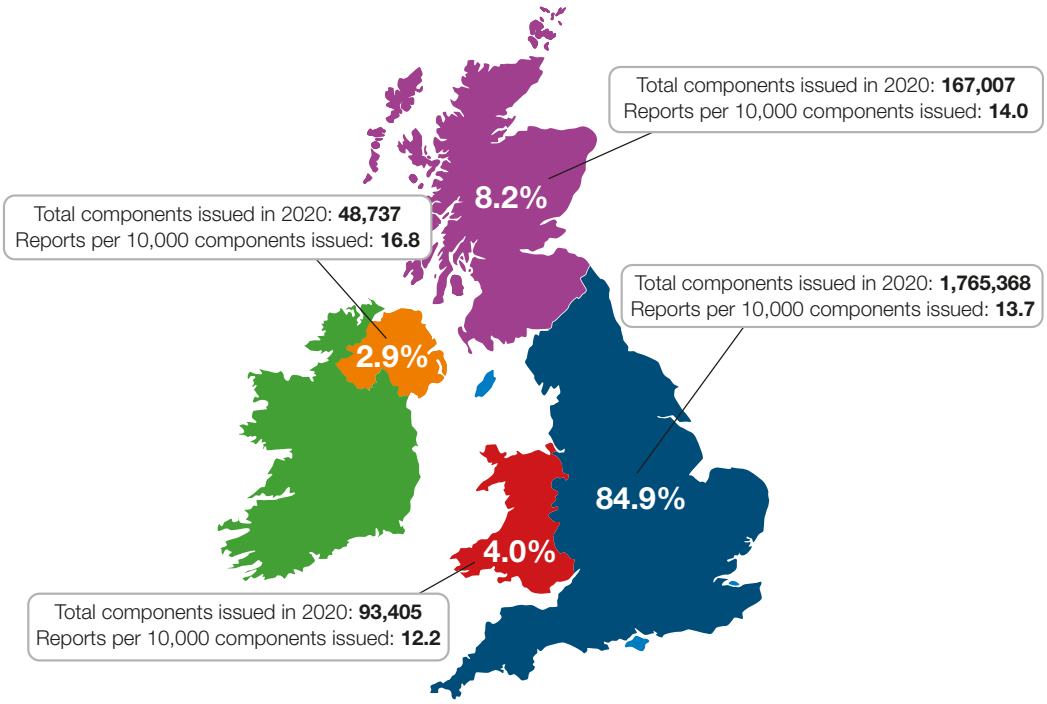


Figure 2.5: Percentage of SHOT reports analysed by UK country (excluding CCP)

Cases included in the 2020 Annual SHOT Report n=3214

The total number of reports analysed and included in the 2020 Annual SHOT Report is 3214. This is a

decrease of 183 from the 3397 reports analysed in the 2019 Annual SHOT Report (Narayan et al. 2020). This includes 29 cases relating to CCP.

In addition to these 3214 reports, there were 61 reports of immunisation against the D-antigen (9 of these were submitted in 2019 but finalised in 2020). These are counted separately as part of a specific stand-alone study.

The total number of 3214 is made up of the 2881 completed reports submitted in 2020 (Figure 2.2) plus 333 reports that were submitted in earlier years, but not finalised until 2020.

The number of reports with potential for patient harm (excluding 'near miss' and 'right blood right patient') is 1877, a slight increase from 2019 (n=1867).

Categorisation of incidents

Every year many cases are moved from the initial category to a more appropriate one by the SHOT Incident Specialists. In 2020, there were 269 transfers between categories in total, which is approximately 7% of all cases submitted to SHOT annually. This is shown in table 2.2 below.

Table 2.2: Number of reports transferred between SHOT reporting categories in 2020

		Transferred to category												
		ADU	ANTID	FAHR	HSE	HTR	NM	RBRP	IBCT-SRNM	TACO	TAD	UCT	IBCT-WCT	Total
Original Category	ADU		3	-	14	1	7	1	-	1	-	-	3	**30**
	ANTID	-		-	-	-	4	-	-	-	-	-	-	**4**
	FAHR	-	-		3	4	-	-	-	2	3	3	-	**15**
	HSE	6	1	-		-	4	8	8	-	-	-	-	**27**
	HTR	-	-	2	-		-	-	1	1	-	-	-	**4**
	NM	12	29	-	3	-		6	9	-	-	-	2	**61**
	PTP	-	-	1	-	-	-	-	-	-	-	-	-	**1**
	RBRP	8	1	-	16	-	10		21	-	-	-	5	**61**
	IBCT-SRNM	1	-	1	1	3	4	4		-	-	-	13	**27**
	TACO	1	-	2	-	-	1	-	-		12	1	-	**17**
	TRALI	-	-	2	-	-	-	-	-	2	5	-	-	**9**
	TTI	-	-	5	-	-	-	-	-	-	-	-	-	**5**
	UCT	-	-	-	-	-	-	-	-	1	-		-	**1**
	IBCT-WCT	1	-	-	1	-	-	1	3	-	-	1		**7**
	Total	**29**	**34**	**13**	**38**	**8**	**30**	**20**	**42**	**7**	**20**	**5**	**23**	**269**

ADU=avoidable, delayed or under/overtransfusion; ANTID=anti-D immunoglobulin; FAHR=febrile, allergic and hypotensive reactions; HSE=handling and storage errors; HTR=haemolytic transfusion reactions; NM=near miss ; RBRP=right blood right patient; IBCT-SRNM=incorrect blood component transfused-specific requirements not met; TACO=transfusion-associated circulatory overload; TAD=transfusion-associated dyspnoea; UCT=uncommon complications of transfusion; IBCT-WCT=IBCT-wrong component transfused

The numbers highlighted in pink are explained further in the paragraph below

The categories that saw the most transfers out to other categories were NM and RBRP (both 61/269, 22.7%), and ADU (30/269, 11.2%). The categories that received the most transfers were IBCT-SRNM (42/269, 15.6%), HSE (38/269, 14.1%) and ANTID (34/269, 12.6%).

The largest number of transfers between a single category was from NM to ANTID (29/269, 10.8%), and RBRP to IBCT-SRNM (21/269, 7.8%). There may be a need for more guidance for reporting in these categories.

Categorisation of incidents can be complex, and not every situation nicely fits a specific set of circumstances. For more help on categorising incidents, please see the latest SHOT reporting definitions document on the SHOT website (see the recommended resources at the end of this chapter), or alternatively contact the SHOT office for advice. We are always happy to help with the appropriate categorisation of an incident.

Analysis of errors by location

The number of incidents reported from the emergency department is the same as in 2019, however the proportion of total reports has increased slightly, so is still on an upward trend overall. The numbers of reports from theatres are higher for 2020, but overall percentage of total reports remains quite consistent with previous years. The number of reports from general wards, and adult critical care have also both increased during 2020, although for both these areas, the trend is downwards since this data has been analysed from 2010.

Unfortunately, there are no denominator data available with regard to the number of transfusions undertaken in each of these areas.

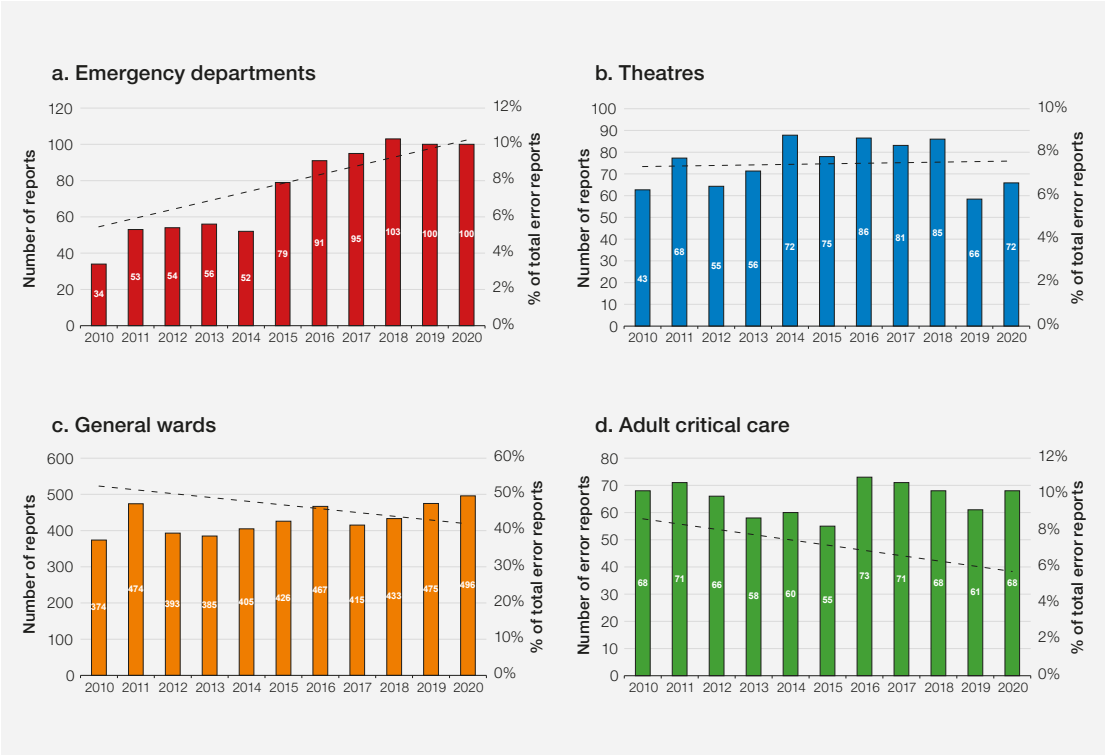


Figure 2.6: Trend of error reports from different departments

SHOT participation benchmarking data

SHOT participation data provides a useful benchmarking tool which is an integral part of continuous improvement in healthcare. Measuring, comparing to similar users, and identifying opportunities for tangible improvements will help improve patient safety. This supports local governance processes as well. Figure 2.7 illustrates how the SHOT participation data can be used to benchmark and drive local improvements in practices.

Data are collated and published annually in the autumn, and the 2020 participation data will be available on the SHOT website during October 2021.

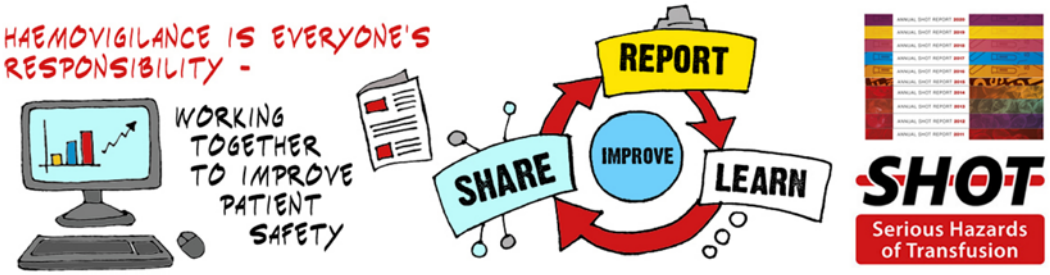
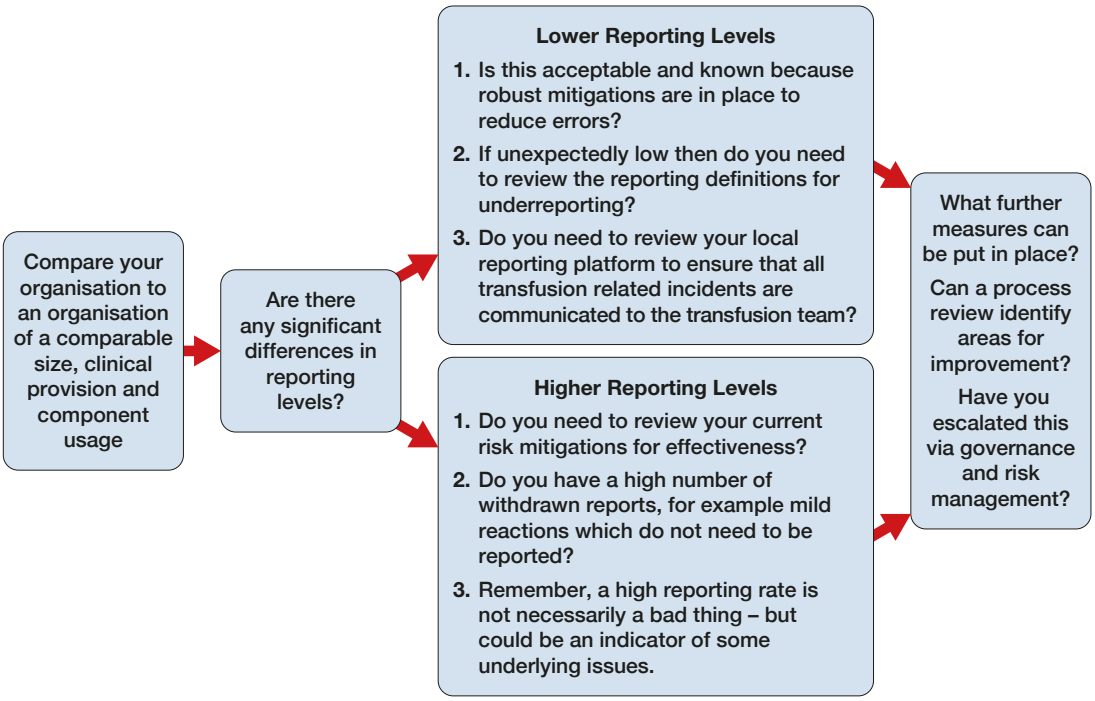


Figure 2.7: Using SHOT participation benchmarking data to drive improvements



All reporters and local governance teams should access and use this participation data to inform local improvements. These discussions should be included in local and regional transfusion meetings.

Conclusion

Participation in UK haemovigilance remains high and has continued throughout the year despite the challenging circumstances of the COVID-19 pandemic.

Reports were submitted from all but two NHS Trusts/Health Boards, however, reporting appears to be reducing over the years from non-NHS organisations.

Participation data, learning points and recommendations from the Annual SHOT Report should be used to improve transfusion safety in all healthcare organisations.

Recommended resources

Definitions of current SHOT reporting categories & what to report
https://www.shotuk.org/resources/current-resources/

SHOT Participation Benchmarking Data
https://www.shotuk.org/reporting/shot-participation-benchmarking/

References

Narayan S (Ed), Poles D, et al. on behalf of the Serious Hazards of Transfusion (SHOT) Steering Group. The 2019 Annual SHOT Report (2020). https://www.shotuk.org/shot-reports/ [accessed 31 March 2021].

Headline Data: Deaths, Major Morbidity and ABO-Incompatible Transfusions

3

Authors: Shruthi Narayan and Debbi Poles

Key SHOT messages

- **Transfusion-associated circulatory overload (TACO) and transfusion delays** are the most common causes of transfusion-related deaths in the UK in 2020 and accounted for 30/39 deaths (76.9%). Some of these could have been prevented and measures must be taken to address these. Vigilant staff, effective communication and collaboration among staff and use of the TACO checklist are all vital in reducing these incidents
- **Investigations of all deaths and learning from serious events.** Incident investigations should be standard in all cases where transfusion may have contributed to the death of a patient, as it provides an opportunity for learning and improvement. An effective investigation includes review of system design and human factors revealing all contributory factors and incidental findings that can then be addressed in the corrective and preventive actions (CAPA). A SHOT guidance tool for TACO incident investigation is now available (see recommended resources)
- **Near miss** events continue to account for most reports submitted to SHOT (1130/3214, 35.2%). Reporting and investigating near misses helps identify and control risks before actual harm results, providing valuable opportunities to improve transfusion safety. Investigations into the cause of near misses will enable a more proactive approach to safety. Potential system failures and hazards can be identified and corrected before harm or injury occurs

Abbreviations used in this chapter

ABOi	ABO-incompatible	**NM**	Near miss
CAPA	Corrective and preventive action	**PAS**	Platelet additive solution
FAHR	Febrile, allergic and hypotensive reactions	**PCC**	Prothrombin complex concentrate
FFP	Fresh frozen plasma	**RCA**	Root cause analysis
Hb	Haemoglobin	**SRNM**	Specific requirements not met
HSCT	Haemopoietic stem cell transplant	**TACO**	Transfusion-associated circulatory overload
IBCT	Incorrect blood component transfused	**UK**	United Kingdom
LIMS	Laboratory information management system	**WBIT**	Wrong blood in tube
NHS	National Health Service	**WCT**	Wrong component transfused

The recommendation from last year remains pertinent:

Recommendation

- National Health Service (NHS) Trusts/Health Boards must use intelligence from all patient safety data including national haemovigilance data to inform changes in healthcare systems, policies, and practices to embed the lessons learnt and truly improve patient safety

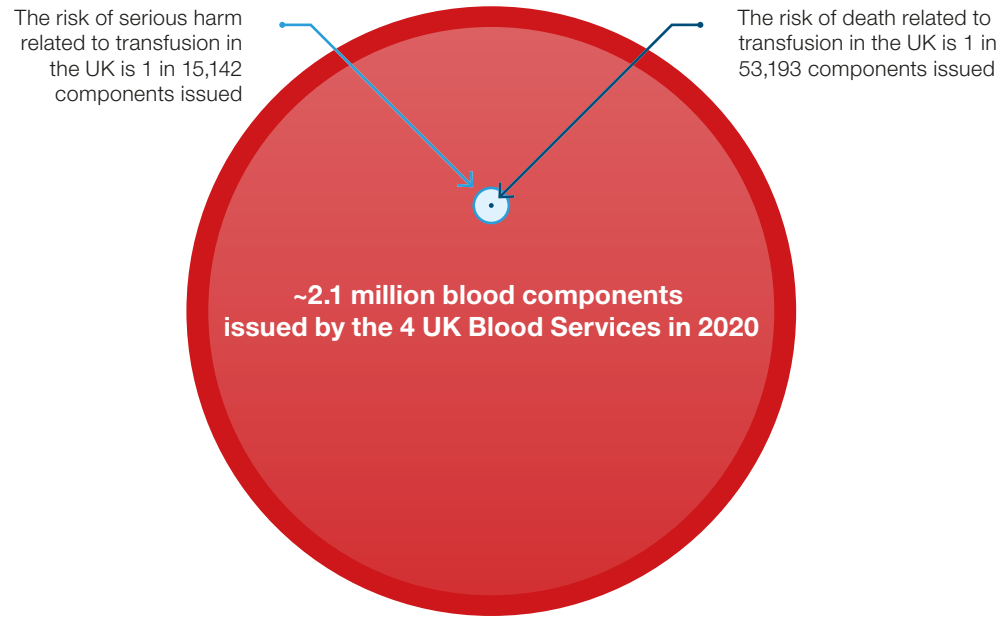
Action: Hospital chief executives and medical directors, National Blood Transfusion Committee (or the equivalent for the devolved countries), hospital transfusion teams

Introduction

Haemovigilance reporting and learning from reports submitted contribute to improving patient safety. These reports provide a mechanism to identify risks so that all healthcare organisations can implement interventions to reduce these risks. Data from SHOT provide valuable information to identify hazards and worthwhile learning opportunities. Data from 2020 show that while transfusions are generally safe in the UK, there are definite areas for concern where actions are urgently needed to improve transfusion safety, and these are elaborated further in this chapter and throughout the Annual SHOT Report.

The risk of death related to transfusion in the UK is 1 in 53,193 components issued and the risk of serious harm is 1 in 15,142 components issued (Figure 3.1).

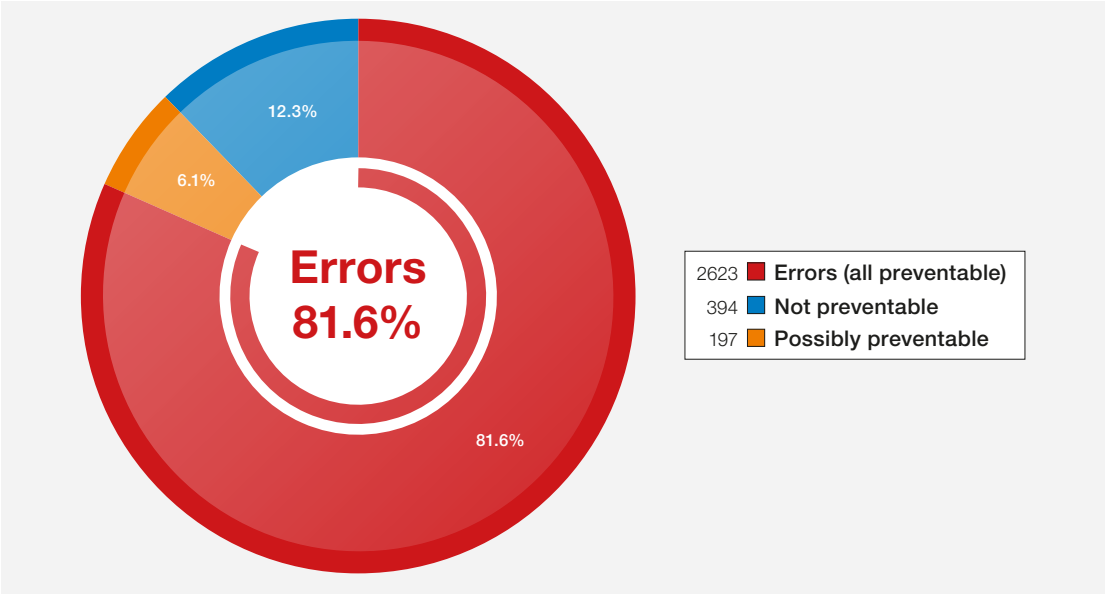
Figure 3.1: Risk of death and serious harm relating to transfusions in the UK in 2020



Note: This is a representative image and not accurate to scale

Serious adverse reactions and events related to transfusion are reported to SHOT and errors continue to account for most of the reports 2623/3214 (81.6%) (Figure 3.2).

Figure 3.2: Errors account for most reports: 2623/3214



Trends in the last few years indicate that while there is a slight downward trend, errors continue (figure 3.3). This means that sustainable systemic improvements to prevent these transfusion errors may not have been fully implemented. Data shows some improvements are being made and every effort must be made in both clinical areas and transfusion laboratories to reduce errors further.

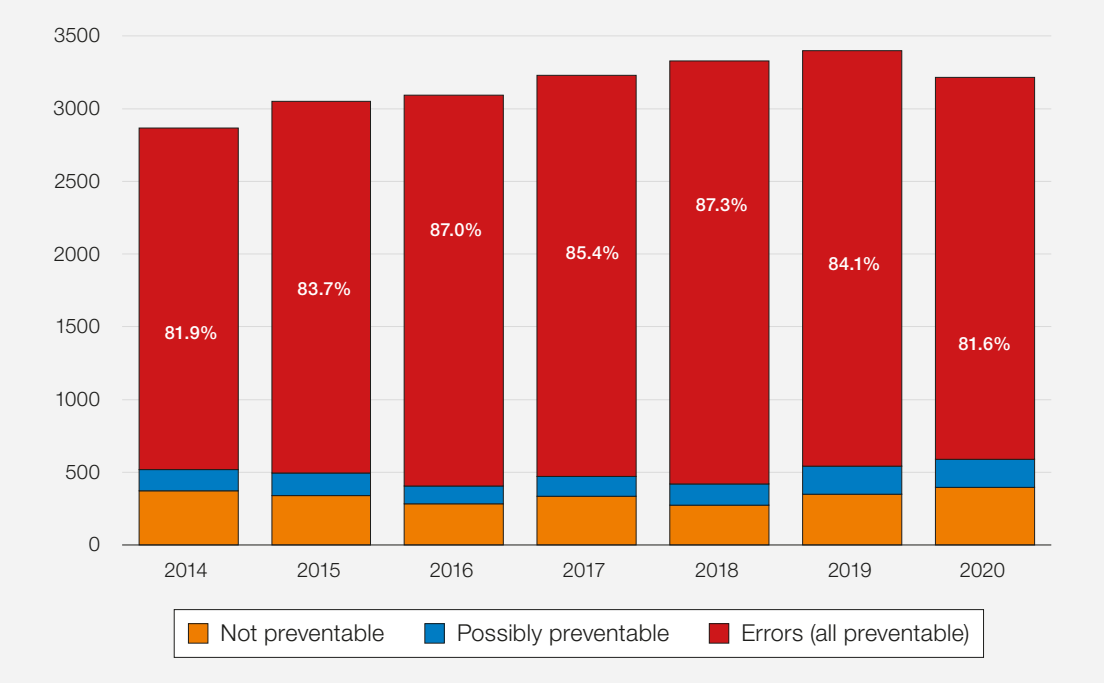


Figure 3.3: Errors as a percentage of total reports 2014-2020

Deaths n=39

There has been a steep increase (17 deaths were reported in 2019) in the number of deaths reported in 2020 related to transfusions. This number includes deaths definitely, probably and possibly (imputability 3, 2, and 1 respectively) related to the transfusion.

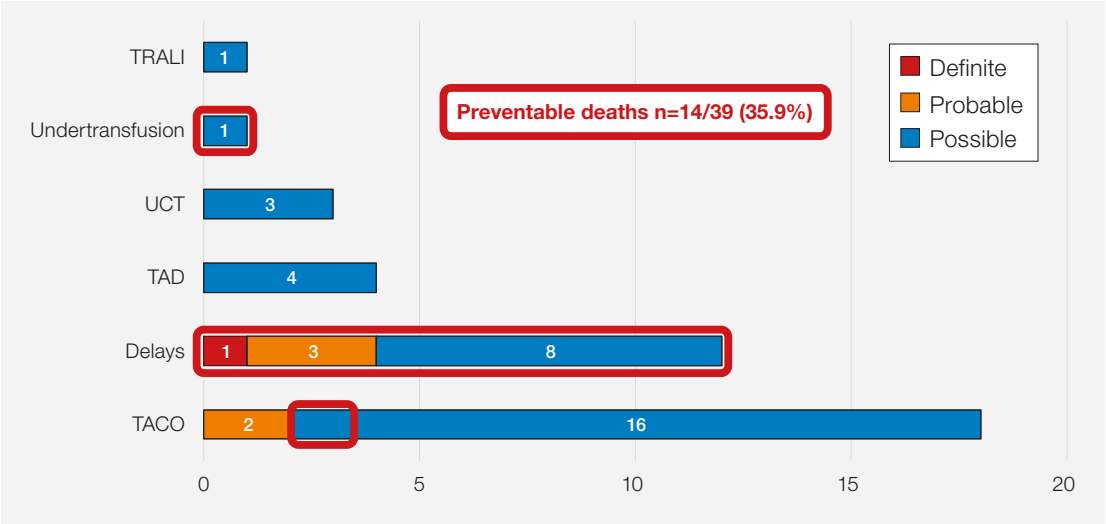
All serious reactions reported to SHOT are assessed for imputability i.e. the relationship of the blood transfusion to the reaction. The imputability criteria are detailed in the table below:

Table 3.1: Grading of imputability

Imputability		
N/A	Not assessable	When there is insufficient data for imputability assessment
0	Excluded or unlikely	When there is conclusive evidence beyond reasonable doubt for attributing the adverse reaction to causes other than the blood or blood components or where the evidence is clearly in favour of alternative causes
1	Possible	When the evidence is indeterminate for attributing the adverse reaction either to the blood or blood component or where there may be alternative causes
2	Likely/probable	When the evidence is clearly in favour of attributing the adverse reactions to the blood or blood component
3	Certain	When there is conclusive evidence beyond reasonable doubt

Deaths reported in 2020 were noted mostly relating to TACO (n=18) and delays (n=12). Pathological reactions, such as, febrile, allergic, hypotensive and haemolytic reactions did not feature as contributory to deaths. Details of reviews into the various reporting categories can be found in the relevant chapters in the report. Key factors identified in deaths relating to TACO and delays include lack of TACO risk assessments in vulnerable patients, delays in recognising major haemorrhage, communication errors and delays in reversal of anticoagulation when patients on anticoagulants present with major bleeding. Serial delays at different transfusion steps are cumulative and can result in harm or death. Transfusions with pulmonary complications contributed most to both deaths and major morbidity. Figure 3.4 shows the distribution of deaths related to transfusion reported in 2020.

Figure 3.4: Deaths related to transfusion (with imputability) reported in 2020 (n=39)



TRALI=transfusion-related acute lung injury; UCT=uncommon complications of transfusion; TAD=transfusion-associated dyspnoea; TACO=transfusion-associated circulatory overload

A detailed review of the transfusion-related deaths in the UK from 2020 can be found in the supplementary information on the SHOT website (https://www.shotuk.org/shot-reports/report-summary-and-supplement-2020/). Suboptimal investigation of these serious incidents is evident with RCA investigations performed and shared with SHOT for the single imputability 3 case and 4 of the 5 cases with imputability 2. RCA was performed for only 18 of the 33 imputability 1 cases, with 7 of these being shared with SHOT. A TACO checklist was stated to have been used pre transfusion in only 4/18 cases. There continues to be a lower threshold to blame individuals and missed opportunities to identify systemic factors that need to be improved when investigating incidents. A human factors driven incident investigation is key to driving sustained improvements in healthcare. Where intervention actions were identified they often referred to review of systems, review of education and/or process mapping with no tangible improvement actions. Reviews and process mapping should be part of the RCA, not cited as an improvement action and this is indicative of an incomplete RCA process. Action plans did not always include responsibilities for implementation, time frames or sustainability of actions, and very few included any review of the effectiveness of the actions.

COVID-19 appears to have contributed in some degree to the increase in transfusion-related deaths, being implicated as a co-morbidity in 5 TACO cases, but was not notable in cases of delayed transfusion, which are reviewed in detail in Chapter 12, Avoidable, Delayed or Under/Overtransfusion (ADU). Despite the pandemic causing a significant strain on health service resources, challenges with patient care were not cited in the investigation reports. Thorough investigation, including identification and implementation of improvement actions, is crucial in all potentially avoidable transfusion reactions and events and should be standard where there has been a death or major morbidity. All incidents should be considered in terms of future potential, it is impossible to know how many lives have been saved because RCA and intervention principles have been applied to near miss events and cases where there is no clinical harm, but it has surely been time well spent.

Trends in transfusion-related deaths

Figure 3.5 shows the distribution of causes of transfusion-related deaths reported between 2010-2020. These demonstrate that the risk of death from transfusions in UK remains very low. Changes in transfusion practices have resulted in a reduction in pathological transfusion reactions and deaths from infections. The main risks however are related to human factors. Pulmonary complications and delays in transfusions are now the main cases of transfusion-related deaths. Use of checklists, embedding the use of electronic identification systems, incorporation of human factors and ergonomics principles in transfusion practices will help in improving decision making in transfusion.

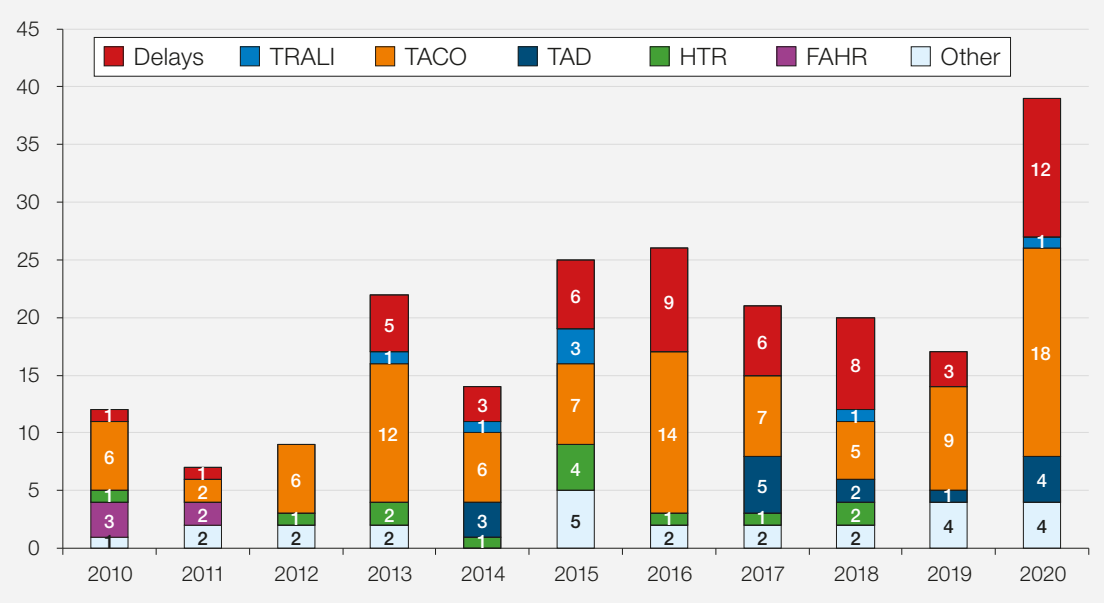


Figure 3.5: Transfusion-related deaths 2010 to 2020 (n=173)

TRALI=transfusion-related acute lung injury; TACO=transfusion-associated circulatory overload; TAD=transfusion-associated dyspnoea; HTR=haemolytic transfusion reaction; FAHR=febrile, allergic and hypotensive reactions

Please refer to the respective Annual SHOT Reports for further details regarding these deaths.

Improved decision making, patient monitoring and education, addressing factors contributing to errors, building safer systems and continued vigilance are vital in improving transfusion safety.

Major morbidity n=137

Febrile, allergic or hypotensive transfusion reactions and pulmonary complications continue to account for most of the cases with major morbidity. These are detailed further in the respective subject chapters in this Annual SHOT Report.

Major morbidity is defined in the SHOT definitions document as:

- Intensive care or high dependency admission and/or ventilation, renal dialysis and/or renal impairment
- Transfusion induced coagulopathy in association with treatment for major haemorrhage (due to the dilution of haemostatic factors following unbalanced resuscitation or overuse of crystalloid/colloid
- Evidence of acute intravascular haemolysis e.g. haemoglobinaemia, gross haemoglobinuria
- Life-threatening acute reaction requiring immediate medical intervention
- Persistent viral infection
- Acute symptomatic confirmed infection
- Sensitisation to D or K in an individual of childbearing potential
- Reaction resulting in a low or high Hb level of a degree sufficient to cause risk to life unless there is immediate medical intervention

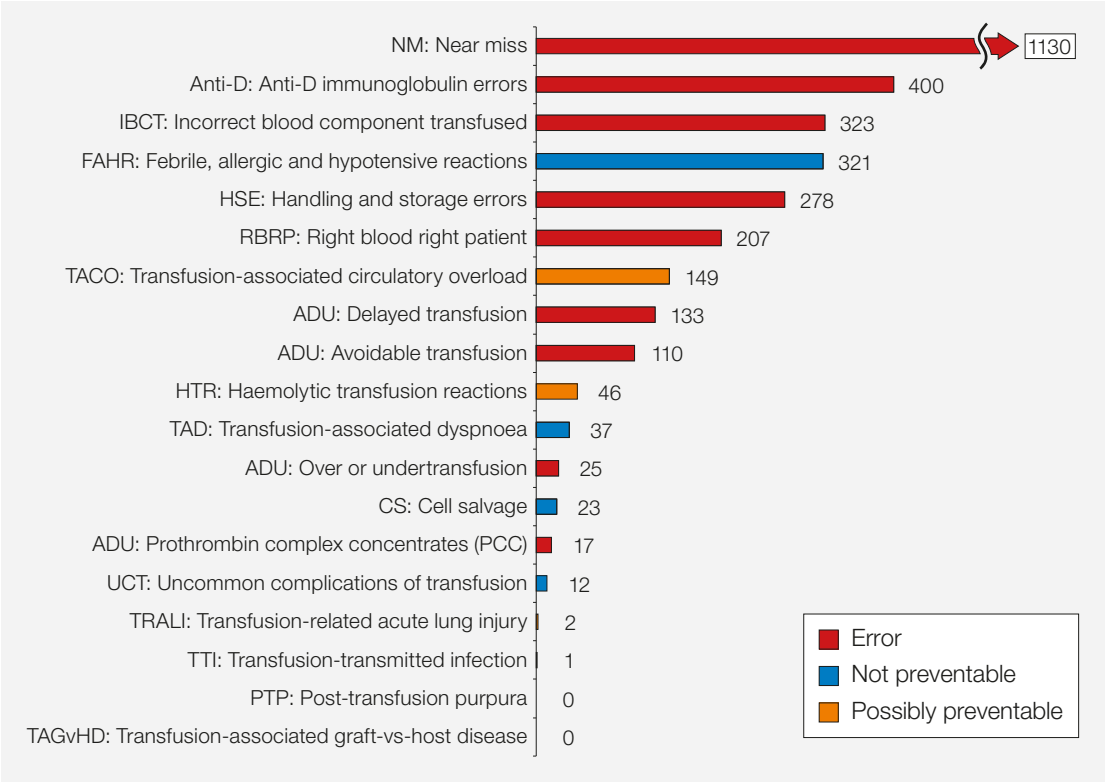
Potential for major morbidity is defined as:

- Potential risk of D or K sensitisation in an individual of childbearing potential

Summary data and risks associated with transfusion

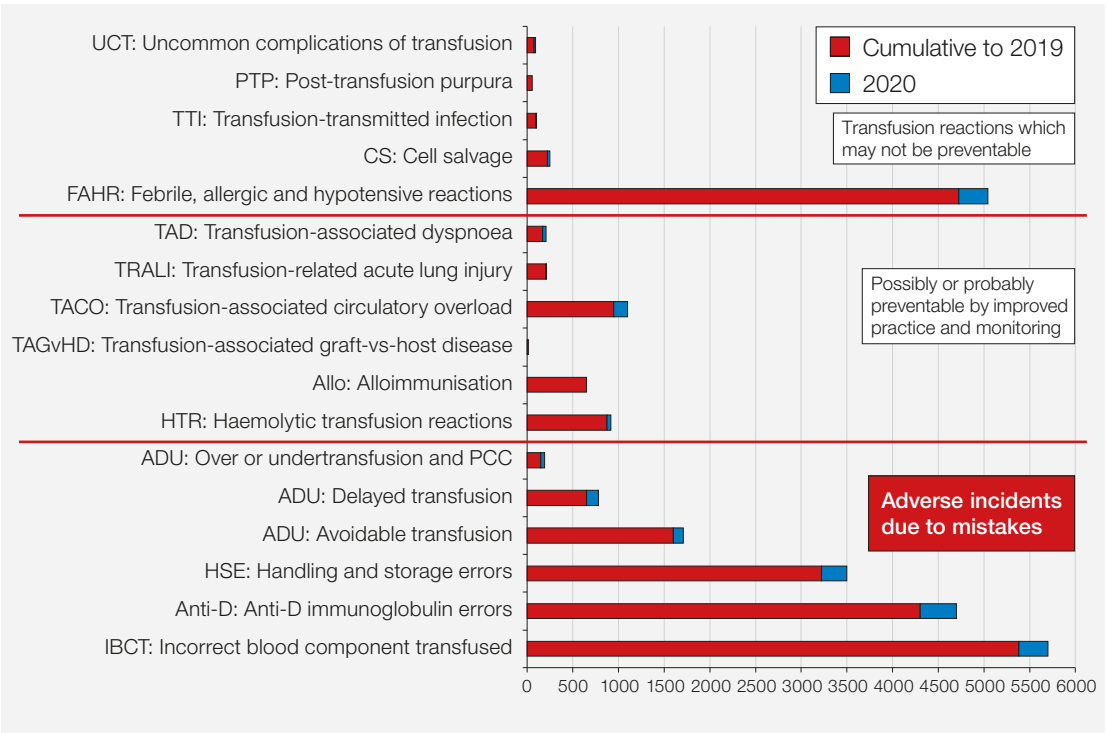
Data collected in 2020 are shown in Figure 3.6. Near miss continues be the category with the highest number of reports (1130/3214, 35.2%). Reporting and investigating near misses helps identify and control risks before actual harm results, providing valuable opportunities to improve transfusion safety.

Figure 3.6: Summary data for 2020, all categories (includes RBRP and NM) (n=3214)



There have been no cases of TA-GVHD or PTP reported in 2020. All transfusion staff need to be aware of these rare complications, prevention strategies and be able to recognise these promptly and manage appropriately. Cumulative data for 24 years are shown in Figure 3.7.

Figure 3.7: Cumulative data for SHOT categories 1996-2020 (n=25218)



**Data on alloimmunisation is no longer collected by SHOT since 2015*

The risk of death related to transfusions in the UK is 1 in 53,193 components and of serious harm 1 in 15,142 components issued in the UK. The risks of transfusion-transmitted infections are much lower than all other transfusion-related complications (see Chapter 21, Transfusion-Transmitted Infections (TTI)).

Cumulative risk data from SHOT

Figure 3.8 shows the number of reactions reported per 10,000 components issued in the UK between 2011-2020. Although red cells are the most common blood component transfused, platelets account for the highest number of reactions reported per 10,000 components. Platelet transfusions are associated with a high frequency of febrile and anaphylactoid reactions (Kiefel 2008). The same pattern is seen in the cases reported to SHOT and these are further elaborated in the FAHR chapter. The incidence of allergic reactions is lower with pooled platelets (suspended in PAS) than apheresis platelets and could most likely be associated with the reduction in plasma content. Reactions to platelets are at least in part caused by release of substances from the platelets themselves and therefore cannot be completely eliminated (Garraud et al. 2016, Maurer-Spurej et al. 2016).

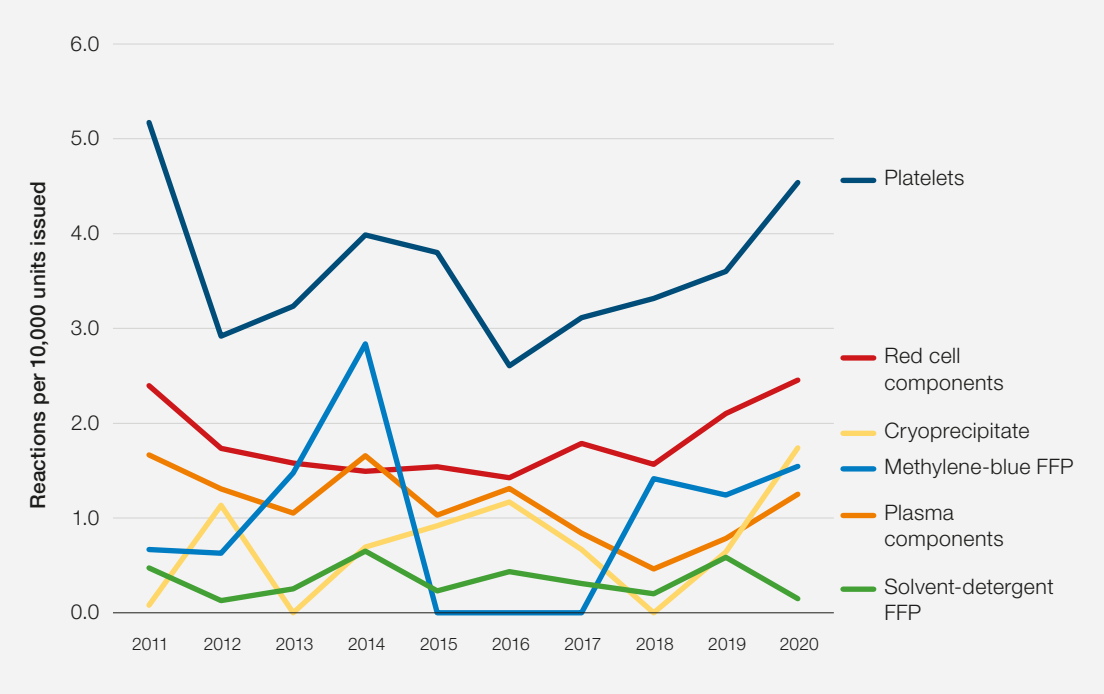


Figure 3.8: Reactions per 10,000 components, by component type 2011-2020

**Not including convalescent plasma*

The following table shows the risk of transfusion reactions based on SHOT data 2011-2020. It should be noted that these are based on the number of blood components issued as accurate data regarding actual number of transfusions is lacking. Notwithstanding a good reporting culture, variations in reporting over the years, changes in definitions, validation, and variation in practices should be considered when interpreting these data. Despite these limitations, the data are useful and provide valuable information about the risks for some of the common transfusion reactions reported to SHOT.

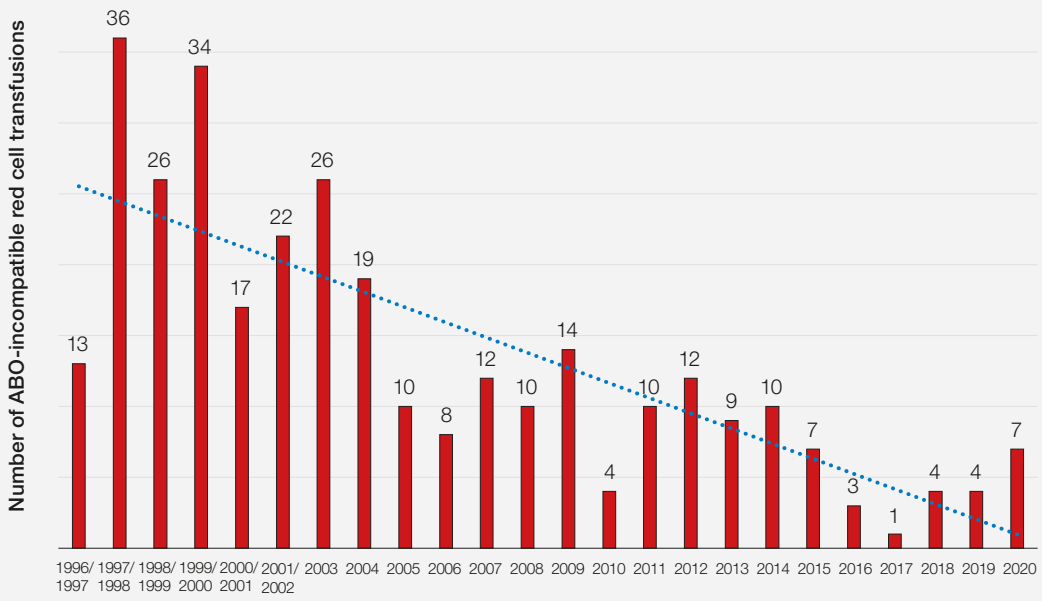
Table 3.2: Risk of transfusion reaction by reaction type 2011-2020

Transfusion reaction	Risk of transfusion reaction based on SHOT data 2011-2020
Febrile, allergic or hypotensive reactions	1 in 7,704
Transfusion-associated circulatory overload	1 in 25,313
Haemolytic transfusion reactions	1 in 57,425
Transfusion-associated dyspnoea	1 in 153,249
Transfusion-related acute lung injury	1 in 417,039
Post-transfusion purpura	1 in 2,543,940
Transfusion-associated graft vs host disease	1 in 25,439,401

ABO-incompatible (ABOi) transfusions n=9

In total, there were 7 ABOi red cell transfusions, 1 ABOi FFP transfusion and 1 related to COVID-19 convalescent plasma reported in 2020. There were no cases of ABOi reported in children. Transfusion took place out-of-hours (20:00-8:00) in 5 of these cases despite the transfusions being reported as elective in 3 of these 5 cases. It is important that unnecessary elective transfusions are avoided out-of-hours in stable patients when staffing levels and senior support available may be low. Staff need to be vigilant and patients need to be monitored closely irrespective of when they are transfused. Administration errors accounted for most of the ABOi transfusions (5/9, 55.6%). Errors at component selection (n=2) and collection (n=2) were seen in the other cases. These errors were not picked up despite staff using a pre-administration checklist in 8/9 (88.9%) cases and worryingly administration checks were not part of routine transfusion practice in one hospital. This is despite repeated SHOT recommendations and a recommendation from the Chief Medical Officer (Department of Health 2017). This safety check applied correctly could potentially have picked up these ABOi transfusions. Figure 3.10 shows the number of ABOi red cell transfusions between 2010 to 2020 that should have been identified at the pre-administration checks. Gaps in staff knowledge, lack of competency training, lone working, staff shortage, confusing SOP, dynamic situations, and high numbers of unqualified staff during the pandemic have been cited as causative and contributory factors. These are further described in Chapter 10, Incorrect Blood Component Transfused (IBCT). Figure 3.9 shows the number of ABOi transfusions reported to SHOT between 1996 and 2020.

Figure 3.9: Number of ABO-incompatible red cell transfusions 1996-2020



There is a slight increase in the number of ABOi reported in 2020 which could reflect the challenges faced in healthcare because of the pandemic. Nevertheless, every effort must be made to address these errors as these can potentially result in patient death and major morbidity.

Data from 2016-2020 show that although there were 19 ABOi red cell transfusions, there were 1495 near misses where an ABOi transfusion would have resulted, the majority of these are WBIT incidents. WBIT constitute the largest subset of near miss cases reported to SHOT in 2020, 673/1130 (59.6%) of all NM events, and these are discussed separately. These may not be detected routinely unless there is a historical record in the transfusion laboratory and demonstrate the importance of the group-check policy (BSH Milkins et al. 2013). These errors, which could have lethal outcomes, demonstrate the importance of positive patient identification at the time of collecting and labelling pre-transfusion samples. As with all NM, WBIT incidents provide valuable opportunities to learn and improve systems. As is evident from the iceberg representation below (Figure 3.11), these occur much more frequently and afford more opportunities to learn than the rarer serious adverse events. When they are not identified or investigated, they are missed opportunities that can contribute to future risks of potentially lethal ABOi.

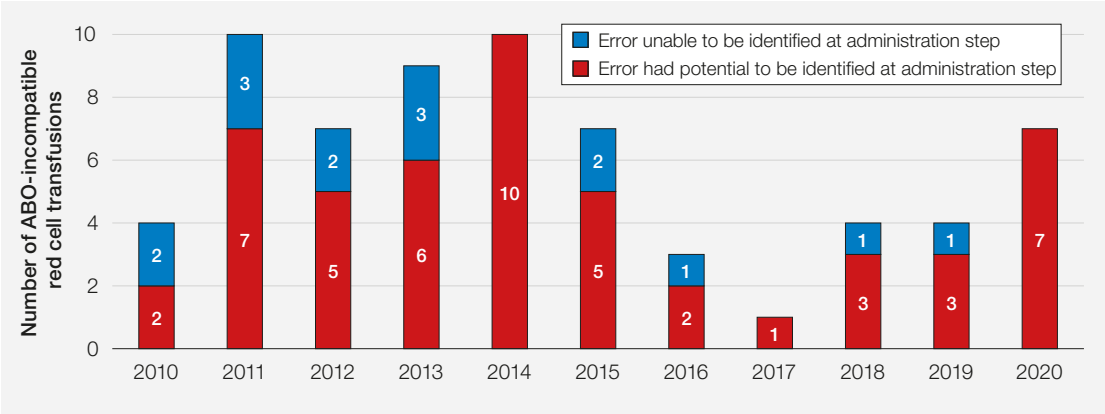


Figure 3.10: ABO incompatible red cell transfusions from 2010 to 2020 showing the importance of the pre-administration checks

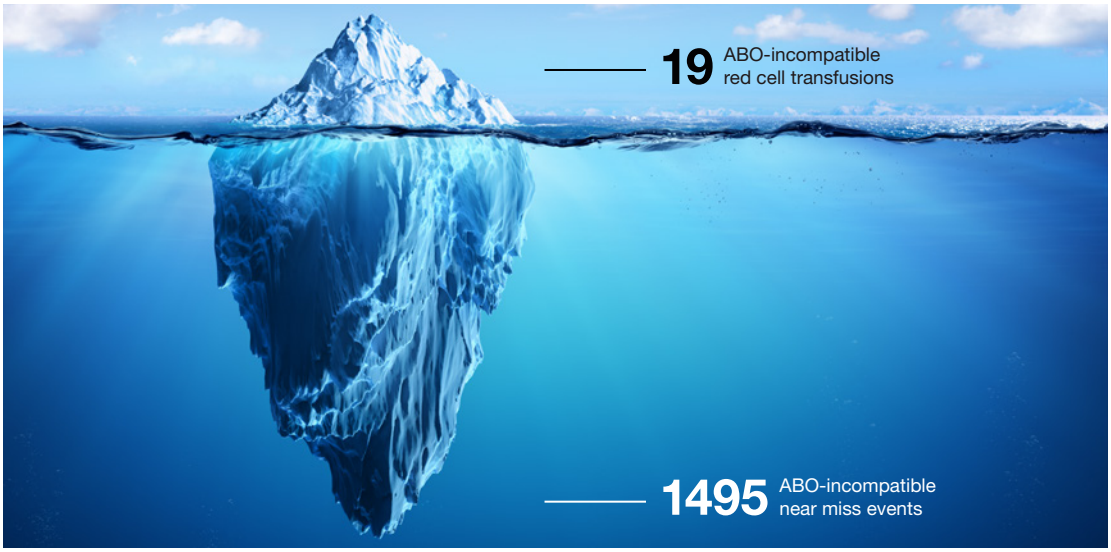


Figure 3.11: ABO-incompatible transfusions 2016-2020: few events (n=19) but many near misses (n=1495)

Investigating these incidents, including WBIT, using human factors principles will help identify the causal and contributory factors; and will inform the corrective and preventive actions to improve patient safety. This year one of the ABOi cases has been worked through using the new SHOT human factors investigation tool (HFIT) (incorporating the Yorkshire Contributory Factors Framework) and the Systems Engineering Initiative for Patient Safety (SEIPS) model to illustrate the benefits of applying human factors principles and systems thinking to incident investigations- both these re-worked investigation reports can be accessed online (https://www.shotuk.org/shot-reports/report-summary-and-supplement-2020/).

Transfusion errors reported in HSCT patients n=44

Transfusion errors continue to be reported in HSCT recipients. Most errors in this group of patients reported in 2020 involved IBCT-WCT (n=17) and IBCT-SRNM (n=15), a similar theme to that reported in the 2019 Annual SHOT Report which included an 8-year review. NM errors (n=12) were those detected prior to the transfusion and included 2 WBIT events. A detailed analysis of these errors can be found in the supplementary information on the SHOT website (https://www.shotuk.org/shot-reports/report-summary-and-supplement-2020/).

Robust communication processes must be in place between the transplant centre, all laboratories providing transfusion support, the referring centre, and any other shared care organisations. Communication must include specific requirements and recommendations for safe ABO/D component support along with the date of the transplant. Laboratories must have reliable processes for adding the specific requirement information to the patient record in the LIMS in a timely manner. Information relating to specific requirements must be easily accessible in the LIMS, flag and alert functionality must be used to its full potential to support safe provision of components. Laboratories must ensure that patients who have received an ABOi HSCT are excluded from electronic issue. These measures will help ensure safer transfusions in these patients.

Conclusion

Incident reporting is vital for improving safety in healthcare. The actual value from local and national reporting lies in learning from the various incidents, recognising gaps in practices, identifying areas for improvement, and carrying out appropriate actions. Recommendations from SHOT following analysis of the transfusion incidents must be used to identify what can be done locally in each Trust or Health Board to improve patient safety. Otherwise we risk collecting reports without positively impacting transfusion safety. Leaders and managers need to be aware of the people-related, cultural, and organisational issues that may prevent lessons from being learned effectively in their organisations. Organisational learning is a key aspect of health and safety management. If reporting and follow-up systems are not fit for purpose, for example if a blame culture acts as a disincentive to reporting near misses, then valuable knowledge will be lost. If the root causes of precursor events are not identified and communicated throughout the organisation, this makes a recurrence more likely. Siloed working in healthcare inhibits organisational learning. All these factors must be addressed to optimise learning and improve systems.

Ensuring transfusion process safety is as important as blood component safety and quality. Potential for serious problems exists at each step in the process of transfusion and learning from incidents reported should drive improvements in healthcare.

Recommended resources

SHOT Bite No. 1a and 1b: Incident Investigation
SHOT Bite No. 17: Near Miss
https://www.shotuk.org/resources/current-resources/shot-bites/

Safe transfusions in transplants document
https://www.shotuk.org/resources/current-resources/

A guidance tool for TACO investigation is available
https://www.shotuk.org/resources/current-resources/

SHOT
Serious Hazards of Transfusion

References

BSH Milkins C, Berryman J, Cantwell C, et al. Guidelines for pre-transfusion compatibility procedures in blood transfusion laboratories. *Transfus Med* 2013;**23(1)**:3-35. http://onlinelibrary.wiley.com/doi/10.1111/j.1365-3148.2012.01199.x/full [accessed 25 March 2021].

BSH Robinson S, Harris A, Atkinson S, et al. The administration of blood components: a British Society for Haematology Guideline. *Transfus Med* 2018;**28(1)**:3-21. http://onlinelibrary.wiley.com/doi/10.1111/tme.12481/full [accessed 25 March 2021].

Department of Health. Safe transfusion practice: use a bedside checklist (CAS) CEM/CMO/2017/005 (2017). https://www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAlert.aspx?AlertID=102663 [accessed 25 March 2021].

Garraud O, Tariket S, Sut C, et al. Transfusion as an Inflammation Hit: Knowns and Unknowns. *Front Immunol* 2016;**7**:534.

Kiefel V. Reactions Induced by Platelet Transfusions. *Transfus Med Hemother*. 2008;**35(5)**:354-358. doi:10.1159/000151350

Maurer-Spurej E, Larsen R, Labrie A, et al. Microparticle content of platelet concentrates is predicted by donor microparticles and is altered by production methods and stress. *Transfus Apher Sci*. 2016;**55(1)**:35-43.

Key Messages and Recommendations 4

Authors: Shruthi Narayan, Jennifer Davies and Mark Bellamy

Key SHOT messages

- **Ensuring transfusion teams are well resourced:** Clinical and laboratory teams can function optimally only if adequately staffed and well resourced. Healthcare leaders and management must ensure that staff have access to the correct information technology (IT) equipment and financial resources for safe and effective functioning
- **Addressing knowledge gaps, cognitive biases, and holistic training:** Transfusion training with a thorough and relevant knowledge base in transfusion to all clinical and laboratory staff along with training in patient safety principles, understanding human factors and quality improvement approaches are essential. It is important that staff understand how cognitive biases contribute to poor decision making so that they can be mitigated appropriately
- **Patient safety culture:** Fostering a strong and effective safety culture that is 'just and learning' is vital to ensure reduction in transfusion incidents and errors, thus directly improving patient safety
- **Standard operating procedures (SOP):** SOP need to be simple, clear, easy to follow and explain the rationale for each step. This will then ensure staff are engaged and more likely to be compliant and follow the SOP
- **Learning from near misses:** Reporting and investigating near misses helps identify and control risks before actual harm results, thus providing valuable opportunities to improve transfusion safety
- **Learning from the pandemic:** The learning from the pandemic experiences should be captured in every organisation, by everyone in healthcare and used to improve patient safety

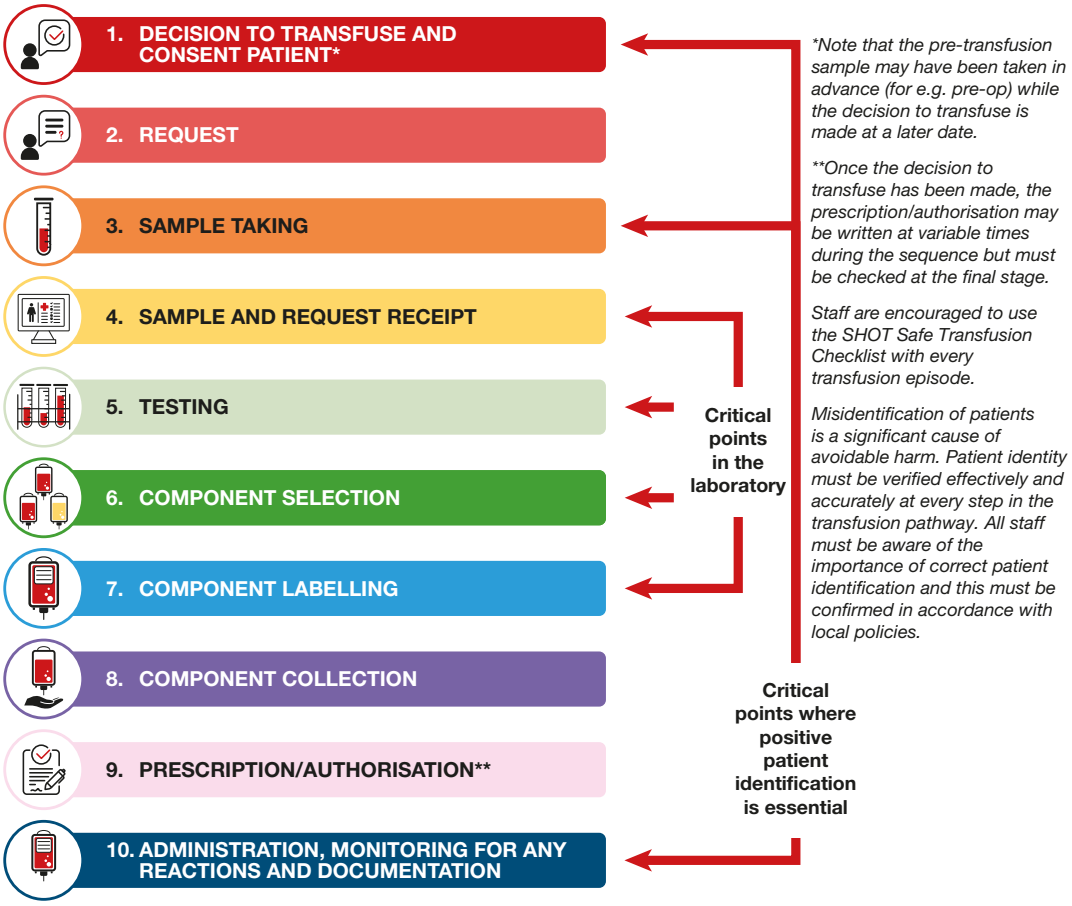
Abbreviations used in this chapter

CAPA	Corrective and preventive action
CQC	Care Quality Commission
EBMS	Electronic blood management system
GI	Gastrointestinal
Hb	Haemoglobin
HFIT	Human factors investigation tool
ICH	Intracranial haemorrhage
IT	Information technology
LIMS	Laboratory information management system
MHP	Major haemorrhage protocol
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NPSA	National Patient Safety Agency
OGD	Oesophago-gastro-duodenoscopy
RCA	Root cause analysis
SaBTO	Advisory Committee on the Safety of Blood, Tissues and Organs
SCRIPT	SHOT UK Collaborative Reviewing and Reforming IT Processes in Transfusion
SOP	Standard operating procedure
UK	United Kingdom
UKAS	United Kingdom Accreditation Service
WCT	Wrong component transfused

Blood transfusion is a critical element of medical and surgical therapies. Transfusions are very safe and effective when used appropriately. The risk of death from transfusions in UK is very low despite the steady increase in the number of reports submitted to SHOT year on year (see Chapter 3, Headline Data: Deaths, Major Morbidity and ABO-Incompatible Transfusions). Changes in transfusion practices have resulted in a reduction in pathological transfusion reactions and deaths from infections. The main risks however are related to human factors. Pulmonary complications and delays in transfusions are now the main causes of transfusion-related deaths. Ensuring transfusion process safety is as important as blood component safety and quality. Potential for serious problems exists at each step in the process of transfusion and learning from incidents reported should drive improvements in healthcare. Figure 4.1 covers the steps in the transfusion process at the recipient end from making the decision to transfuse to administration of blood and monitoring for any reactions. The nine steps referenced in previous SHOT reports have been updated following feedback from transfusion colleagues to include the decision to transfuse and patient consent.

Use of checklists, embedding the use of electronic identification systems and incorporation of human factors and ergonomics principles in transfusion practices will help to improve decision making in transfusion. The key messages and recommendations from the previous Annual SHOT Reports remain relevant and all healthcare organisations involved in transfusion are encouraged to continue implementing these and ensuring measures have been effective.

Figure 4.1: Ten steps in transfusion



All staff involved in blood transfusions need to have basic knowledge of blood components, indications for use, alternative options available, risks and benefits and possible reactions and their management. SaBTO released an updated set of recommendations to NHS Trusts/Health Boards on patient consent for a blood transfusion. These guidelines were approved and released by SaBTO in December 2020 (SaBTO 2020) and supersede the previous SaBTO 'Patient consent for blood transfusion guidelines from 2011'. Table 4.1 highlights the key aspects that need to be covered when consenting patients for transfusions.

	Key aspects to be covered when consenting patients for transfusion
1	Patient and/or family/carer have been provided with relevant information about blood transfusions that would help in their decision-making process
2	The reason for the transfusion has been discussed
3	The benefits of the transfusion have been explained
4	Transfusion risks, both short and long-term risks have been discussed with the patient and/or family/carer (including any additional risks pertinent to long term multi-transfused patients)
5	The risks, benefits, and consequences of NOT accepting blood transfusion have been elaborated
6	Transfusion issues specific to the patient have been highlighted
7	Relevant alternative options have been discussed including how they might reduce the need for a transfusion
8	The transfusion process has been explained
9	The need for any specific requirements for blood components and rationale, including need for anti-D Ig post transfusion as appropriate has been elaborated and relevant patient information leaflet has been provided
10	Patient and/or family/carer has also been informed that once transfused, they are no longer eligible to donate blood
11	Patients and carers/family have been given the opportunity and been encouraged to ask questions
12	Patient and/or family/carer is aware that if they change their mind at any point before the transfusion, they are entitled to withdraw their consent, and this should be documented and managed appropriately
13	Synopsis of discussions and decisions taken documented in patient's clinical notes

Table 4.1: Consenting patients prior to transfusions (based on the SaBTO guidance and NICE guidance NG24)

The Safe Transfusion Checklist that is available to download from the SHOT website covers most aspects of the transfusion process at the bedside (https://www.shotuk.org/resources/current-resources/). The ABCDE approach to transfusions shown below helps in the transfusion decision-making process.

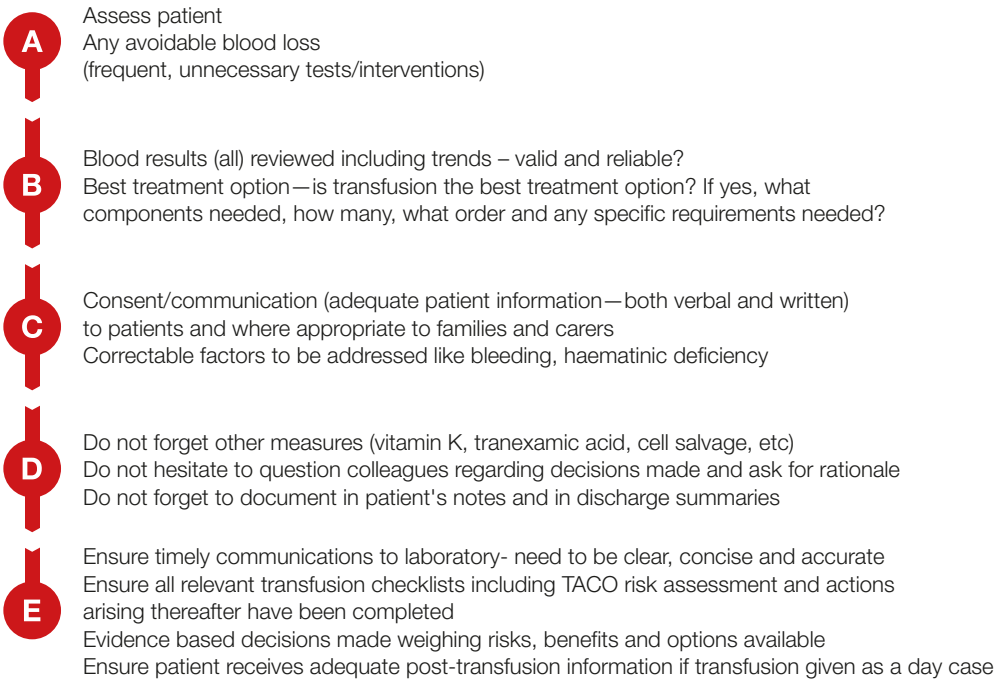


Figure 4.2: The A-E Decision Tree to facilitate decision making in transfusion

Key SHOT recommendations for 2020

The main SHOT recommendations from the preceding years remain pertinent as improvements still need to be made to address gaps previously identified. The first NHS-wide Patient Safety Syllabus (AoMRC, 2020) supports a transformation in patient safety education and training in the NHS for all healthcare professionals. It highlights the importance of human factors principles and promotes a systems approach to patient safety. The following are the key recommendations based on the emerging themes from the 2020 Annual SHOT Report. For the first time a gap analysis tool has been developed by the SHOT team to help local organisations to identify key areas for improvement (link provided in the recommended resources at the end of the chapter).

Addressing transfusion delays

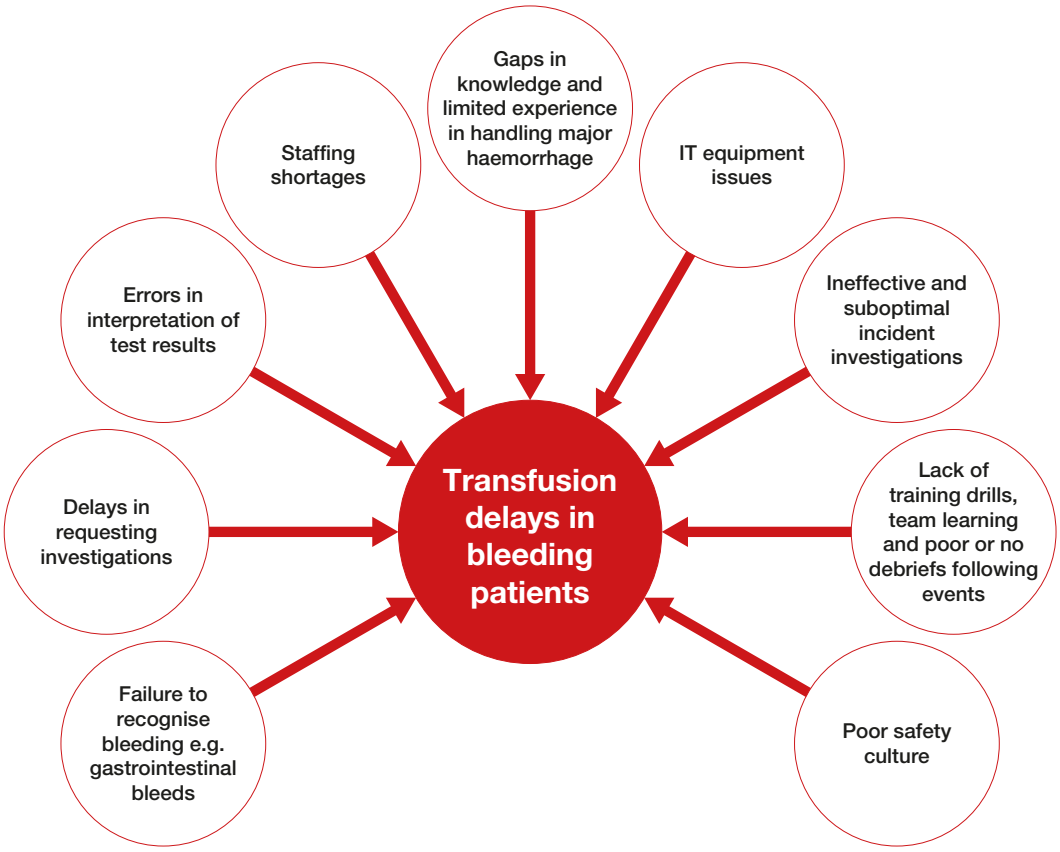
The number of cases of transfusion delays reported to SHOT are increasing year on year and contribute significantly to transfusion-related patient deaths. These delays are largely avoidable, and serial Annual SHOT Reports have highlighted that measures need to be taken by clinical and laboratory transfusion teams to address delays and improve safety. Transfusion delays have been reported in adults and children. Instances where laboratory test results have not been interpreted correctly resulting in delays in accessing specialist help have also been reported.

It is concerning that delays have been reported in relation to MHP activation including delays in anticoagulant reversal where every minute counts. A published review of 680 trauma patients noted that every minute of delay from activation of the MHP to delivery of components increased the odds of death by 5% (Meyer et al. 2017).

It is now more than 10 years since the NPSA published their Rapid Response Report (NPSA 2010). This alert was issued in relation to 11 deaths and 83 incidents of harm due to delays reported over a 4-year period. The number of reports submitted to SHOT as 'delayed transfusions' are increasing year on year and 133 cases were reported in 2020 with 12 cases resulting in patient death. The increase in both total number of reported delays and deaths is of concern. The most important factor contributing to delay is poor communication. Guidelines published in 2015 recommend that all staff 'involved in frontline care must be trained to recognise major blood loss early, know when to activate/trigger the local major haemorrhage protocol and take prompt and appropriate action' (BSH Hunt et al. 2015) and good communication is essential. The key components of a MHP are listed in recent review (Booth and Allard 2018) and include scope, activation method, choice of components, communication, stand-down, and regular review including training and drills. The evidence from SHOT reporting suggests that there is room for improvement.

Factors contributing to transfusion delays in bleeding patients is shown in Figure 4.3. Serial delays at different transfusion steps are cumulative and can result in patient harm or death. Details about the cases reported to SHOT can be found in Chapter 12a, Delayed Transfusions.

Figure 4.3: Factors contributing to transfusion delays in bleeding patients



Gastrointestinal bleeding can be deceptive, the severity is often masked, diagnosis may be delayed; hypotension and tachycardia are important clinical signals. NICE guidelines recommend that patients with an upper gastrointestinal bleed should have an OGD within 24 hours (of admission) (NICE 2012). Patients with upper GI bleeding should have a Blatchford score recorded to assess the bleeding risk (Banister et al. 2018; Chatten et al. 2018). Patients with evidence of GI haemorrhage require close monitoring, timely investigation, and appropriate transfusion; this may be incremental to keep up with bleeding, keeping a close watch on the Hb and clinical signs of bleeding.

Obstetric haemorrhage can be rapid and massive; it is vital that major haemorrhage protocols work smoothly and quickly. Improving staff knowledge and training drills and learning to work together as teams are essential. In MH scenarios there must be a process for safe concessionary release of red cells for patients with antibodies. In complex cases transfusion experts should be contacted for advice to ensure appropriate and timely management.

Systemic shortcomings should be identified and urgently addressed to reduce the time between decision to transfuse to actual transfusion. These include review of the porter services and emergency back-up arrangements. Where the use of refrigerators has to be suspended there must be clear communication of alternative procedures for emergencies. The management of major haemorrhage continues to require improvement in many hospitals with attention to streamlining communication, training, and drills. Communication between hospitals during patient transfer must be comprehensive and include all laboratory information. Clinicians must provide laboratory staff with relevant clinical information so that they provide appropriate interpretation of results and be open to challenge by laboratory staff. A holistic systems approach to incident investigation, reviewing timelines and mapping events throughout the patient journey would help to identify missed learning opportunities. Seeking urgent specialist input especially in cases with haemolysis, and/or a positive antibody screen will help prevent unnecessary delays. No patient should die from want of blood.

Main recommendation 1

- Transfusion delays, particularly in major haemorrhage and major trauma situations, must be prevented. Delays in provision and administration of blood components including delays in anticoagulant reversal, particularly in patients with intracranial haemorrhage (ICH), can result in death, or serious sequelae. Every minute counts in these situations

Actions required:

Multidisciplinary hospital transfusion committees should:

- Ensure that procedures are in place detailing identification, escalation and blood provision in major haemorrhage and trauma cases
- Ensure procedures are agreed by relevant clinical and laboratory groups, are accessible, and incorporated in regular training and simulation exercises
- Ensure that procedures are in place detailing appropriate use of anticoagulant reversal agents without requirement for approval by a consultant haematologist
- Ensure appropriate use and access to anticoagulant reversal agents is incorporated into regular training for clinical and laboratory staff
- Consider implementation of a fixed dose regime for prothrombin complex concentrates, with rapid access for ICH cases

Pathology laboratory management should:

- Ensure that procedures are in place enabling rapid provision of blood components in complex situations, using concessionary release pathways
- Ensure major haemorrhage, trauma and concessionary release procedures are incorporated into regular training and competency-assessment for all staff working in transfusion laboratories

SHOT
Serious Hazards of Transfusion

Reliable and robust IT systems to support transfusion practices

IT systems are integral to the safety and efficiency of the transfusion chain vein-to-vein, right from donor management to donation management and processing to issue to hospitals and transfusions to patients. Electronic bedside identification systems using hand-held computers and portable printers will minimise the risk of wrong transfusions caused by blood sampling error for compatibility testing and patient identification error before blood administration. Fully automated hospital transfusion laboratory immunohaematology testing systems together with LIMS help reduce hospital transfusion laboratory errors. Remote electronic blood release systems, an extension of the hospital transfusion laboratory LIMS to refrigerators in the clinical arena may aid the safe release of computer crossmatch-compatible blood. Computer transfusion requests would guide clinicians in making appropriate requests, and connectivity with electronic patient records and hospital transfusion laboratory LIMS would provide clinical decision support and thus help prevent human errors. EBMS are invaluable in the collection and administration of blood components as a second check to prevent errors, and provide detailed audit trails, helping improve transfusion safety.

SHOT has highlighted the importance of IT in preventing human errors and the need for effective implementation of appropriate IT solutions in safe transfusions for the last 2 decades. The use of computerised identification systems to avoid patient identification errors was first mentioned in the Annual SHOT Report for 1999-2000 (Love et al. 2001). This was a key SHOT recommendation in the 2017 Annual SHOT Report, 'All available information technology (IT) systems to support transfusion practice should be considered and these systems implemented to their full functionality. Electronic blood management systems should be considered in all clinical settings where transfusion takes place. This is no longer an innovative approach to safe transfusion practice; it is the standard that all should aim for' (Bolton-Maggs et al. 2018). SHOT has strongly supported the use of IT to reduce human errors in transfusion medicine. This has also been supported by NICE (NICE NG24, 2015). The NICE guidance states 'consider using a system that electronically identifies patients to improve the safety and efficiency of the blood transfusion process'.

The adoption and widespread use of IT in transfusion still lags behind its knowledge and awareness of impact on safety. The key to closing this gap is for healthcare leaders to make this a key priority and invest in safety.

The 2018 SHOT recommendations survey highlighted that there are significant gaps in IT adoption and use across the NHS and competing priorities, stretched resources and finance were commonly cited as barriers (https://www.shotuk.org/resources/shot-surveys/). Responses were received from SHOT reporters. Of concern there were several comments stating senior leaders and managers failed to recognise the importance of IT in improving transfusion safety.

A multicentre study, the first of its kind, demonstrated a lower incidence of IBCT-WCT and near-miss IBCT-WCT with electronic patient identification systems compared to manual processes, thus demonstrating the application of information technology in minimising wrong transfusions through the reduction of human steps that are prone to errors (Murphy et al. 2019).

A 3-year retrospective review (2016 to 2018) of near miss SHOT reports identified with an IT element highlighted the importance of electronic systems in the detection and reporting of errors, but also show where design and implementation flaws introduce errors (Davies et al. 2020). Greater reliance

on IT makes thorough system validation critical. Robust systems are needed to ensure patient specific requirement flags are added to LIMS. Drop down lists are ergonomically dangerous, if present LIMS should include a validation function for confirmation of the entered reaction pattern against the selected blood group during any manual entry of blood groups.

The Department of Health and Social Care of the United Kingdom released 'The future of healthcare: our vision for digital, data and technology in health and care' in 2018 (DHSC 2018). This sets out plans for a truly joined-up health and care, designed around the needs of patients and their care networks, with good integration of physical and digital services. The vision is to have a safe and secure data infrastructure that protects the health and care system. Patients and local organisations would be able to make the right technology choices for their own area, while also maintaining high quality systems than can communicate across the entire NHS, achieving better, safer, more targeted care.

NHS Digital has published a draft of a new framework that will set out the core standards on technology and data by which all IT systems and digital services in the NHS must abide. Greater standardisation of data, the right infrastructure and platforms, secure systems and interoperability will ensure that patient care is more joined-up, safer and more efficient. All these elements are critical to the safe and successful use of technology, ensuring that systems talk to each other and that the right data get to the right place at the right time. Interoperability or the lack of it has been a major impediment in transfusions. Connected systems ensure that clinicians have immediate access to relevant and appropriate patient data, both clinical and laboratory, from care providers and settings. Data can be communicated between systems with absolute fidelity, eliminating misinformation and misunderstandings (NHS Digital 2020).

IT systems support staff to administer blood components safely and appropriately. Electronic systems are vital in the detection and reporting of errors, but for IT systems to be effective and reliable, they should be designed and implemented appropriately with a robust validation process. Staff must be trained and should have access to subject matter experts. IT system design and implementation flaws introduce errors. Reliance on IT does not equate to complacency. Greater reliance on IT makes thorough system validation critical. Robust systems are needed to ensure patient-specific requirement flags are added to LIMS. Recognising the urgent need for improvements in this area, SHOT is aiming to bring together transfusion experts to work with IT experts and the manufacturers of these systems to ensure we have the best possible outcomes for our patients. The SHOT UK Collaborative Reviewing and reforming IT Processes in Transfusion (SCRIPT) group was initiated by the SHOT IT and laboratory working expert group members in 2020. The SCRIPT work will include the specification and implementation of IT systems as well as promoting interoperability, raising the profile of transfusion requirements within IT systems, and could also include training transfusion experts in IT and IT experts in transfusion.

SCRIPT work plans include:

1. A survey completed by SHOT reporters giving a UK-wide picture of IT systems that support transfusion – this has been completed and is undergoing analysis
2. To engage with software providers and with healthcare IT strategy groups and individuals
3. To run a SCRIPT workshop in collaboration with key stakeholders with both transfusion personnel and IT providers to inform and educate about transfusion IT and identify areas for improvement
4. To support and maintain a community of practice within transfusion IT

Further information about the SCRIPT work can be accessed on the SHOT website (https://www.shotuk.org/resources/current-resources/script/)

Main recommendation 2

- Effective and reliable transfusion information technology (IT) systems should be implemented to reduce the risk of errors at all steps in the transfusion pathway, provided they are configured and used correctly

Actions required:

Hospital senior management should:

- Ensure transfusion IT systems that support good practice and safe patient care, as recommended by the hospital transfusion committee or equivalent, are implemented across the organisation

Transfusion IT providers should:

- Ensure systems are compliant with the relevant current national legislation, guidelines, and recommendations
- Ensure systems support safe practice using appropriate alerts with consideration to reduce risk of alert fatigue

Pathology laboratory management should:

- Ensure that all transfusion IT systems are used to their full potential, are compliant with relevant national legislation, guidelines, and recommendations and are regularly validated
- Ensure that use and understanding of the transfusion IT systems is incorporated into staff training and regular competency-assessment

Hospital IT management should:

- Consider the impact of changes to, or implementation of, any clinical IT system on the delivery of the transfusion service, including planned downtime events
- Review opportunities to improve transfusion safety, from the decision to transfuse through to the administration and monitoring of the transfusion, by harnessing interoperability between clinical IT systems and transfusion IT systems

Investigating incidents

Investigating incidents is integral to providing a safe transfusion service and preventing patient harm. The quality and safety risk in the context of the patient should be central to all investigations. Effective incident investigation processes can reduce error, improve practice and lead to safer systems. Learning from experiences can prevent harmful incidents from recurring- safety is enhanced by learning from all incidents.

Incident investigations often are inadequate and fail to identify causes of failure or improvement actions to reduce recurrence. Introduced into SHOT reporting in 2016, the HFIT results have shown that investigations disproportionately blame individuals while system failures are overlooked (see Chapter 8, Human Factors in SHOT Error Incidents). Re-training or supervising one individual will not fix the system or prevent recurrence of errors. To truly improve practice, provide safe processes and reduce risk a systems-based approach to investigating incidents is required. A systems-based approach to the investigation of incidents and moving to a just and learning culture is essential. Incorporating a just and learning culture in all NHS organisations and moving away from a blame culture was a key SHOT recommendation in 2018 (Narayan et al. 2019) – this is fundamental for a good safety culture in any organisation.

Regulatory guidelines and standards require that incidents, or non-conformances, are identified, investigated and that actions are taken to reduce the risk of recurrence:

- Good Practice Guidelines 2018 (9.4) include the requirement for an appropriate level of RCA and identification of CAPA (Council of Europe 2018)

- UKAS ISO15189:2012 includes identification of the root causes, implementation of CAPA and review of the effectiveness of the actions (UKAS 2019)
- NHS England and NHS Improvement provide standardised tools and templates for patient safety incident investigations, guides to duty of candour and supporting a just culture (NHS England n.d.)
- CQC regulation 12: safe care and treatment require that incidents are reviewed, thoroughly investigated by competent staff and monitored to make sure that action is taken to remedy the situation, prevent further occurrences and make sure that improvements are made as a result (CQC 2014)

Incident analysis is part of the incident management continuum in every organisation and needs to be reviewed regularly. Thorough incident investigations using human factors principles will help identify the causal and contributory factors; and will inform the corrective and preventive actions to improve patient safety. This year one of the ABOi cases has been worked through using the new SHOT HFIT framework (incorporating the Yorkshire Contributory Factors Framework) and the Systems Engineering Initiative for Patient Safety (SEIPS) model to illustrate the benefits of applying human factors principles and systems thinking to incident investigations- both these re-worked investigation reports can be accessed online (https://www.shotuk.org/shot-reports/report-summary-and-supplement-2020/).

Main recommendation 3

- Effective investigation of all incidents and near miss events, application of effective corrective and preventive actions, and closing the loop by measuring the effectiveness of interventions should be carried out to optimise learning from incidents

Actions required:

Risk management departments should:

- Provide support and training for all staff involved in transfusion-related incident investigation
- Ensure procedures and templates are available that include consideration of human factors and a system-based approach to investigation, include plans for corrective and preventive actions and a process for reviewing the effectiveness of the actions
- Provide a platform to share learning from transfusion errors and near miss events across the whole organisation

Pathology laboratory management should:

- Ensure capacity plans include provision of adequate staffing to support robust investigation of all transfusion-related incidents and near miss events
- Ensure that staff involved in incident investigation have received adequate training, including human factors and a system-based approach to investigation
- Provide support with implementation of effective corrective and preventive actions, ensuring that these are forcing functions* wherever possible

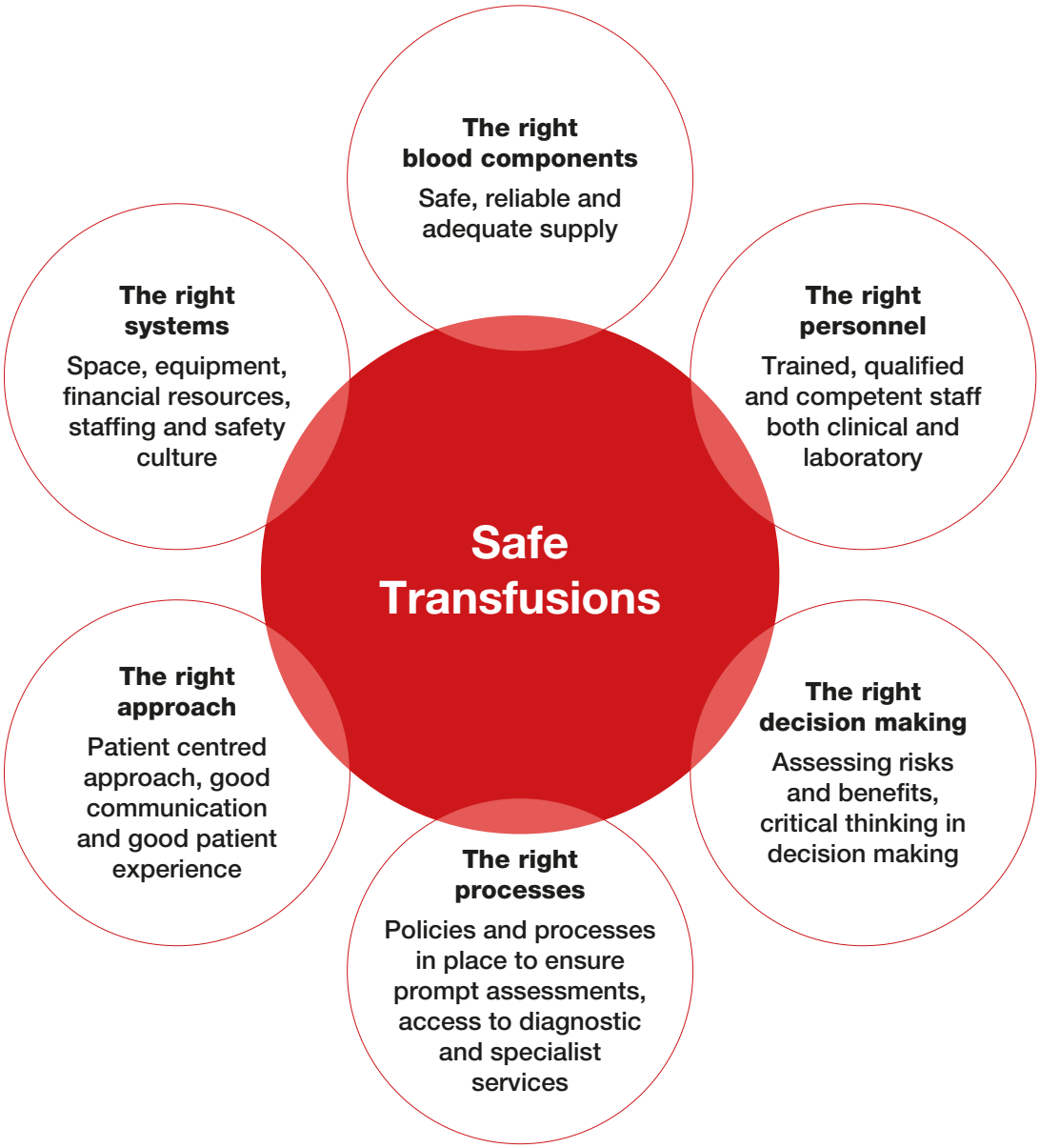
A **forcing function is an aspect of a design that prevents the user from taking an action without consciously considering information relevant to that action (e.g. rule in LIMS that does not allow issue of ABOi red cell units).*

Framework for safe transfusions in the NHS

The 10 'Rs' framework discussed in the 2019 Annual SHOT Report based on the 10' R's safe prescribing and safe administration of medications acknowledges that the responsibility for managing the environment where transfusions take place and the responsibility for safe transfusions is a multi-disciplinary concern (Narayan et al. 2020). It is therefore clear that the actions needed to address transfusion errors should be multifaceted. Transfusion errors are often the result of faulty systems, processes, and conditions that lead people to make mistakes. The key to eradicating transfusion errors and advancing patient safety is to create systems for healthcare delivery that doctors, nurses, and others providing patient care can rely on.

At a macro-system level all the following aspects (Figure 4.4) are vital for safe transfusions in healthcare:

Figure 4.4: Framework for safe transfusions



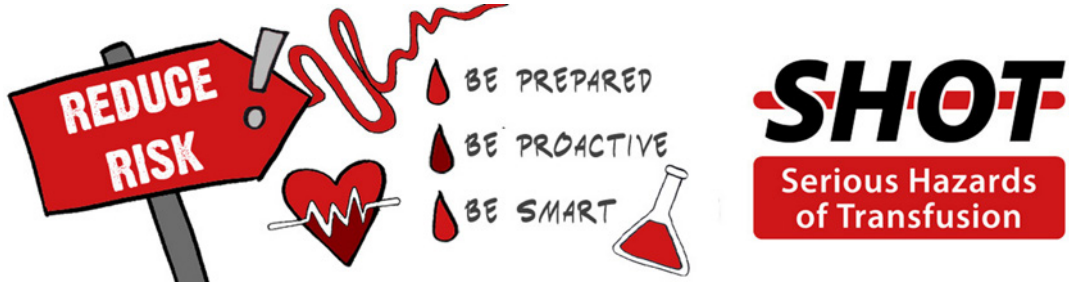
Systems-based strategies with a collaborative effort by everyone in healthcare comprising frontline staff, supporting workforce including those in management and executives, are needed urgently to bring about sustainable and tangible improvements in patient safety.

Recommended resources

SHOT Bite No. 1a and 1b: Incident Investigation
SHOT Bite No. 8: Massive Haemorrhage – Delays
SHOT Bite No. 13: Information Technology in Transfusion – Highlights and Lessons
SHOT Bite No. 16: Errors with Prothrombin Complex Concentrate
SHOT Bite No. 17: Near Miss
https://www.shotuk.org/resources/current-resources/shot-bites/

2020 Annual SHOT Report gap analysis tool for all recommendations
https://www.shotuk.org/shot-reports/report-summary-and-supplement-2020/

SHOT educational video about transfusion delays in major haemorrhage can be accessed at the link
https://www.shotuk.org/resources/current-resources/videos/



References

Academy of Medical Royal Colleges (2020) National patient safety syllabus V2.0 https://www.aomrc.org.uk/patientsafety/ [accessed 28 June 2021]

Banister T, Spiking J and Ayaru L. Discharge of patients with an acute upper gastrointestinal bleed from the emergency department using an extended Glasgow-Blatchford Score. *BMJ Open Gastro* 2018;**5**:e000225.

Bolton-Maggs PHB (Ed), Poles D, et al. on behalf of the Serious Hazards of Transfusion (SHOT) Steering Group. The 2017 Annual SHOT Report (2018). https://www.shotuk.org/shot-reports/ [accessed 14 April 2021].

Booth C and Allard S. Major haemorrhage protocols. *ISBT Sci Ser* 2018;**13(3)**:219-228.

BSH Hunt BJ, Allard S, Keeling D, et al. A practical guideline for the haematological management of major haemorrhage. *Br J Haematol* 2015;**170(6)**:788-803.

Care Quality Commission. Regulation 12: Safe care and treatment (2014) https://www.cqc.org.uk/guidance-providers/regulations-enforcement/regulation-12-safe-care-treatment [accessed 14 April 2021].

Chatten K, Purssell H, Banerjee AK, et al. Glasgow Blatchford Score and risk stratifications in acute upper gastrointestinal bleed: can we extend this to 2 for urgent outpatient management? *Clin Med (Lond)* 2018;**18(2)**:118-122.

Council of Europe. Good Practice Guidelines for Blood Establishment Required to Comply with Directive 2005/62/EC, 15/02/2018 https://www.edqm.eu/en/good-practice-guidelines-blood-establishments [accessed 14 April 2021].

Department of Health and Social Care. Policy Paper: The future of healthcare: our vision for digital, data and technology in health and care. Published Oct 2018 https://www.gov.uk/government/publications/the-future-of-healthcare-our-vision-for-digital-data-and-technology-in-health-and-care/the-future-of-healthcare-our-vision-for-digital-data-and-technology-in-health-and-care [accessed 14 March 2021].

Davies J, McGrann A, Poles D, et al. A 3-year review of the information technology related near miss reports to SHOT. *Vox Sang* 2020:**115(1)**;3-387.

Love EM, Jones H et al. on behalf of the Serious Hazards of Transfusion SHOT Steering Group. The SHOT Annual Report 1999-2000 (2001) https://www.shotuk.org/shot-reports/ [accessed 14 April 2021].

Meyer DE, Vincent LA, Fox EE, et al. Every minute counts: time to delivery of initial massive transfusion cooler and its impact on mortality. *J Trauma Acute Care Surg* 2017;**83(1)**:19-24.

Murphy MF, Addison J, Poles D, et al. Electronic identification systems reduce the number of wrong components transfused. *Transfusion* 2019;**59(12)**:3601-3607. https://onlinelibrary.wiley.com/doi/10.1111/trf.15537 [accessed 14 April 2021].

Narayan S (Ed), Poles D, et al. on behalf of the Serious Hazards of Transfusion (SHOT) Steering Group. The 2018 Annual SHOT Report (2019). https://www.shotuk.org/shot-reports/ [accessed 14 April 2020].

Narayan S (Ed), Poles D, et al. on behalf of the Serious Hazards of Transfusion (SHOT) Steering Group. The 2019 Annual SHOT Report (2020). https://www.shotuk.org/shot-reports/ [accessed 14 April 2020].

NHS Digital. NHS digital, data and technology standards framework. (2020) https://digital.nhs.uk/about-nhs-digital/our-work/nhs-digital-data-and-technology-standards/framework#introduction [accessed 14 April 2021].

NHS England. Patient safety incident investigation (PSII) (n.d.) https://www.england.nhs.uk/patient-safety/patient-safety-investigation/ [accessed 14 April 2021].

NICE. Acute upper gastrointestinal bleeding in over 16s: management. Clinical Guideline 141 (2012). https://www.nice.org.uk/guidance/CG141/chapter/1-Guidance#timing-of-endoscopy [accessed 14 April 2021].

NICE guideline (NG24) Blood transfusion (2015) https://www.nice.org.uk/guidance/ng24/chapter/Recommendations#patient-safety [accessed 04 May 2021].

NPSA. NPSA Rapid Response Report: 'The transfusion of blood and blood components in an emergency' (2010). https://www.transfusionguidelines.org/document-library/documents/npsa-rapid-response-report-the-transfusion-of-blood-and-blood-components-in-an-emergency-21-october-2010-pdf-100kb [accessed 14 April 2021].

SaBTO. Guidelines from the expert advisory committee on the Safety of Blood, Tissues and Organs (SaBTO) on patient consent for blood transfusion. (2020) https://www.gov.uk/government/publications/blood-transfusion-patient-consent [accessed 14 April 2021].

COVID-19 and Haemovigilance

5

Authors: Shruthi Narayan, Jennifer Davies, Debbi Poles, Victoria Tuckley, Simon Carter-Graham, Emma Milser and Fahim Ahmed

The SHOT Steering Group and Working Expert Group would like to extend their heartfelt gratitude to all our reporters and indeed everyone in the transfusion community and the wider NHS for their contributions during the pandemic. During these times of crisis, everyone has come through by supporting each other and working together. Staff have been working tirelessly to ensure patient care is not compromised. Haemovigilance reporting continued. The period of the pandemic was also a period of accelerated transformation across services – this was only possible through the dedication of all our colleagues in the transfusion community. From the introduction of a new blood component (COVID-19 convalescent plasma, CCP), new CCP trials run during the pandemic, continuing education and training of staff, introduction of electronic systems and digital acceleration, this was a period of transformation. Our ability to adapt, innovate and grow during these unprecedented circumstances has been extraordinary. When faced with the very worst, we have seen the transfusion community come together, helping, and supporting each other. It is the kindness and support that we give to each other that will help us get through these unprecedented times. For this and everything, we extend our sincere appreciation and gratitude.

Key SHOT message

- Experiences during the pandemic have stressed the importance of collaboration, communication, and co-operation to help reduce risks and improve safety

Abbreviations used in this chapter

ADE	Antibody-dependent enhancement	**NHS**	National Health Service
CAS	Central alerting system	**RCA**	Root cause analysis
CCP	COVID-19 convalescent plasma	**RCT**	Randomised controlled trial
ECMO	Extracorporeal membrane oxygenation	**RECOVERY**	Randomised Evaluation of COVID-19 therapy
HCWLN	Health & Care Women Leaders Network	**REMAP-CAP**	Randomised, embedded, multi-factorial, adaptive platform trial for community-acquired pneumonia
HTT	Hospital transfusion team	**SAE**	Serious adverse event
ICU	Intensive care unit	**SAR**	Serious adverse reaction
IgG	Immunoglobulin G	**SARS-CoV-2**	Severe acute respiratory syndrome coronavirus 2
JPAC	Joint UKBTS Professional Advisory Committee	**TACO**	Transfusion-associated circulatory overload
MHRA	Medicines and Healthcare products Regulatory Agency	**TAD**	Transfusion-associated dyspnoea
NBTC	National Blood Transfusion Committee	**UK**	United Kingdom

Recommendation

- All National Health Service (NHS) organisations should ensure that learning from the pandemic experiences is captured and used to improve patient safety

Action: All NHS organisations

COVID-19 pandemic and impact on transfusions

The COVID-19 pandemic has massively disrupted and exacerbated the shortcomings in healthcare but has also served as a catalyst for much needed transformation, which occurred at an accelerated pace. The challenge now is to harness all the learning from experiences and build on the momentum from efforts during the pandemic to improve systems further. This new chapter will specifically cover the influence of the pandemic on haemovigilance.

The COVID-19 pandemic has had major implications for blood transfusions. This period has been marked by uncertain demand patterns. Elective and non-COVID-19 related care largely stopping during the pandemic. The demand for blood reduced during the first peak but was as predicted during the second wave with continuation of most services in the NHS. The NBTC Emergency Planning Working Group produced the Emergency Preparedness, Resilience and Response guidance for hospital transfusion teams in 2020 and an emergency preparedness gap analysis tool both of which can be accessed from the JPAC website (link provided in references). The NBTC also produced guidance for appropriate specification for emergency red cells and a platelet shortage plan in October and November 2020.

The four UK Blood Services worked collaboratively to ensure a continuing safe supply of blood during the pandemic. COVID-19 challenged donor selection practices, balancing the need to supply whilst ensuring donor safety. Donor haemovigilance was particularly important given donors were recovering from an emerging illness (see Chapter 7, Donor Haemovigilance). Donor selection guidelines were regularly reviewed and updated in line with international guidance. Revised collection guidelines ensured donor, donation, and staff safety.

To date, there has not been any evidence of transmission of SARS-CoV-2 via transfusion of blood components, and this risk is therefore currently theoretical and considered highly unlikely. The pandemic has had an impact on blood supplies through reduced blood donation and reduced availability of appropriate collection facilities. It is the responsibility of Blood Services to take steps to assess, plan, and respond to the challenges appropriately and proportionately after undertaking a data-driven risk assessment (WHO 2021).

Nightingale hospitals

New pop-up COVID-19 hospitals were set up as temporary hospitals in the UK as part of the response to the COVID-19 pandemic. This reflected wider NHS re-structuring to prepare for the pandemic and anticipated strain on NHS services. They principally include the eight NHS England Nightingale Hospitals (London, Birmingham, Bristol, Cumbria, Exeter, Harrogate, Manchester, and Sunderland), NHS Scotland's Louisa Jordan hospital, NHS Wales' Dragon's Heart Hospital, and the Northern Irish Health and Social Care site at Belfast City Hospital. The field hospitals were intended to be used to treat critical care patients who were regarded as being less severely ill, while the most severely ill patients were treated in mainstream NHS hospitals. Transfusion needs were predicted to be low at these sites, nevertheless a transfusion service needed to be established within a tight time frame ensuring full traceability with staff trained and competent in transfusion-related procedures including recognition, management and reporting of transfusion reactions. Transfusion services set up at these sites is a testament to the incredible work of clinical and laboratory transfusion staff from local hospitals supported by the UK Blood Services. SHOT is planning a survey to capture learning from establishing these transfusion services at the pop-up sites later this year and results will be shared widely.

Blood use in COVID-19 patients

Transfusion requirements in COVID-19 patients is low even in those who are critically ill (Barriteau et al. 2020). Sanz et al. (2020) showed that bleeding, mostly related to the use of anticoagulants, was the main indication for red blood cell transfusion in patients with COVID-19. A single centre experience showed that red cell concentrates were the most frequently transfused component in COVID-19 infected patients with higher use during veno-venous ECMO (Doyle et al. 2020). This study from the international Extracorporeal Life Support Organisation Registry provides data on 1035 ECMO-supported patients with COVID-19 who received care in 36 countries and showed that in patients with COVID-19 who received ECMO, both estimated mortality 90 days after ECMO and mortality in those with a final disposition of death or discharge were less than 40%. This supports the use of ECMO in refractory COVID-19-related respiratory failure.

Impact on staff

Undoubtedly, staff working in the NHS are its greatest asset and are key to delivering high-quality care. Poor workforce planning, weak policies and funding shortages which are longstanding and worsened during the pandemic have resulted in a workforce crisis. These staffing challenges across the NHS invariably impact transfusion practices as blood transfusions occur in various medical, surgical, and obstetric settings and across adult and paediatric patients. These challenges are not only in the clinical but also in the transfusion laboratory setting. Serial UKTLC surveys have highlighted staffing concerns both with numbers and skill mixes (Bolton-Maggs et al. 2019; UKTLC, 2019). Many reports submitted to SHOT have highlighted the challenges with reduced staffing due to any reason (redeployment, sickness, etc) during the pandemic with staff unfamiliar with transfusion practices needing to undertake these roles with little or no training/supervision reflective of the challenging circumstances. One of the greatest challenges lies in nursing, with nearly 38,000 vacancies (one in ten posts). Unfilled vacancies increase the pressure on staff, leading to high levels of stress, absenteeism, and turnover (Kings Fund 2021). This has been compounded by the COVID-19 pandemic which has exacerbated long term issues such as chronic excessive workload, burnout and inequalities experienced by ethnic minority staff.

The NHS Confederation (2021) and HCWLN have recently undertaken a survey to gather information about the impact COVID-19 has had on all health and care workers, the survey closed on 5th March 2021 and results are awaited. In June 2020, the HCWLN commissioned a survey to better understand the impact the pandemic has had on women working across health and care services. Over 1,300 women responded, and the report describes the struggles, pains and fears women working in health and care services have faced during the pandemic. The physical and emotional impact due to caring responsibilities both in and outside of work are significant. It also draws out some of the positive experiences, such as opportunities for learning and the strength of support many have received from their managers and provides valuable recommendations. With NHS staff being predominantly female (77%), this is very pertinent and the recommendations in this report along with the NHS People Plan for 2020/21 and People Promise (links provided in the reference list) will help improve staff well-being with several measures being identified that organisations need to be equipped with.

Digital acceleration

Healthcare has undergone a rapid digital progression in 2020. This has been a period of great innovation and use of digital technology for both patients and staff, while supporting enhanced quality of care and increased efficiency. From telephone/video consultations for patients, electronic patient records, electronic decision-making systems, electronic prescribing to virtual staff inductions, virtual training for healthcare professionals, team meetings and collaborations using platforms such as Zoom, Microsoft Teams or Skype, this has truly been a period of digital transformation in the NHS.

However, there needs to be a huge cultural change before a fully digital NHS can become a reality. Lack of digital awareness, reluctance to fund digital solutions, insufficient resources, and lack of universal solutions results in each institution trying to find optimal solutions that fit in with their outdated legacy systems. Barriers to interoperability have been highlighted which need to be addressed urgently. Any solution for a clinical setting should be designed with patients and users in mind. Clinicians are rarely

consulted about digital solutions, and this is critical to have meaningful transformation and uptake. It is important to ensure that digital inclusion tools and effective broadband are available to all so that health inequalities are not further exacerbated, and every effort must be made to improve digital literacy of patients.

COVID-19 convalescent plasma (CCP)

CCP, donated by persons who have recently recovered from COVID-19, is the acellular component of blood that contains antibodies, including those that specifically recognise the SARS-CoV-2 virus. These antibodies, when transfused into patients infected with SARS-CoV-2, are thought to exert an antiviral effect, suppressing virus replication before patients have mounted their own humoral immune responses. Safety and efficacy of CCP were tested as part of two large randomised controlled trials in the UK. Early in the pandemic, the Chief Medical Officers of England, Wales, Scotland and Northern Ireland, and the NHS Medical Director, wrote to all doctors in the UK strongly encouraging participation in the national randomised trials in COVID-19, CCP was included as part of RECOVERY and REMAP-CAP trials (CAS Alert April 2020 and links to trial websites provided in the references section).

REMAP-CAP included CCP as a treatment randomisation option (CCP versus standard care +/- other randomised treatments) in adults admitted to ICU within the preceding 48 hours with confirmed COVID-19 and patients received up to two ABO-compatible CCP on study day 1 and day 2. Early findings from REMAP-CAP established that treatment with CCP provided no benefit for the general critically ill population with COVID-19. There was no evidence of harm associated with CCP and enrolment of severely ill COVID-19 patients to this arm of REMAP-CAP study was stopped early January 2021.

The RECOVERY trial was an investigator-initiated, individually randomised, controlled, open-label, adaptive platform trial to evaluate the effects of potential treatments in patients hospitalised with COVID-19. Hospitalised patients of any age were eligible for the trial if they had clinically suspected or laboratory-confirmed SARS-CoV-2 infection and no medical history that might, in the opinion of the attending clinician, put them at significant risk if they were to participate in the trial. Between 28 May 2020 and 15 January 2021, 5795 patients were randomly allocated to receive CCP and 5763 to usual care alone. Data from RECOVERY has shown that among patients hospitalised with COVID-19, high-titre CCP did not improve survival or other pre-specified clinical outcomes (The RECOVERY Collaborative Group 2021).

Following these results from REMAP-CAP and RECOVERY, the Chief Medical Officers of England, Wales, Scotland and Northern Ireland, and the NHS Medical Director, wrote to all doctors in UK in March 2021 recommending that CCP must NOT be used in the management of hospitalised patients with confirmed or suspected SARS-CoV-2 infection (CAS Alert March 2021).

CCP is a blood component and as such all SAE and SAR related to CCP are reportable to the MHRA and SHOT in the UK as part of the national haemovigilance scheme. Data from SHOT helped inform safety data regarding CCP and provided a unique opportunity to collaborate and have direct input into clinical trials from a haemovigilance perspective. Just over 13,000 units of CCP were transfused under the two trials with only 14 confirmed SAR (from RECOVERY and REMAP-CAP) equating to a risk of SAR of 1 in 958 units of CCP, over the trial period. The most common reactions seen in CCP recipients were febrile, allergic, or hypotensive reactions and pulmonary reactions (TACO/TAD). No reactions have been noted to be definitely related to CCP. Cases which were submitted during 2020 are counted in the figures for this Annual SHOT Report and are covered in more detail in the respective chapters. Of note, there were no reports of ADE related to CCP administration. ADE refers to a form of immune enhancement, a poorly understood group of phenomena occurring when components of the immune system that usually protect against viral infections somehow end up being counterproductive. Antibodies created during a first-time infection could, under very specific circumstances, end up enhancing the disease rather than protecting against subsequent infections. While there is a theoretical risk that antibodies in CCP could enhance disease via ADE, literature available shows that CCP therapy is safe (Lee et al. 2020). This has been corroborated by the UK trials. Errors were reported relating to CCP use, and these have been covered in respective chapters and reflect challenges faced by staff during the pandemic along with the dynamic situations when managing seriously ill patients deteriorating rapidly.

The two large RCT from UK have helped establish the evidence that CCP does not improve survival or other clinical outcomes in patients hospitalised with COVID-19. A systematic review and meta-analysis published in February 2021 confirmed that treatment with CCP compared with placebo or standard of care was not significantly associated with a decrease in all-cause mortality or with any benefit for other clinical outcomes. The certainty of the evidence was low to moderate for all-cause mortality and low for other outcomes (Janiaud et al. 2021). However, a recent small scale (160 patients) randomised, double-blind, placebo-controlled trial of CCP with high IgG titres against SARS-CoV-2 in older adult patients within 72 hours after the onset of mild COVID-19 symptoms showed that early administration of high-titre CCP to mildly ill infected older adults reduced the progression of COVID-19 (Libster et al. 2021). While this is encouraging, further large-scale trials are needed in this subset of patients.

The CCP trials also helped increase transfusion awareness in frontline staff. At the time of closure, there were 226 hospitals in the UK open to CCP in the RECOVERY trial and 122 sites recruited to REMAP-CAP (staff received training before opening). The need for the administration checklist and TACO checklist prior to CCP and transfusion safety messages were cascaded to staff at these sites and helped raise awareness of transfusion and haemovigilance issues.

Haemovigilance reporting during the pandemic

Just over 2 million blood components were issued in 2020 from the 4 UK Blood Services. A total of 4063 reports were received by SHOT in 2020 equating to 19.6 reports per 10,000 components issued which continues a steady upward trend from the preceding years despite all the challenges.

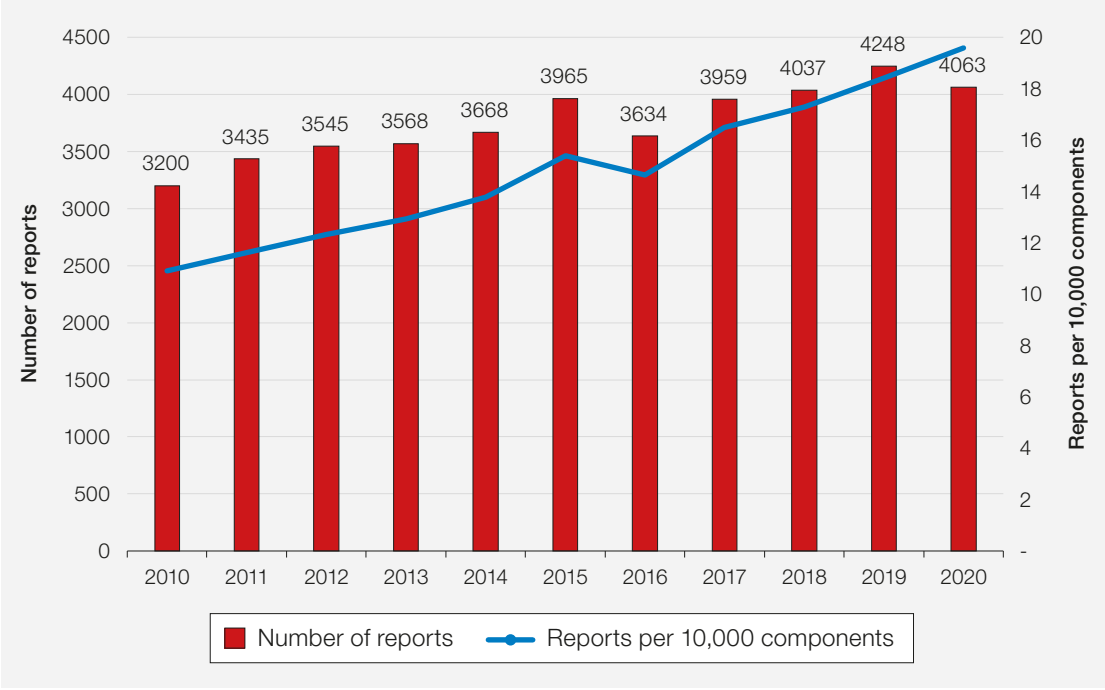


Figure 5.1
Trend in reports per 10,000 components issued in the UK

The variation in the number of reports submitted at different periods in the year has been described further in Chapter 2, Participation in United Kingdom (UK) Haemovigilance. The distribution of the reports across the reporting categories is similar to preceding years apart from a large increase in febrile, allergic and hypotensive reactions. Errors continue to account for majority of the reports and whilst pressures relating to the pandemic have been identified as contributory to some of these, there does not seem to be any steep increase in the proportion of errors. RCA summaries submitted have highlighted the staffing challenges including staff shortages, staff unfamiliar with transfusions, hyperdynamic situations with critically ill patients, and challenges with carrying out tasks with full personal protective equipment in COVID-19. These have been alluded to in the respective chapters.

It is encouraging to see haemovigilance activities continue despite challenges faced by frontline staff because patient safety is a priority. The 2019 SHOT recommendations survey showed that 98.9% of

respondents continued with haemovigilance reporting, however, 67% noted difficulties in obtaining information due to restricted access to clinical areas, staff redeployment and staffing levels. Investigating incidents was also reported to be challenging due to these factors (SHOT Recommendations survey 2019 https://www.shotuk.org/wp-content/uploads/myimages/2019-Recommendations-Survey.pdf).

Several factors emerge as being key to haemovigilance reporting during the pandemic:

- **The importance of electronic reporting**: the pandemic underlines how electronic or paperless reporting is the most effective and reliable reporting method. Reporting to SHOT has been paperless since 2005
- **Established communication channels with haemovigilance staff**: proactive communications help understand challenges and requirements, helps to engage with key stakeholders and resolve issues in a timely manner
- **Importance of a robust, reliable, and responsive team of haemovigilance experts**: Haemovigilance plays a fundamental role in enhancing transfusion safety by learning from reports submitted and then putting in place system changes to prevent them in future. Haemovigilance reporting is useless if it does not result in quality improvement. Learning from intelligence gathered from haemovigilance reporting is vital and this is only possible with access to subject matter experts who will be able to review submitted reports and recognise trends and actions that need to be taken
- **An established reporting culture:** Cultivating an atmosphere where people have the confidence to report safety concerns without fear or blame and trust that the information, they submit will be acted upon is vital for any reporting system including haemovigilance. When there is an established reporting culture, staff are themselves motivated to continue reporting in the interest of patient safety even in challenging times
- **Robust business continuity and contingency plans in healthcare organisations** help teams identify, prioritise actions and allocate resources proportionately when faced with staffing challenges and unprecedented demands on care provision as seen during the pandemic. Minimum staff needed for governance activities must be identified. Whilst safety reporting is important, and should continue especially during these challenging periods to help identify emerging risks, patient care takes precedence
- **Relevant meaningful outputs from the haemovigilance system and feedback loops:** supporting educational materials and safety alerts as appropriate from haemovigilance schemes, digital learning resources to support staff learning are important to optimise patient safety. Feedback loops help understand challenges, prompt behaviour change and establishes an adaptive haemovigilance system
- **Collaboration with international haemovigilance experts and sharing resources and experiences:** When faced with these unprecedented challenges, sharing experiences, issues faced, and solutions applied helped teams and organisations to learn from each other. This helped ensure appropriate measures could be instituted in a timely manner. The pandemic is borderless so should patient safety learning be

It is important to look back and acknowledge progress with respect to transfusion safety. Although the COVID-19 pandemic has forced major changes and challenges for the NHS, we have seen staff and systems rise to meet these. New ways of working, improved cooperation, collaboration and communication have been amply demonstrated, all contributing to patient safety despite the ongoing challenges.

Highlights of lessons learnt through the COVID pandemic

Author: Julie Staves, Transfusion Laboratory Manager at Oxford Radcliffe Hospitals NHS Trust

The National Transfusion Laboratory Managers and Practitioner groups in England worked together to produce a summary of the lessons learnt through the pandemic.

The highlights of this included:

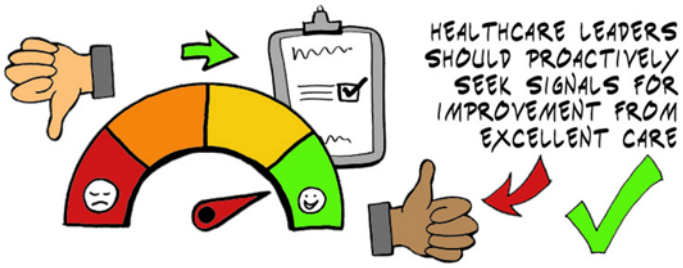
- Stock management is key to ensuring adequate supplies of blood components whilst not limiting wastage. Reviewing stock levels frequently is important to react to changing situations quickly
- Maintaining traceability remained a legal responsibility and changes were needed for clinical areas treating infectious patients. This included quarantining tags. Overall Trusts using electronic systems found the impact less
- The use of satellite refrigerators caused issues in lots of hospitals. Management were keen to purchase new refrigerators or re-site existing refrigerators. The logistics of this were often complex and the impact on the HTT was not considered. Maintenance of refrigerators was more complex especially in COVID-19 'hot' areas
- Training of clinical staff was difficult, but the need also increased as staff were redeployed. The use of e-learning was well used and most adapted sessions to make the most of electronic remote meeting capacity

Overall, the HTT worked hard at maintaining standards and found taking a safe but adaptable approach was the best way forward.

Conclusion

While we may feel the urge to bury the past year for obvious reasons, we must harness a growth mindset and learn from experiences, grow stronger and build safer systems, being wiser from the challenges we have faced together. There is much to take away from our pandemic experiences, the most important being that despite personal and professional challenges, the transfusion community and indeed the whole NHS came together, worked, and supported each other and all those who needed our help. It was resilience in action that helped navigate the uncertain and challenging times. It is also important to recognise and acknowledge that it is people who matter. Ensuring staff safety and wellbeing with adequate resources and a good safety culture will automatically translate to improved staff engagement, safer systems, and better patient outcomes. Sharing experiences and developing expert consensus based on emerging evidence has certainly helped transfusion services during the pandemic (Stanworth et al. 2020).

As we tentatively look towards a recovery from the pandemic, it is an opportunity to collectively reflect, grieve, learn, and develop as a global community.



SHOT
Serious Hazards of Transfusion

References

Barriteau CM, Bochey P, Lindholm PF, et al. Blood transfusion utilization in hospitalized COVID-19 patients. *Transfusion*. 2020;**60(9)**:1919-1923. doi:10.1111/trf.15947.

Bolton-Maggs, P., Mistry, H., Glencross, H., Rook, R. and (2019), Staffing in hospital transfusion laboratories: UKTLC surveys show cause for concern. Transfusion Med, **29**: 95-102. https://doi.org/10.1111/tme.12593

CAS Alert: Novel Coronavirus: Clinical Trials. April 2020. https://www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAlert.aspx?AlertID=103012 [accessed 27 April 2021].

CAS Alert: Convalescent Plasma in the Management of Hospitalised Patients with COVID-19. March 2021. https://www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAlert.aspx?AlertID=103152 [accessed 27 April 2021].

Doyle AJ, Danaee A, Furtado CI, et al. Blood component use in critical care in patients with COVID-19 infection: a single-centre experience. *B J Haem* 2020;**191(3)**:382-385.doi: 10.1111/bjh.17007.

Janiaud P, Axfors C, Schmitt AM, et al. Association of Convalescent Plasma Treatment With Clinical Outcomes in Patients With COVID-19: A Systematic Review and Meta-analysis. *JAMA* 2021;**325(12)**:1185-1195. doi:10.1001/jama.2021.2747.

Lee WS, Wheatley AK, Kent SJ, et al. Antibody-dependent enhancement and SARS-CoV-2 vaccines and therapies. *Nat Microbiol* 2020;**5(10)**:1185-1191 https://doi.org/10.1038/s41564-020-00789-5 [accessed 27 April 2021].

Kings Fund. NHS Workforce: our position. Part of The King's Fund position. 2021 https://www.kingsfund.org.uk/projects/positions/nhs-workforce [accessed 27 April 2021].

Libster R, Perez Marc G, Wappner D, et al. Early High-Titer Plasma Therapy to Prevent Severe Covid-19 in Older Adults. *N Engl J Med* 2021;**384**:610-618. DOI: 10.1056/NEJMoa2033700.

JPACa. NBTC Emergency Planning Working Party publications. (n.d.) https://www.transfusionguidelines.org/uk-transfusion-committees/national-blood-transfusion-committee/working-groups [accessed 27 April 2021].

JPACb. Welcome to the National Blood Transfusion Committee. (n.d.) https://www.transfusionguidelines.org/uk-transfusion-committees/national-blood-transfusion-committee [accessed 27 April 2021].

NHS Confederation. Impact of COVID-19 on staff working in health and care sectors. 2021 https://www.nhsemployers.org/news/2021/02/impact-of-covid-19-on-the-health-and-care-workforce [accessed 27 April 2021].

NHS People Plan for 2020/2021 – action for all of us. https://www.england.nhs.uk/ournhspeople/ [accessed 04 May 2021].

NHS: Our NHS People Promise. https://www.england.nhs.uk/ournhspeople/online-version/lfaop/our-nhs-people-promise/ [accessed 04 May 2021].

RECOVERY trial. 2021 https://www.recoverytrial.net/ [accessed 27 April 2021].

REMAP-CAP trial. 2021 https://www.remapcap.org/ [accessed 27 April 2021].

Sanz C, Faundez A, García Carulla A, et al. Hemorrhage Is a Major Cause of Blood Transfusion in COVID-19 Patients. *Blood* 2020;**136(1)**:21-22. https://doi.org/10.1182/blood-2020-138830 [accessed 27 April 2021].

Stanworth S, New H, Apelseth T, et al. Effects of the COVID-19 pandemic on supply and use of blood for transfusion. *Lancet Haematol* 2020;**7(10)**:e756-764. https://www.thelancet.com/journals/lanhae/article/PIIS2352-3026(20)30186-1/fulltext [accessed 27 April 2021].

The RECOVERY Collaborative Group, Horby PW, Estcourt L, et al. Convalescent plasma in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial. *medRxiv* 2021 doi: https://www.medrxiv.org/content/10.1101/2021.03.09.21252736v1 [accessed 27 April 2021].

UKTLC 2019 survey. Accessible on the SHOT website. https://www.shotuk.org/uktlc-survey-2019/ [accessed 04 May 2021].

WHO. Maintaining a safe and adequate blood supply and collecting convalescent plasma in the context of the COVID-19 pandemic. 2021. https://www.who.int/publications/i/item/WHO-2019-nCoV-BloodSupply-2021-1 [accessed 27 April 2021].

Acknowledging Continuing Excellence in Transfusion (ACE) 6

Authors: Shruthi Narayan, Jennifer Davies, Debbi Poles, Emma Milser, Simon Carter-Graham, Victoria Tuckley and Fahim Ahmed

With contributions from Heidi Doughty, Terrie Perry, Fiona Regan, Megan Rowley, and Charlotte Silver

Definition:

Exceptional transfusion practice by a team or department, that was above and beyond routine practice and has widespread learning opportunities.

Abbreviations used in this chapter

ACE	Acknowledging Continuing Excellence in Transfusion	**NM**	Near miss
AI	Appreciative inquiry	**SAE**	Serious adverse event
NHS	National Health Service	**SAR**	Serious adverse reaction

Introduction

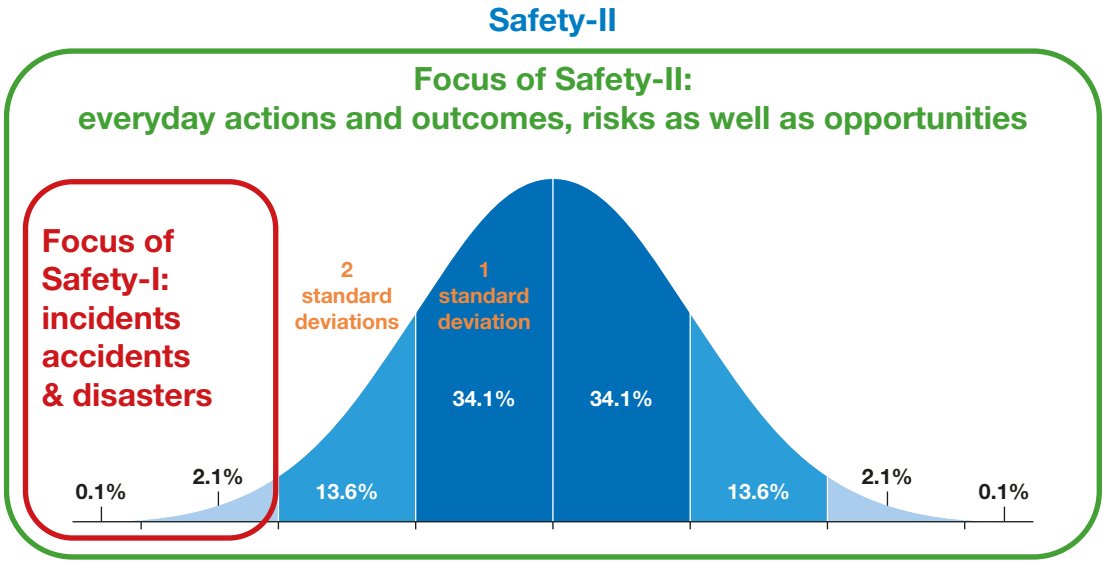
ACE was introduced in the 2019 Annual SHOT Report with a dual aim of recognising exceptional practice by teams or departments above and beyond routine practice and recognising innovative solutions to previous adverse events. Whilst SHOT continues to report on adverse transfusion incidents and reactions, it has always been acknowledged that excellence is highly prevalent and identifying this in the report will provide new opportunities for local learning and improving resilience and staff morale, contributing to a holistic approach to patient safety.

Incident investigations may recognise aspects of good practice or praise individuals for their actions but is mainly focussed on the errors and interventions for prevention of recurrence. This is the traditional Safety-I, or risk management, approach. Safety-II is a proactive approach looking at safe episodes of care to inform improvement in healthcare systems. Safety-II approach helps understand how things go right to explain how occasionally things go wrong and continuously aim to anticipate developments and events. This reframing of safety has major implications for the way we design our systems and the role of people within them. These affect everything, from our approaches to incidents, to quality improvement, to the way we train and lead teams. Learning from how things go right, rather than wrong, is an important element of Safety-II and is especially powerful since things go right much more often than they go wrong (Figure 6.1, Hollnagel 2015). Learning how staff provide good care under difficult circumstances means we can ensure it happens more often.

We hope to promote a safer culture by looking at both instances of ‘what went wrong’ and ‘what went right’. It is clear that there is a place for both Safety-I and Safety-II approaches. Safety-II does not replace Safety-I, they complement each other and provide a different and valuable perspective.

Appreciative inquiry (AI) is an effective tool to help reframe safety issues and improve patient care. It is an engaging, inclusive, and collaborative way of exploring issues in healthcare, especially because it aligns neatly with the Safety-II paradigm. AI focuses on acknowledging strengths and values of individuals and organisations while understanding, accepting, and searching for positive meanings. It is effective at improving teamwork and helps improve team performance. This tool can be used as a framework for improvement projects or system-wide change (Bushe 2011, Trajkovski 2013).

Figure 6.1: From Safety-I to Safety-II



Note: this figure is from James Christie's Blog, adapted from the Safety-I and Safety-II diagrams from the document 'From Safety-I to Safety-II: A White Paper (EUROCONTROL, 2013) and 'A White Paper on Resilience Engineering for ATM (EUROCONTROL, 2009)

Recommendation

- All National Health Service (NHS) organisations should provide education and resources to support an effective safety culture based on a proactive approach to patient safety

Action: All NHS Trusts/Health Boards

Safety culture

SHOT has repeatedly promoted the importance of a 'just and learning culture' in healthcare, a culture in which individuals are not held accountable for systems failures over which they have no control and a culture in which learning from experiences is encouraged. By supporting staff to be open about mistakes, feel confident to speak up about potential risks and not fear blame, the organisation can learn valuable lessons and use this knowledge to ensure that errors are not repeated. We have provided the human factors toolkit (see Chapter 8, Human Factors in SHOT Error Incidents) within the SHOT incident reporting platform enabling reporters to incorporate a systems-based approach into their investigations and avoid placing blame on individuals.

Fostering a strong and effective safety culture is also vital to reduce transfusion incidents thus directly improving patient safety. This environment promotes effective leadership and teamwork, a feeling of psychological safety for the staff, inclusivity, trust and respect, a shared vision and above all, an openness and support for learning.

The Health Foundation developed a framework for measuring and monitoring safety. This sought to shift an organisation's thinking from reliance on regulatory compliance as a guarantor of safety (a mindset of assurance) to a proactive approach of measurement and monitoring (a mindset of enquiry) (Chatburn et al. 2018). This framework encompasses five core dimensions of safety as shown below in Figure 6.2.

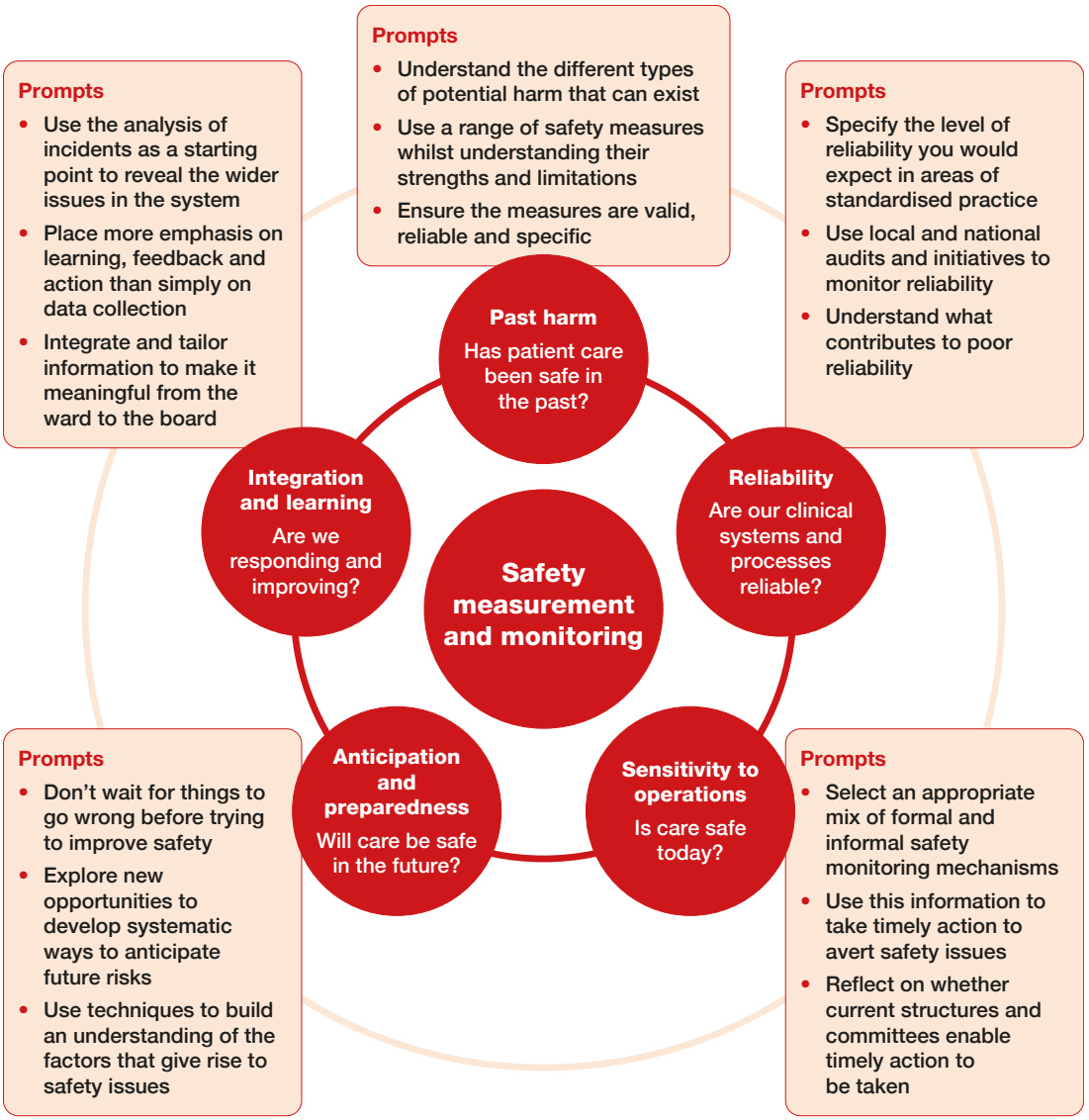


Figure 6.2: The framework for measuring and monitoring safety – and useful prompts for using it in practice (from the Health Foundation, 2018)

Using these core dimensions in their entirety can encourage organisations to take a holistic and proactive view of patient safety and support a cultural shift from the traditional risk management viewpoint. For a framework such as the one above to be effective it needs committed leadership from individuals that understand the concepts of Safety-I and Safety-II (Hollnagel et al. 2015), sufficient resources to implement and sustain this approach and a process for translating this for front line staff. The NHS Improvement's 'A Just Culture guide' also provides a powerful tool to help promote cultural change in organisations or teams where a blame culture is still prevalent (NHSI 2018).

Serial Annual SHOT Reports have shown a good, strong reporting culture in the UK. The participation data is reassuring and reports, including near miss events, continue to be submitted to SHOT year on year, even during the pandemic year 2020. Proactive, preventative, and predictive measures that provide information about the performance of healthcare activities are vital and help prevent incidents and improve safety. NM have potentially predictive qualities because they can help uncover hazards, risks, process weaknesses and patterns that can be addressed to avoid future incidents. Near miss reporting should be encouraged and reporting must be made as easy as possible. NM year on year constitute the biggest reporting category in SHOT and these have been picked up by vigilant staff (see Chapter 13, Near Miss (NM) Reporting). Learning from NM and improving systems will help reduce actual events and improve safety. As noted in Chapter 2, Participation in UK Haemovigilance, areas of underreporting have been recognised, possibly due to staff shortages and inadequate resources which need to be addressed and investigated further. One of the key 2019 SHOT recommendations was that all National Health Service (NHS) organisations should embrace Safety-II approach as a complement

to Safety-I, should analyse where and when things go wrong, proactively seek to prevent, eliminate risks and promote compliance with Safety-II by developing ways to support, augment and encourage these (Narayan et al. 2020).

ACE reports

A new reporting category was introduced by SHOT in January 2021 – reporters can submit instances of exceptional transfusion practice by a team or department, that was above and beyond routine practice and has widespread learning opportunities. Reporting in this category is not included in the participation data for SAE and SAR. Further information about this category and illustrative cases can be accessed from the SHOT website. It is hoped that this will encourage local processes to be put in place to recognise excellent contributions by individuals or teams and promote sharing best practices between teams.

SHOT have convened an ACE working group, the aim of this group is to promote reporting in this category, to review reports submitted to other categories, and withdrawn SHOT reports, for ACE aspects that can be shared as good practice. Some reported cases are withdrawn each year, as upon expert review, it is agreed that the clinical/laboratory teams have consciously made transfusion decisions taking into account the overall clinical picture of the patient and assessing risks and benefits. In such cases, individuals or teams may have identified learning that can be shared with the wider transfusion community to avoid similar scenarios, outside the confines of expected contingency planning. An example of such a report submitted included one that related to a full power outage which disconnected analysers, blood component storage devices, computer systems and telephone lines in a hospital transfusion laboratory. This report demonstrated the power of individuals working together to ensure that patient care was not adversely affected during this challenging time. SHOT was able to share the learning from this event, and the importance of robust contingency plans, via a national patient safety notice (available on the SHOT website https://www.shotuk.org/resources/current-resources/).

It is important to recognise that transfusion support is an essential element of modern healthcare and therefore should be considered in disaster preparedness. In addition, many national civil contingency arrangements require healthcare providers to demonstrate that they can deal with emergencies while maintaining critical services. Emergency preparedness is essential to provide a co-ordinated response to the event, maintain business continuity and guide recovery to ‘business as usual’. Any response should be flexible and scalable to deal with a variety of emergency incidences including combinations of escalating and unexpected events. The emergency response involves a mixture of plans, procedures, and improvisation (Alexander 2015). All give the opportunity to demonstrate excellence. Lessons identified should be captured during post event reviews as soon as practicable after the incident. Debriefing should be used to thank staff and recognise achievements. The principles of joint organisational learning should then be used across the global transfusion community to share excellence and continually improve the dynamic process of transfusion disaster preparedness.

Patient perspective

Author: Charlotte Silver (Lay Member)

Having received blood components throughout my life due to a rare and chronic blood condition, I welcome the addition of the ACE chapter. Learning from excellence is important in all areas of life but in a clinical setting it is nothing short of essential in order to enable more lives like mine to be saved and improved.

As an experienced patient I am reassured by comprehensive, timely, bedside checks and recognise their vital importance. I have the confidence to speak up if checks are not done in part or in full and have raised this as a concern in the past, however many patients may not recognise that a check has not been completed in full or they may not feel comfortable to speak up. As a patient you feel vulnerable, with little control over your treatment, you are reliant on excellent communication with medical staff and the lack of free movement due to being hooked up to machines can compound the feeling of being vulnerable.

Untimely and unclear communication between clinical teams makes me extremely nervous and adds extra anxiety to my appointments. I would rather my treatment was delayed whilst the hospital team check and recheck my treatment plan and/or bloods and this be communicated to me honestly, promoting respect and trust between patient and clinician.

I recognise just how hectic and stressful hospitals are and I am forever grateful and in awe of those who provide patient care. Behaviour change, such as taking time to acknowledge and learn from continuing excellence is a slow process made harder in busy and challenging circumstances. However, the COVID-19 pandemic has shown that it is possible to still create a nurturing culture of learning from excellence. As a patient I am reassured to know that there are steps being taken to acknowledge and learn from excellence and hope that this initiative will be taken up by all clinicians as it will be beneficial to not only clinicians but also patients.

Conclusions

There are several instances in reports submitted to SHOT where staff have demonstrated excellence in communication and collaboration to ensure safe transfusions. We encourage reporting all these instances where staff have taken proactive measures to improve communication, reduce delays and ensure safe bedside checks. If your team or organisation has made an extraordinary response in the face of adversity, or the unprecedented challenges of the pandemic, please share this via an ACE submission. If you have implemented an improvement action or identified a further measure for safety in a risk assessment, that has worked well, is sustainable and transferrable to other organisations this should be reported.

Learning from excellence has a valuable role to play in haemovigilance schemes and SHOT strongly encourages submissions to ACE. Learning from excellence and sharing good practice acts as a proactive safety measure in the absence of patient harm. As the number of SHOT-ACE reports increase, a repository of good practice will be developed and shared on the SHOT website. Sharing a single organisation's learning or good practice on a national repository can translate into avoidance of patient harm across a multitude of other organisations.

Combining Safety-I and Safety-II approaches will help provide a more holistic understanding of the underlying reasons for errors and procedural violations. This will help identify aspects of practice that could benefit from targeted interventions to help support staff in providing safe patient care. Reporting and studying success augments learning, enhances patient outcomes and experience through quality improvement work and positively impacts resilience and culture in the workplace.

Recommended resources

SHOT Safety Notice 01: Emergency preparedness in the transfusion laboratory in case of total power outage
https://www.shotuk.org/resources/current-resources/

ACE reporting - ACE definitions
https://www.shotuk.org/resources/current-resources/

ACE reporting – illustrative examples
https://www.shotuk.org/resources/current-resources/

SHOT
Serious Hazards of Transfusion

References

Alexander DE. Disaster and Emergency Planning for Preparedness, Response, and Recovery. Oxford Research Encyclopedia of Natural Hazard Science. 2015. https://doi.org/10.1093/acrefore/9780199389407.013.12 [accessed 27 April 2021].

Bushe GR. Appreciative inquiry: Theory and critique. In Boje, D., Burnes, B. and Hassard, J. (eds.) The Routledge Companion To Organizational Change 2011. (pp. 87103). Oxford, UK: Routledge.

Chatburn E, Macrae C, Carthey J, et al. Measurement and monitoring of safety: impact and challenges of putting a conceptual framework into practice. *BMJ Quality & Safety* 2018;**27(10)**:818-826. https://qualitysafety.bmj.com/content/27/10/818 [accessed 27 April 2021].

EUROCONTROL: A White Paper on Resilience Engineering for ATM. 2009. https://www.eurocontrol.int/sites/default/files/2019-07/white-paper-resilience-2009.pdf [accessed 05 May 2021].

EUROCONTROL: From Safety-I to Safety-II: A White Paper. 2013. https://www.skybrary.aero/bookshelf/books/2437.pdf [accessed 05 May 2021].

Hollnagel E, Wears RL and Braithwaite J. (2015) From Safety-I to Safety-II: A White Paper. The Resilient Health Care Net: Published simultaneously by the University of Southern Denmark, University of Florida, USA, and Macquarie University, Australia. https://www.england.nhs.uk/signuptosafety/wp-content/uploads/sites/16/2015/10/safety-1-safety-2-whte-papr.pdf [accessed 27 April 2021].

James Christie's Blog: The dragons of the unknown; part 6 – Safety II, a new way of looking at safety. https://clarotesting.wordpress.com/2018/10/25/the-dragons-of-the-unknown-part-6-safety-ii-a-new-way-of-looking-at-safety/ [accessed 05 May 2021].

Narayan S (Ed), Poles D, et al. on behalf of the Serious Hazards of Transfusion (SHOT) Steering Group. The 2019 Annual SHOT Report (2020). https://www.shotuk.org/shot-reports/ [accessed 27 April 2021].

NHS Improvement: A just culture guide https://www.england.nhs.uk/patient-safety/a-just-culture-guide/ [accessed 27 April 2021].

Trajkovski S, Schmied V, Vickers M, et al. Using appreciative inquiry to transform health care. *Contemp Nurse* 2013;**45(1)**:95-100.

Donor Haemovigilance

7

Authors: Dr Lorna McLintock, Clinical Lead for Blood Donation, SNBTS
Dr Shruthi Narayan, SHOT Medical Director and Consultant in Donor Medicine, NHSBT
Dr Kathryn Maguire, Consultant in Transfusion Medicine, NIBTS
Dr Stuart Blackmore, Consultant in Donor Medicine, WBS
Sue Mackinnon, Lead Quality and Governance Nurse, WBS

With contribution from Dr Ibrahim Magzoub, NIBTS

Definition:

Donor haemovigilance refers to the systematic monitoring of adverse reactions and incidents during the blood donor's journey, with a view to improving donor experience and safety.

Serious adverse reaction: An unintended response in a donor or a patient associated with the collection or transfusion of blood or blood components that is fatal, life threatening, disabling, incapacitating, or which results in, or prolongs, hospitalisation or morbidity (according to Article 3(h) of directive 2002/98/EC).

Key SHOT messages

- The overall incidence of serious adverse events of donation (SAED) remains low. The rate of SAED for 2020 in the United Kingdom (UK) was 0.22 per 10,000 donations
- Experience during the COVID-19 pandemic has shown that the UK Blood Services and the transfusion community work in an adaptive and collaborative way which is important in improving donation and transfusion safety
- Vasovagal events and bruising were more common in COVID-19 convalescent plasma (CCP) donors by both whole blood and plasmapheresis compared with regular whole blood and platelet donors

Abbreviations used in this chapter

ACE-2	Angiotensin converting enzyme 2
ACS	Acute coronary syndrome
AF	Atrial fibrillation
BP	Blood pressure
BSQR	Blood Safety and Quality Regulations
CCP	COVID-19 convalescent plasma
GP	General practitioner
JPAC	Joint United Kingdom (UK) Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee
RECOVERY	Randomised Evaluation of COVID-19 Therapy
REMAP-CAP	A Randomised, Embedded, Multi-factorial, Adaptive Platform Trial for Community-Acquired Pneumonia
RTC	Road traffic collision
SAED	Serious adverse event of donation
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
SNBTS	Scottish National Blood Transfusion Service
UK	United Kingdom
VVR	Vasovagal reaction

NHSBT	NHS Blood and Transplant	**WB**	Whole blood
NIBTS	Northern Ireland Blood Transfusion Service	**WBS**	Welsh Blood Service
NICE	National Institute for Health and Care Excellence		

Recommendation

- The collection of a new blood component(s) requires a proactive adaptable whole system approach, including donor engagement and education, donor selection, donation process development and post-donation care procedure that includes adverse event recording and monitoring. Learning from the experiences during the pandemic must be incorporated to improve systems and processes

Action: United Kingdom (UK) Blood Services

Introduction

Blood donation is an uneventful experience for most donors, but as with any clinical intervention, there are associated risks. European legislation (European Blood Directives 2002/98/EC and 2005/61/EC) which has been subsequently transposed into UK law through the BSQR mandates that donors are made aware of these risks and that good governance processes exist to identify and mitigate risks, thus improving donor and donation safety. This chapter covers serious complications of blood donation reported in the UK in 2020 and, specifically, key aspects of CCP collections.

Serious adverse events of donation

UK Blood Services have implemented the 'Standard Surveillance of Complications Relating to Blood Donations' (Goldman et al. 2016) and individually record and monitor complications relating to blood donations referred to as adverse events of donation. SAED are those which either result in donor hospitalisation, interventions, significant disability/incapacity persisting for >1-year post donation or rarely death.

The UK Blood Services have ten reporting categories for SAED, and incidence rates are included in this chapter. The overall incidence of the SAED for the UK Blood Services from January to December 2020 was 0.22 per 10,000 donations, which has been stable for the last few years.

Assigning severity rating and imputability status (the strength of relation between donation and complication) is challenging, especially when information is incomplete, and some terms, such as long-term pain and/or disability, are subjective. There are currently no uniform objective criteria to separate levels of severity or imputability and there is considerable variation in how this is recorded (Land et al. 2018).

Recording imputability status for donor events, whilst not a mandatory requirement under BSQR, is assessed and documented for every SAED as follows:

- 3. Definite or certain link to donation
- 2. Probable or likely link to donation
- 1. Possible link to donation
- 0a. Link to donation unlikely
- 0b. Link to donation excluded

Occasionally, it is clear that the reported post-donation complication is unrelated or very unlikely to be related to the donation event itself. For example, a donor developing a complication relating to diverticulitis requiring admission within 24 hours of donation. Hence the risk of SAED in the UK is calculated using all reported cases in the first instance and in addition, the risk after excluding those that are clearly not related to donation, see Table 7.3.

Data

A total of 1,742,217 whole blood and component donations were collected by the 4 UK Blood Services in 2020. This is summarised in the Table 7.1 below:

Donations from 2020		NHSBT	SNBTS	NIBTS	WBS
Whole blood (including CCP from WB) donations	Donations from male donors	672,387	59,661	19,007	37,208
	Donations from female donors	699,770	76,349	19,821	43,745
	Donations from new donors	100,848	11,105	3, 201	9,433
	Donations from repeat donors	1,271,309	124,905	35,627	71,520
Apheresis (includes plateletpheresis and plasmapheresis)	Donations from male donors	88,823	6,945	3,340	2633
	Donations from female donors	11,115	621	343	449
	Donations from new donors	24,564	90	37	168
	Donations from repeat donors	75,374	7,476	3,646	2914
Total number of donations in 2020		**1,472,095**	**143,576**	**42,511**	**84,035**

Table 7.1: Cumulative donation data from the 4 UK Blood Services for the period January to December 2020

Table 7.2 summarises the number of SAED by category for all 4 UK Blood Services combined for period January to December 2020.

SAED category		Total number
01.	Death within 7 days of donation	0
02.	Hospital admission within 24 hours of donation	6
03.	Injury resulting in a fracture within 24 hours of donation (including fractured teeth)	10
04.	RTC within 24 hours of donation	2
05a.	Problems relating to needle insertion persisting for more than one year (this mainly includes suspected or confirmed nerve and tendon injuries)	17
05b.	Problems relating to needle insertion requiring hospitalisation/intervention (this mainly includes vascular complications)	0
06.	ACS diagnosed within 24 hours of donation	2
07.	Anaphylaxis	0
08.	Haemolysis	0
09.	Air embolism	0
10.	Other event	1
Total reported SAED in 2020		**38**

Table 7.2: SAED by category in 2020

Table 7.3 details the total number of whole blood and component donations and the total number of SAED reported for each of the 4 UK Blood Services for 2020. This equates to 0.22 SAED per 10,000 donations (irrespective of imputability) or 1 SAED per 45,848 donations. This is a very similar rate to the previous 4 years. Table 7.3 also gives a summary of total number of SAED excluding imputability scores of 0a, 0b for 2020.

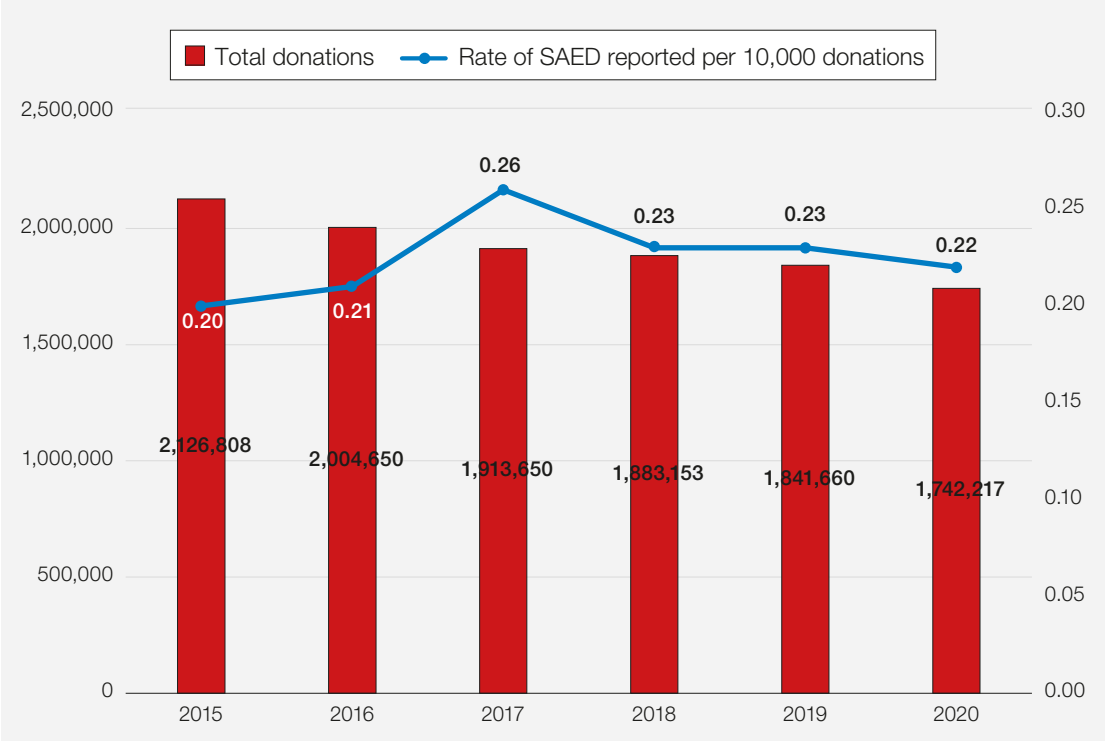
Table 7.3: Summary of total donations for the 4 UK Blood Services and total numbers of SAED for 2020

	NHSBT	SNBTS	NIBTS	WBS
Whole blood donations	**1,372,157**	**136,010**	**38,828**	**80,953**
Apheresis donations including CCP	**99,938**	**7,566**	**3,683**	**3,082**
Total donations	**1,472,095**	**143,576**	**42,511**	**84,035**
	Total donations in the UK: 1,742,217			
Total number of SAED in the calendar year 2020	**31**	**6**	**0**	**1**
Total number of SAED excluding those cases unlikely or not related to blood donation	**29**	**6**	**0**	**1**
Rate of total SAED per 10,000 donations in UK for 2020 (all submitted reports irrespective of imputability)		**0.22**		
Rate of SAED per 10,000 donations in UK for 2020 excluding those cases unlikely or not related to donation		**0.21**		

Comparison of trends with previous years

The rate of SAED has remained stable the last few years.

Figure 7.1: Rate of SAED reported per 10,000 donations in the UK from 2015-2020



Impact of the COVID-19 pandemic on donor haemovigilance and collection of COVID-19 convalescent plasma (CCP)

The 4 UK Blood Services have worked collaboratively to initiate CCP collection to support randomised clinical trials of patients seriously unwell with COVID-19 (REMAP-CAP and RECOVERY) in line with guidance from the 4 UK Chief Medical Officers (issued April 2020). These trials showed no benefit from treatment with CCP and collection stopped in March 2021 (The RECOVERY Collaborative Group, 2021). Each Blood Service took a different approach to CCP collection. This is described in Table 7.4.

CCP donations from 2020	NHSBT	SNBTS	NIBTS	WBS
Total	33,301	4,227	593	1,242
Plasmapheresis	33,301	1,321	47	71
Whole blood (WB)	-	2,906	556	1,171
Donor sex	M/F	M/F	M/F	M
Pre-assessment	Telephone/email and info on web	Telephone	Telephone	Face to face
Donors questioned about long COVID	Relevant questions included later	yes	yes	yes
Total number of SAED in the calendar year 2020	1	1	0	0
Rate of total SAED per 10,000 donations in UK for 2020 (all submitted reports irrespective of imputability)	0.5 per 10,000, double that of overall rate, possibly reflecting the fact that despite satisfying the donor selection guidelines, these are still patients following a recent COVID-19 infection			

Table 7.4: COVID-19 convalescent plasma collection by Blood Service

** At NHSBT, CCP collection by WB was done only on the initial collections (<100) to validate and finalise the collection, manufacturing, and testing process*

Donor selection guidelines

Chapter 3 of Guidelines for the Blood Services in the UK (JPAC 2018) states that only persons in good health shall be accepted as donors of blood or components for therapeutic use. COVID-19 challenged donor selection practices balancing the need to supply whilst ensuring donor safety. Donor haemovigilance was particularly important given donors were recovering from an emerging illness.

Donor selection guidelines were reviewed and updated regularly based on evolving information on COVID-19 to allow the rapid implementation of collection of CCP.

Adverse events in CCP donors

Adverse event data from UK Blood Services demonstrated that

- Feeling faint was more common in CCP donors than non-CCP donors for both whole blood and plasmapheresis donations
- Bruising was more common in CCP donors than non-CCP donors (plasmapheresis compared to platelet apheresis)
- 2 SAED in CCP donors (one ACS, 1 severe VVR) equating to an SAED rate of 0.5 per 10,000 CCP donations

CCP collections by apheresis were started across NHSBT early in the pandemic to support the clinical trials (REMAP-CAP and RECOVERY). Apheresis collections avoid unnecessary red cell loss in the donor and optimise the volume of plasma that can be collected. Cumulative data from NHSBT showed that approximately 12% of CCP attendances resulted in at least one adverse event, reported within 7 days of attendance. Donors experiencing an adverse event were more likely to be first-time donors. The risk of having any adverse event falls from 15% for first-time donors to 7% for repeat donors.

As CCP was also collected through whole blood donations (4,077 donations from SNBTS and WBS), comparison was possible between adverse events in CCP and non-CCP donors following whole blood donation. VVR were more common in CCP donors (vasovagal rate in CCP donors from SNBTS was 27.87 vs 13.39 per 1,000 attendances in non-CCP whole blood donors). The age profile was the same in both groups although there were a higher number of first-time donors in the CCP donor cohort (SNBTS 24% vs 8%). This highlights there was something different about the CCP donors compared to non-CCP donors. Adverse event data relating to CCP reported from NIBTS were small and have not been included in the comparison between CCP and non-CCP whole blood donors here.

The higher rate of VVR in these donors is likely to be multifactorial. Reasons for this may include increased donor anxiety or reduced nutrition following COVID-19. Other factors such as vasodilation,

vascular dysregulation, or subclinical cardiac dysfunction secondary to recent COVID-19 infection may be contributory. SARS-CoV-2 (the virus causing COVID-19) binds to the ACE-2 receptor, a key component of the renin angiotensin aldosterone system which regulates fluid and electrolyte balance, systemic vascular resistance, and blood pressure. ACE-2 is expressed on respiratory and gut epithelial cells but also on vascular endothelial cells where blockade (or downregulation) will cause vasodilation. Hypotension due to vascular dysregulation may result and could explain increased VVR rates.

The phenomenon of 'long-COVID' and evidence of persisting subclinical cardiac dysfunction in a proportion of patients may explain the higher incidence of post-donation hypotension in CCP donors irrespective of known confounding factors such as gender, new/repeat and collection method. Given that COVID-19 is increasingly recognised as a multisystem disease with cardiac, neurological and renal sequelae that can give rise to fatal vasoplegia in some people, it seems reasonable to hypothesise that something similar is happening in the systemic circulation resulting in increased rates of VVR.

The following caveats need to be considered when interpreting adverse events in CCP donors:

- While there was significant collaboration between the UK Blood Services, recruitment, donor assessment and collection methods differed between services and changed over time
- Staff familiarity and experience with CCP collection may have been limited initially but will have increased during the pandemic
- There is a higher proportion of new and returning donors amongst CCP donors, but this has changed with time
- The incidence of adverse events in CCP donors may be artificially high due to the low total number of donations compared to non-CCP donors

Case 7.1: Acute coronary syndrome in a new CCP donor

A first time CCP donor in his 50s who had last donated blood in 1993. The donor donated CCP by plasmapheresis 4 months after he was diagnosed and hospitalised with COVID-19. The donation was uneventful but the next day the donor experienced a brief episode of very sharp central chest pain and felt sweaty and 'not right' following exercise. He was admitted to hospital and diagnosed with acute coronary syndrome and sinus bradycardia. Aspirin, clopidogrel, ramipril, isosorbide mononitrate and simvastatin were commenced. The donor developed further similar symptoms while awaiting coronary angiogram. This demonstrated coronary artery disease for which angioplasty and stenting were performed. All symptoms subsequently resolved. The donor has been withdrawn from further donations.

Cardiac complications can occur in donors with pre-existing heart disease stressing the need for careful donor selection and a robust pre-donation assessment to identify risk factors. Around 20% of hospitalised COVID-19 patients have underlying cardiovascular disease (Zou et al. 2020). Acute myocardial injuries in patients with COVID-19 include acute coronary syndromes, arrhythmias, cardiac arrest, cardiogenic shock, cardiomyopathy, heart failure, myocarditis, pericarditis, and pericardial effusion (NICE 2020a). Common cardiovascular symptoms of ongoing symptomatic or post COVID-19 syndrome include chest tightness, chest pain and palpitations (NICE 2020b). A study of patients with COVID-19 (49% with mild or moderate COVID-19) showed 78% had evidence of cardiac involvement on biochemical or imaging markers and 60% of ongoing myocardial inflammation at 2-3 months independent of pre-existing conditions, severity or overall course of illness (Puntmann et al. 2020).

Careful assessment of donors recovering from COVID-19 is required, including consideration of cardiac symptoms, and is reflected in JPAC guidance recovery from coronavirus (JPAC n.d.).

Case 7.2: Delayed vasovagal reaction resulting in damage to donor teeth

A female donor in her 40s who had previously donated 20 times uneventfully had a delayed vasovagal reaction (faint) several hours post donation in the middle of the night when she got up. The donor had consumed alcohol and reported feeling 'quite tipsy' when going to bed. She had fainted whilst downstairs and was found by a family member with front two teeth damaged significantly needing

emergency dental surgery the following week. She was withdrawn from future donations.

A VVR is a general feeling of discomfort and weakness with anxiety, dizziness, and nausea, which may progress to loss of consciousness. Syncope, or transient loss of consciousness, is the major cause of immediate morbidity of medical significance during blood donation and is the most severe of a spectrum of VVR, which range from mild pre-syncopal symptoms to severe reactions involving syncope. VVR is associated with hypotension and relative bradycardia. VVR can result in an unexpected fall which can lead to injuries. The overall prevalence of VVR in whole blood donors is estimated to be between 1.4 and 7% (moderate reactions) and between 0.1 and 0.5% (severe reactions) (Amrein et al. 2012). VVR have significant implications not only for the welfare of donors but also staff time and training, the management of donor sessions and perhaps more crucially on the retention of donors and security of the blood supply (France et al. 2004).

Several factors, both physiologic and psychological can contribute to VVR. The reaction is generated by the autonomic nervous system and further stimulated by psychological factors and the volume of blood removed, relative to the donor's total blood volume. VVR that occur after the donor has left the donation session are of concern, due to the potential for the donor to come to harm (Kamel et al. 2010). These are delayed reactions and are a poorly understood complication of blood donation. They are thought to occur because of failure of the donor's normal compensatory reflexes to respond to the volume loss associated with donation. Inadequate fluid intake post donation, prolonged standing and high environmental temperature are recognised factors increasing the risk of a delayed VVR.

Many studies have shown that female gender is associated with VVR, both immediate and delayed, highlighting the gender differences in incidences of adverse reactions (Garozzo et al. 2010). Gender differences in autonomic functions are associated with differences in BP. There are also gender differences in the renin angiotensin system and the effects of bound angiotensin II type 2 receptor on renal vascular resistance. Renal sympathetic nervous activity is the main cause of vascular resistance in the evaluation of BP in female subjects.

Unlike immediate VVR, the risk of a delayed reaction is not significantly higher in first time, inexperienced and younger donors compared to experienced, regular, and older donors. It is possible that experienced donors become complacent about following advice to increase their fluid intake following donation, thereby increasing their risk of a delayed reaction.

Post-donation information must be provided to all donors. This should include the risk of delayed reactions and advice on maintaining post-donation fluid intake, and avoidance of known precipitating factors such as overheating and prolonged standing. The mechanism for delayed VVR remains poorly understood. Understanding the physiological basis of such reactions may lead to the development of appropriate interventions to reduce their likelihood.

Prevention is important as blood donors who experience VVR are less likely to give blood again (Eder et al. 2012). Reducing adverse events improves donor retention. Therefore, it is important to understand and prevent adverse events related to blood donation and to improve blood donation safety.

Case 7.3: Irregular pulse detected at a routine pre-donation check in a regular platelet donor

A male platelet donor in his 30s, with no history of cardiac issues, was found to have an irregular pulse rate on a routine pre-platelet donation check. The donor had donated upward of 25 whole blood and platelet donations uneventfully. He was not accepted for donation and was deferred pending further investigation. A preliminary diagnosis of AF was made by the GP and he was referred to a cardiologist.

AF is characterised by a rapid, irregular heartbeat and is the most common heart rhythm irregularity. The irregular cardiac rhythm can cause the formation of blood clots which increases the risk of stroke by fivefold (NICE 2019). The risk of a serious adverse event is also significantly increased should a donation take place whilst a donor is experiencing AF.

JPAC guidance states that, as a minimum, the pulse must be taken on entry to the apheresis programme (JPAC 2018). Pulse checks are undertaken prior to apheresis donations due to potential adverse cardiac effects of citrate. Following cardiology review it was concluded that the irregular pulse was due to sinus arrythmia and AF was ruled out, the donor was reinstated.

This case has been included to highlight the precautionary approach in selecting donors and the proactive approach taken in the UK Blood Services to ensure donor safety- this is especially relevant in the case of CCP donors who may have silent cardiac effects following COVID-19. A pre-apheresis donation pulse check on donors is a simple, cost-effective safety measure which identifies potential issues so that further specialist investigation and intervention can take place, thus protecting donor health and preventing serious adverse events.

Conclusion

The implementation of CCP collection increased collaboration across the UK Blood Services with regular reviews and shared learning. The identification of increased adverse events in CCP donors and emerging evidence on ongoing and post COVID-19 symptoms ('long-COVID') led to the expansion of the JPAC donor selection guidance 'recovery from coronavirus infection' in an attempt to defer donors with 'long-COVID'. It should be highlighted that these questions apply to all donors recovering from COVID-19 and not just CCP donors. A good donor haemovigilance system is vital in helping improve donor and donation safety. Effective public awareness campaigns on the importance of maintaining an adequate national blood supply, the continuing need for blood donors and safety of the donation process should be disseminated continuously, using different communication platforms to reach all segments of the population (WHO 2021).

References

Amrein K, Valentin A, Lanzer G, et al. (2012) Adverse events and safety issues in blood donation - a comprehensive review. *Blood Rev* 2012;**26(1)**:33-42.

BSQR. The Blood Safety and Quality Regulations. 2005. http://www.legislation.gov.uk/uksi/2005/50/contents/made [accessed 27 April 2021].

CAS Alert: Convalescent Plasma in the Management of Hospitalised Patients with COVID-19. March 2021. https://www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAlert.aspx?AlertID=103152 [accessed 27 April 2021].

Eder AF, Notari EP, Dodd RY. Do reactions after whole blood donation predict syncope on return donation? *Transfusion* 2012;**52(12)**:2570-6.

EU directives: https://ec.europa.eu/health/blood_tissues_organs/blood_en [accessed 27 April 2021] then click Blood-Legislation and guidelines to expand list and select the option below:

> Directive 2002/98/EC of the European Parliament and of the Council of 27 January 2003 setting standards of quality and safety for the collection, testing, processing, storage and distribution of human blood and blood components and amending Directive 2001/83/EC OJ L 33, 8.2.2003. https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32002L0098 [accessed 27 April 2021].

France CR, France JL, Roussos M, et al. Mild reactions to blood donation predict a decreased likelihood of donor return. *Transfus Apher Sci* 2004;**30(1)**:17-22.

Garozzo G, Crocco I, Giussani B, et al. Adverse reactions to blood donations: the READ project. *Blood Transfus* 2010;**8(1)**:49-62.

Goldman M, Land K, Robillard P, et al. Blood donation associated risks; data from a Swiss regional haemovigilance program. *Vox Sang* 2016:**110(2)**:185-188.

JPAC. Guidelines for the Blood Transfusion Services in the UK. Whole Blood and Components. 2018. https://www.transfusionguidelines.org/dsg/wb [accessed 27 April 2021].

JPAC. Coronavirus Infection. (n.d.) https://www.transfusionguidelines.org/dsg/wb/guidelines/coronavirus-infection [accessed 27 April 2021].

JPAC. Latest updates: Coronavirus Infection No 04-2021, No 64-2020, No 29-2020, No 13-2020, No 9-2020, No8-2020, No 3-2020. https://www.transfusionguidelines.org/dsg/wb/latest-updates [accessed 27 April 2021].

Kamel H, Tomasulo P, Bravo M, et al. Delayed adverse reactions to blood donation. *Transfusion* 2010;**50(3)**:556-565.

Land K, Townsend M, Goldman, et al. International validation of harmonized definitions of complications of blood donations. *Transfusion* 2018:**58(11)**:2589-2595.

Puntmann V, Ludovica Carerj M, Wieters I, et al. Outcomes of cardiovascular magnetic resonance imaging in patients recently recovered for coronavirus disease 2019 (COVID-19). *JAMA Cardiol* 2020;**5(11)**:1265-1273.

NICE guideline (NG128) Stroke and transient ischaemic attack in over 16s: diagnosis and initial management. Published 01 May 2019. https://www.nice.org.uk/guidance/ng128 [accessed 28 April 2021].

NICE. COVID-19 rapid guideline: acute myocardial injury. 2020a. https://www.nice.org.uk/guidance/ng171/resources/covid19-rapid-guideline-acute-myocardial-injury-pdf-66141956176837 [accessed 27 April 2021].

NICE. COVID-19 rapid guideline: Managing the long term effects of COVID-19. 2020b. https://www.nice.org.uk/guidance/ng188/resources/covid19-rapid-guideline-managing-the-longterm-effects-of-covid19-pdf-66142028400325 [accessed 27 April 2021].

RECOVERY trial. 2021 https://www.recoverytrial.net/ [accessed 27 April 2021].

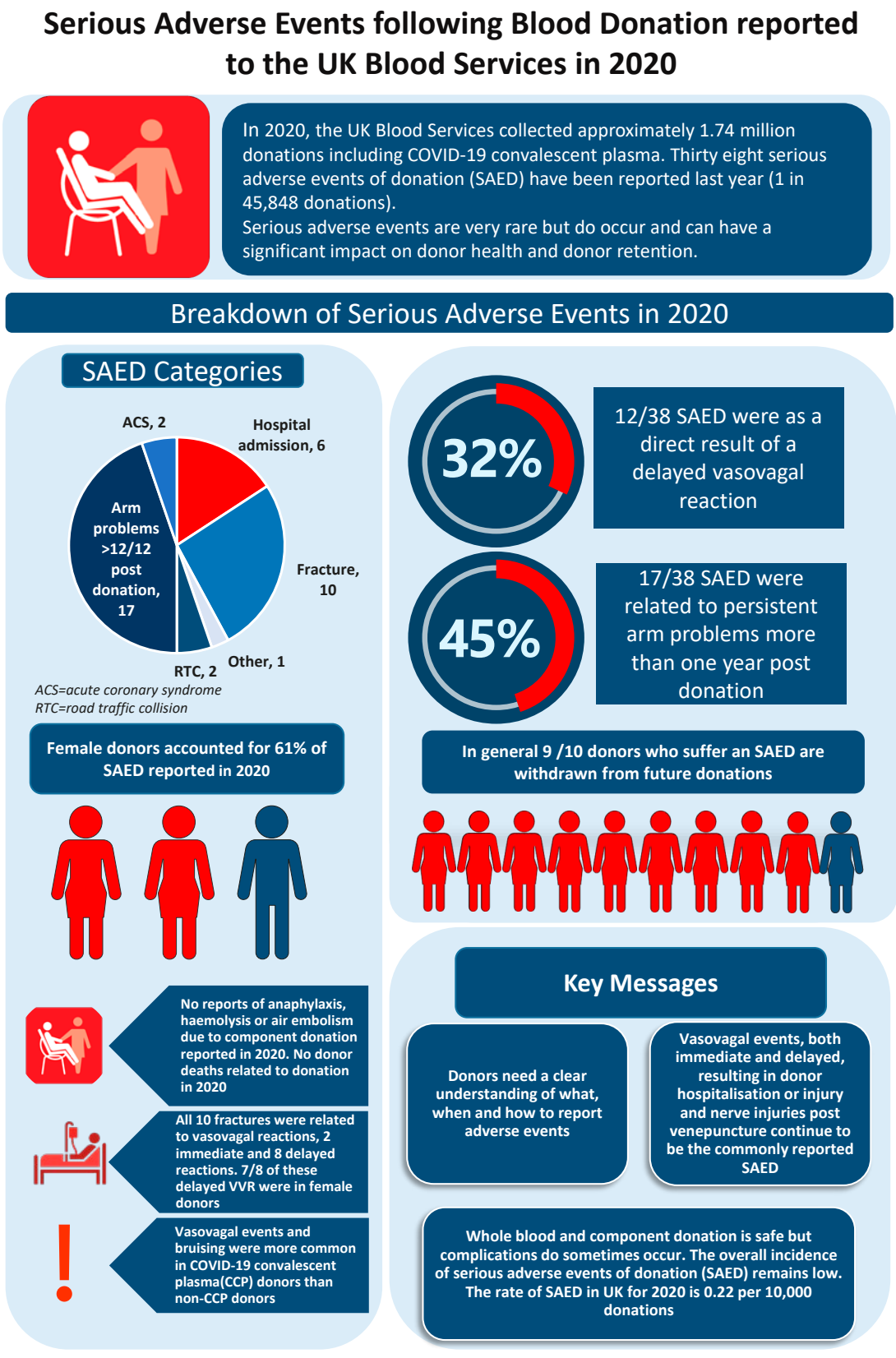
REMAP-CAP trial. 2021 https://www.remapcap.org/ [accessed 27 April 2021].

The RECOVERY Collaborative Group, Peter W Horby, Lise Estcourt et al. Convalescent plasma in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial. medRxiv 2021.03.09.21252736; doi: https://doi.org/10.1101/2021.03.09.21252736 [accessed 27th March 2021].

WHO. Maintaining a safe and adequate blood supply and collecting convalescent plasma in the context of the COVID-19 pandemic. 2021. https://www.who.int/publications/i/item/WHO-2019-nCoV-BloodSupply-2021-1 [accessed 27 April 2021].

Zou F, Qian Z, Wang Y, et al. (2020) Cardiac Injury and COVID-19: A Systematic Review and Meta-analysis. CJC Open 2020;**2(5)**:386-394. https://doi.org/10.1016/j.cjco.2020.06.010 [accessed 27 April 2021].

Figure 7.2: Serious Adverse Events following Blood Donation reported to the UK Blood Services in 2020



ERROR REPORTS

8 Human Factors in SHOT Error Incidents n=2623

Author: Alison Watt and Emma Milser

Recommendations

- Staff involved in investigating incidents should be fully trained in techniques for effective investigations, including an understanding of human factors methods
- Investigations should identify, and include improvement actions, for all the contributory factors involved
- The nine key principles outlined in the white paper titled 'Learning from Adverse Events' published by the Chartered Institute of Ergonomics and Human Factors (CIEHF, 2020) should be applied to investigating transfusion incidents in order to help with understanding a human factors perspective. A link to the paper is in the chapter resources section

Action: Hospital risk departments, hospital transfusion committees, hospital transfusion teams

Abbreviations used in this chapter

BMS	Biomedical scientist	**IT**	Information technology
CIEHF	Chartered Institute of Ergonomics and Human Factors	**RCA**	Root cause analysis
HF	Human factors	**SEIPS**	Systems Engineering Initiative for Patient Safety
HFIT	Human factors investigation tool	**WEG**	Working Expert Group
LIMS	Laboratory information management system	**YCFF**	Yorkshire Contributory Factors Framework

Introduction

There were 2623 error cases reported in 2020, which is 234 fewer than in 2019 (n=2857). This is consistent with an overall reduction in adverse incident reports made to SHOT in 2020 and the reasons for this are discussed in Chapter 5, COVID-19 and Haemovigilance.

This chapter represents the final year's analysis of the original HF question set that formed the SHOT HFIT between 2016 and 2020 (Watt 2020). From January 2021 the HFIT questions were restructured because the overriding outcome from the five years of this study showed a disproportionate emphasis on the culpability of individual staff members (Figure 8.1). Therefore, the questions have been expanded to request more detail about the system and organisational elements of error incidents. The scoring has also been refined to a five-Likert scale (Likert 1932) so causation can be estimated using the guidance: 0 – None, 1 – Barely, 2 – A little, 3 – Some, 4 – A lot, 5 – Fully.

The new HFIT questions are based on the YCFF (Lawton et al. 2012) and further information about this framework can be found on their website (Improvement Academy 2021). To assist reporters when answering the new HFIT questions, a revised tuition package is available on the SHOT website along with two new HF videos created by SHOT, with other additional HF resources: a recording from the SHOT HF webinar held in 2020 and an interview with the author of the SHOT HF chapter. Links to all these resources can be found in the resources section later in the chapter.

Analysis of the SHOT HFIT (2016-2020)

Distribution of scores for HFIT

Over the 5 years of this study the distribution of scores given to the four human factors has not changed substantially, as shown in Figure 8.1. The initial impact of the self-learning material seemed to be that slightly less responsibility was assigned to staff members, but although that early reduction has been maintained, the decrease has not continued. In 2020 over half of all scores were still assigned to staff members with no major difference of scoring between those that have or have not used the learning material. Therefore, the HFIT questions have been changed from January 2021 to encourage reporters to examine error incidents in more depth.

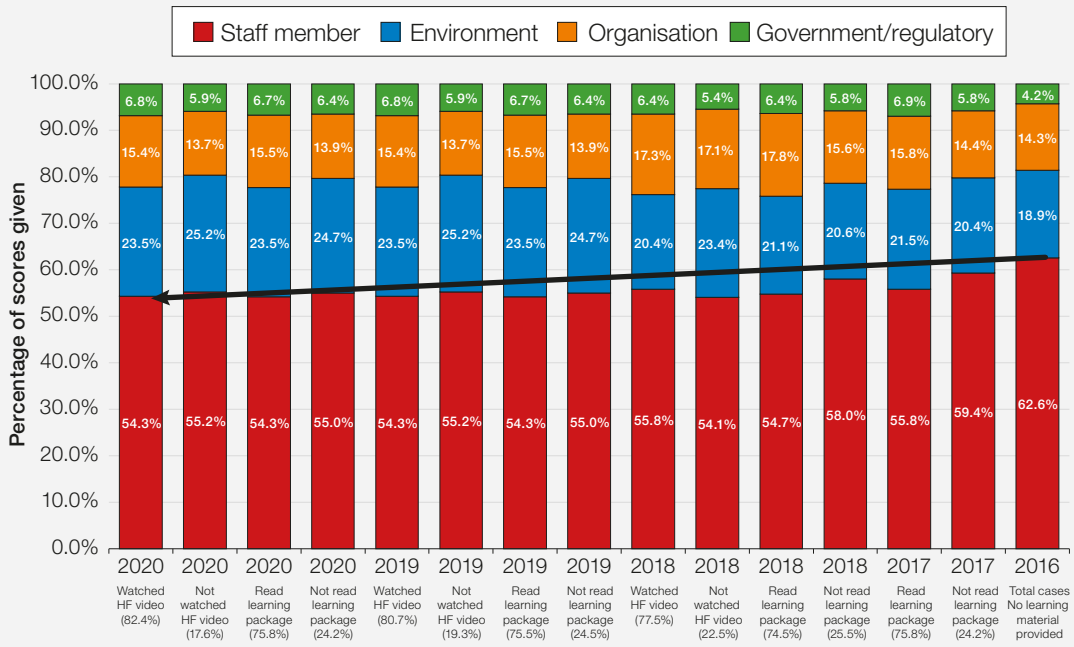


Figure 8.1: Evaluation of uptake of self-learning opportunity and comparative percentages of scores for human and organisational factors

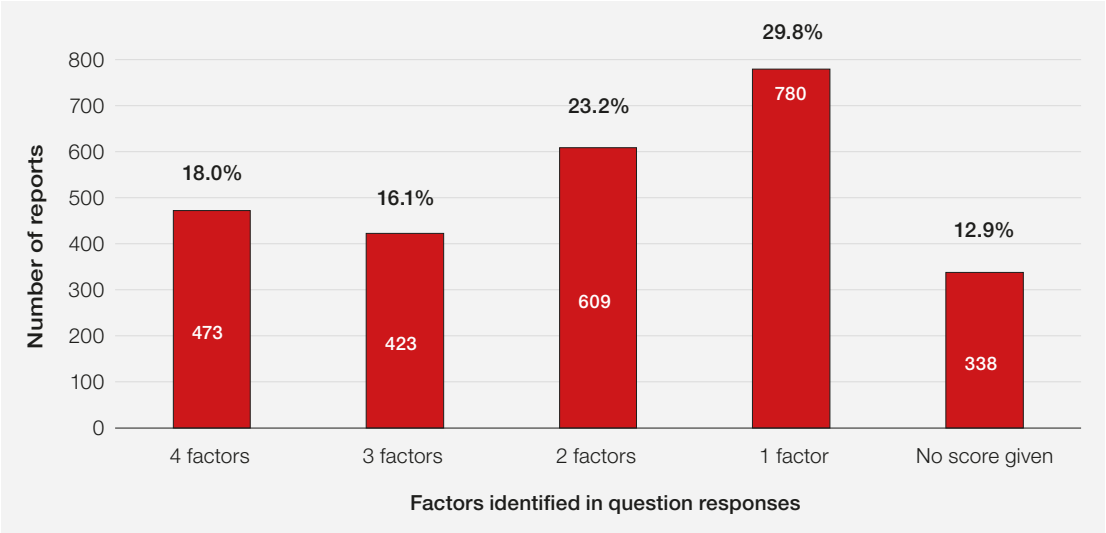
Learning points

- A better understanding of the rationale and scoring of the HFIT questions is essential so that appropriate responses are recorded to help drive local improvements. While self-learning material is available and useful, it is acknowledged that access to local human factors experts and incorporation of human factors driven incident investigation frameworks is important to sustain changes in practice
- Responses to the HFIT questions show a slight preference for videos as a learning tool; SHOT has produced two videos specifically on human factors

Variability in HFIT scoring

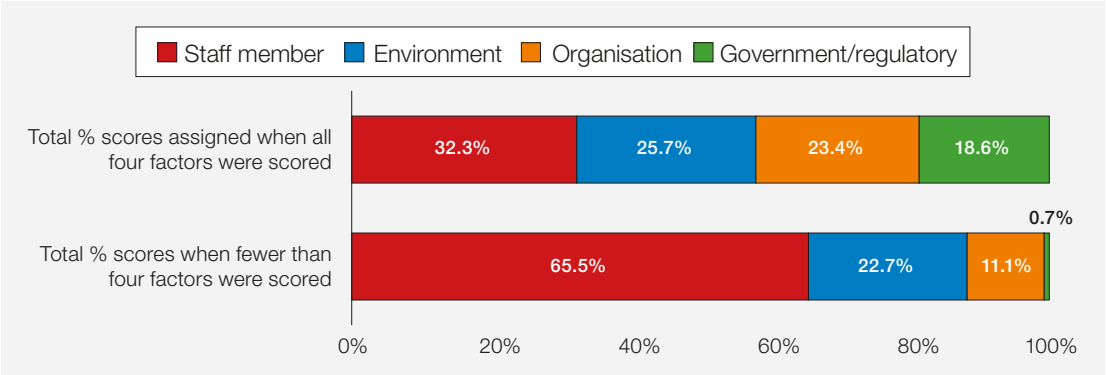
In 2020, as in previous years, there is considerable variability in whether scores are assigned to all four factors (Figure 8.2) and nearly a third are only given a score for one factor (780/2623, 29.8%) Of these, the vast majority are allocated a single score for the culpability of staff members (745/780, 95.5%).

Figure 8.2: Assessment of whether multiple contributory factors were assigned HF scores (2020)



There is a more equitable spread of percentage scores between the different factors when comparing cases where all four factors have been scored (473/2623, 18%) against cases where fewer than four factors were assigned a score (2150/2623, 82%) (Figure 8.3). From these percentages, the blame assigned to staff members was twice as high when fewer than four factors were scored (65.5%), as when all four factors were given a score (32.3%).

Figure 8.3: Comparison of percentages when the incident was scored for all four of the human and system factors or for fewer than four factors (2020)



Case 8.1 demonstrates that scoring 10/10 for the single factor of staff culpability could mean further learning from an incident is reduced. This case shows there were system and organisational problems, but the emphasis on staff issues implies opportunities to resolve other problems may have been overlooked. In addition, scoring like this may make staff colleagues feel that their organisation does not have a just culture (Dekker 2012).

Case 8.1: COVID-19-related organisational problems, but the report identifies only staff issues

An emergency patient was admitted straight to theatre during the night. Red blood cell units were removed from the recovery room refrigerator by order of the anaesthetist and kept near the patient in theatre for the duration of the surgery. No temperature-controlled storage box was requested from the laboratory. Due to the units being out of temperature-controlled storage for over 4 hours, and their close-proximity to a suspected COVID-19 positive patient they were wasted.

This near miss case was scored 10/10 for the extent to which the cause was attributable to unsafe practice by individual staff member(s) and no scores were assigned to other factors. The main suggested change was staff-related, i.e. all staff to acknowledge that they have received and understood new information before proceeding with their duty. However, further information revealed this was the first COVID-19 patient in theatre and the operation was during a night shift, so there was reduced staffing and a lack of senior staff to contact for advice. The theatre policy was unclear at this time regarding COVID-19 'hot' areas and staff did not want to go from a 'hot' area to a 'cold' area for blood if needed.

The guidance regarding handling and storage of blood components for COVID-19-related cases was not clear at the time, or had not been well communicated, as exemplified by staff not asking for a temperature-controlled blood storage box. The main contributory factors were environmental due to enforced COVID-19 adaptations and organisational due to poor communication of the changes. Reduced staffing at night could be due to Government-level funding factors, which may affect the staffing complement. The scoring could have been much more evenly spread between system factors, presenting better opportunities for learning. From the information supplied, it appears the level of staff culpability was minimal and it was not clear why it warranted a score of 10/10. While acknowledging that SHOT may not have the full details of events in this case, it is likely that over-scoring staff culpability could contribute to staff demoralisation if people perceive they are being blamed unfairly.

Evaluation of one change to make incident less likely to recur

Useful information is elicited from responses to the question 'If you could change one thing to make this incident less likely to happen again, what would it be?'. Figure 8.4 shows a categorisation of the main suggestions made in 2020 and indicates mostly changes to the local environment (357/970, 36.8%) or organisation-wide modifications (419/970, 43.2%), despite the overall tendency to score staff members as being most culpable (Figure 8.5).

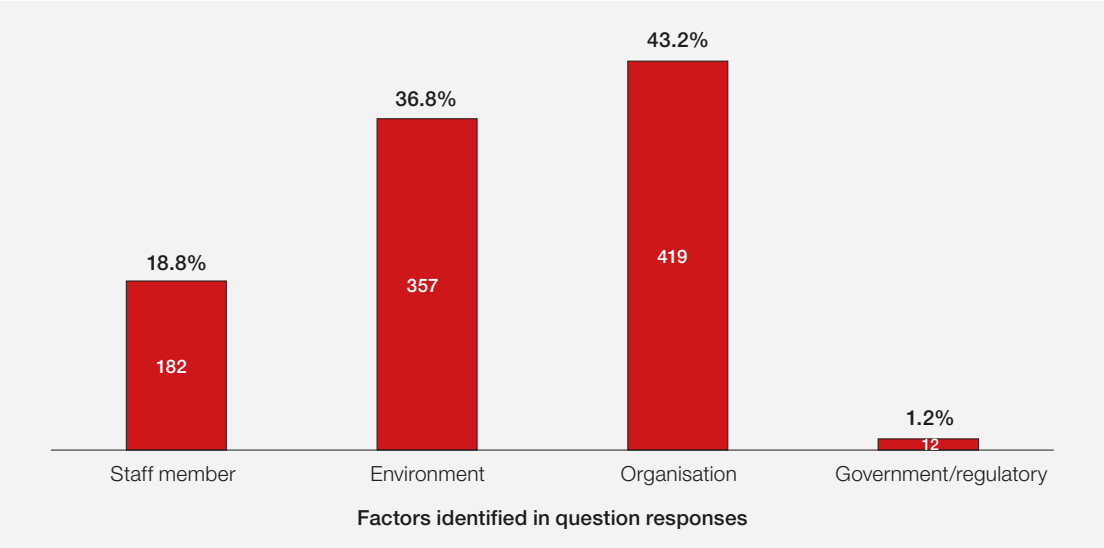


Figure 8.4: Factors identified for one change likely to reduce recurrence of the incident (n=970 responses) (2020)

A comparison was made of the factors identified as possible improvements as shown in Figure 8.4 against the actual HFIT scores assigned in these same cases (n=970). The outcome is shown in Figure 8.5 and demonstrates again that despite high scores attributed to staff, the preferred resolutions are system and organisational rather than staff related.

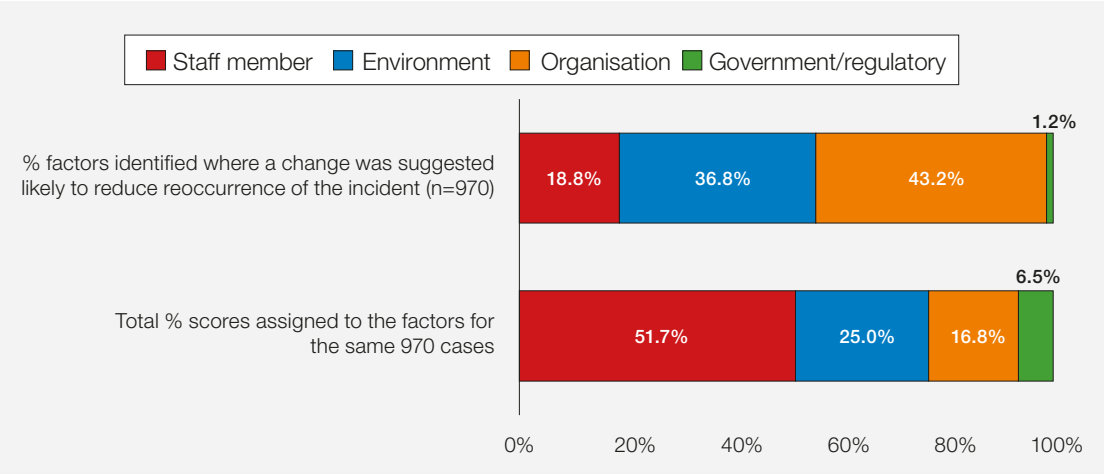


Figure 8.5: Percentages of the types of factors identified where a change was suggested (n=970) compared to percentages of HFIT scores in the same cases (2020)

Case 8.2 shows that there was inferred involvement of environmental and organisational issues in the incident which resulted in two appropriate system changes. However, no HFIT scores were given for these factors, with maximum scoring allocated for staff only.

Case 8.2: Near miss scored 10/10 for staff only, but interim change made to environment and major organisational improvement planned

A patient required a transfusion of irradiated platelets. During the pre-administration check of the unit of platelets in the clinical area, it was noted that the identification label containing the patient details stated that the component was irradiated. Despite this the clinical staff detected that the irradiation blue-dot indicator sticker (RadTag®) was missing from the unit. They alerted the laboratory staff; the unit was returned to the laboratory and it was confirmed that non-irradiated platelets had been issued. An incorrect transfusion that did not meet the patient's special requirements was prevented by diligent checking.

The BMS issuing the component had not checked for an irradiation sticker and an HFIT score of 10/10 was assigned to the staff member, with no scores for any other factors. However, it was identified that an organisational change of an upgrade to the LIMS was required, because at the time of this incident the LIMS did not have a function to stop non-irradiated components from being issued to patients known to require irradiated components. Whilst awaiting the IT change to be installed, an environmental change was implemented with a yellow tag being introduced and attached to all non-irradiated platelet units to ensure that they stood out to staff when issuing components. By scoring the HFIT for these system changes that were identified for the corrective and preventative actions, a more equitable spread of scores across different factors may have resulted.

Conclusion

The HFIT has been revised and it is anticipated that the new format will inspire incident investigators to focus less on individual failures and more on examining underlying system failures. In the supplementary information to this chapter SHOT HF experts have included a case study which has been reworked using the updated HFIT. The same case has also been analysed using the SEIPS framework, a conceptual model that depicts how work systems affect patient safety and help drive improvements (Holden, 2020).

The key message is to highlight system and organisational problems and implement appropriate interventions to reduce risk of error recurrence.

Incident investigation should always include consideration of the impact of human factors. There may not necessarily be a single root cause, many incidents are multifactorial. Identification of all factors contributing to the error will enable robust interventions to be implemented for each of the factors highlighted. Local investigators should have appropriate training in the investigation process, which should include the importance of human factors. A white paper published by the Chartered Institute of Ergonomics and Human Factors (CIEHF 2020) aimed to help organisations understand a human factors approach to investigating and learning from adverse events. The paper discusses how organisations learn, or fail to learn, from adverse events and provides nine key principles, with practical guidance, which organisations can apply to capture the human contribution to adverse events. It is recommended that these principles are applied to the investigation of adverse events in transfusion.

Key SHOT messages

- The new questions in the human factors investigation tool (HFIT) are available in the human factors tuition package section of the SHOT website https://www.shotuk.org/reporting/human-factors-tuition-package/. Changes to questions are made in January each year, so reporters are strongly encouraged to download the HFIT dataset every year and use these questions as a structure for local investigations of error incidents
- Human Factors (HF) should be incorporated into local incident investigations. Where system and organisational problems are identified, these can be translated into local improvements. Such system changes can reduce the likelihood of a similar incident recurring

Recommended resources

SHOT Human Factors Tuition Package
https://www.shotuk.org/reporting/human-factors-tuition-package/

SHOT Human Factors videos
https://www.shotuk.org/resources/current-resources/videos/

SHOT Bites No. 1a, 1b and 12 that cover investigating incidents and cognitive bias
https://www.shotuk.org/resources/current-resources/shot-bites/

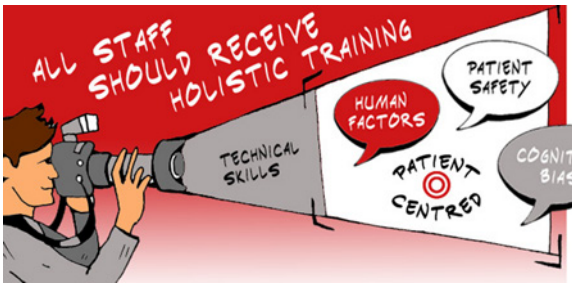
SHOTcast Human Factors
https://www.shotuk.org/resources/current-resources/shot-casts/

CIEHF Learning from adverse events
https://www.ergonomics.org.uk/CIEHFLearningfromAdverseEvents

SHOT Human Factors webinar
https://www.youtube.com/watch?v=ie0UK9R5IbM

Yorkshire Contributory Factors Framework
https://improvementacademy.org/tools-and-resources/the-yorkshire-contributory-factors-framework.html

Supplementary material ABOi case worked through using HFIT and SEIPS
https://www.shotuk.org/shot-reports/report-summary-and-supplement-2020/



SHOT
Serious Hazards of Transfusion

References

Card AJ (2017) The problem with '5 whys'. BMJ Qual Saf, **26(8)**, pp.671-677.

CIEHF (2020) Chartered Institute of Ergonomics and Human Factors (CIEHF) White Paper on Learning from Adverse Events https://www.ergonomics.org.uk/CIEHFLearningfromAdverseEvents [accessed 15 March 2021].

Dekker S. (2012) Just Culture: Balancing safety and accountability. Ashgate Publishing, Ltd.

Holden RJ, Carayon P. SEIPS 101 and seven simple SEIPS tools. BMJ Qual Saf 2021;0:1–10. doi:10.1136/bmjqs-2020-012538 https://qualitysafety.bmj.com/content/qhc/early/2021/05/25/bmjqs-2020-012538.full.pdf [accessed 28 June 2021]

Improvement Academy (2021) Yorkshire Contributory Factors Framework https://improvementacademy.org/tools-and-resources/the-yorkshire-contributory-factors-framework.html [accessed 15 March 2021].

Isherwood, P, and Waterson, P. (2021). To Err Is System; a Comparison of Methodologies for the Investigation of Adverse Outcomes in Healthcare. Journal of Patient Safety and Risk Management 26, no. **2**: pp.64–73.

Lawton R, McEachan RR, Giles SJ et al. (2012) Development of an evidence-based framework of factors contributing to patient safety incidents in hospital settings: a systematic review. BMJ Qual Saf, **21(5)**, pp.369-380.

Likert, R. (1932). A technique for the measurement of attitudes. Archives of Psychology, **22**, 140, pp.5-55.

Peerally MF, Carr S, Waring J et al. (2017) The problem with root cause analysis. BMJ Qual Saf, **26(5)**, pp.417-422.

Watt AJ (2020) The application of human factors to the blood transfusion process. PhD thesis available at https://repository.lboro.ac.uk/articles/The_application_of_human_factors_to_the_blood_transfusion_process/12489734 [accessed 15 March 2021].

9 Adverse Events Related to Anti-D Immunoglobulin (Ig) n=400

Author: Courtney Spinks and Jennifer Davies

Definition:

An adverse event related to anti-D immunoglobulin (Ig) is defined as related to the prescription, requesting, administration or omission of anti-D Ig which has the potential to cause harm to the mother or fetus immediately or in the future. This category also includes events relating to the administration of anti-D Ig following transfusion of D-mismatched platelets.

Key SHOT messages

- Errors relating to cell-free fetal deoxyribonucleic acid (cffDNA) accounted for 47 cases, an increase from 2019. Continued reporting to SHOT helps promote learning from these events
- Review protocols and standard operating procedures (SOP) to reduce incorrect omission of routine antenatal anti-D Ig prophylaxis (RAADP) and anti-D Ig post potentially sensitising event (PSE)

Abbreviations used in this chapter

BSH	British Society for Haematology
cffDNA	Cell-free fetal deoxyribonucleic acid
G&S	Group and screen
HDFN	Haemolytic disease of the fetus and newborn
IBGRL	International blood group reference laboratory
IUD	Intrauterine death
Ig	Immunoglobulin
LIMS	Laboratory information management system
NICE	National Institute for Health and Care Excellence
NIPT	Non-invasive prenatal testing
NHSBT	National Health Service Blood and Transplant
PCR	Polymerase chain reaction
PSE	Potentially sensitising event
SOP	Standard operating procedure
RAADP	Routine antenatal anti-D Ig prophylaxis
UKAS	United Kingdom Accreditation Service
WBIT	Wrong blood in tube

Recommendations

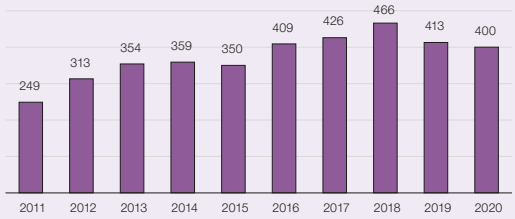
- Planned routine appointments must include processes to ensure that D-negative women receive routine antenatal anti-D Ig prophylaxis (RAADP) as appropriate
- Review processes to ensure that anti-D Ig post potentially sensitising event (PSE) is administered before patients are discharged from hospital
- Processes should be in place to ensure that cell-free fetal deoxyribonucleic acid (cffDNA) D type results are reviewed prior to order or administration of anti-D Ig or RAADP
- Laboratory processes should include appropriate actions to be taken when cffDNA D type is discrepant with cord D type

Action: Maternity services, laboratory management

Headline data 2020

Number of reports n=400
Deaths n=0
Major morbidity n=0

Anti-D reports by year



Demographic data

Male n=0
Female n=400
Adults n=395
Paediatric n=5

Potential for major morbidity n=275

Late/omitted RAADP n=136
Late/omitted anti-D following a PSE (including delivery) n=139

Introduction

In 2019 SHOT received 413 reports of errors relating to anti-D Ig, in this reporting year there was a nominal reduction with a total of 400 reported errors. Interestingly very few referenced the changes to practice that must have been introduced to manage patient and staff safety during the COVID-19 pandemic. Most errors (335/400, 83.8%) occurred in the clinical area. Omission or late administration of anti-D Ig accounted for 275/400 (68.8%) cases, there were 57/400 cases (14.3%) where anti-D Ig was administered to an individual with a D-negative infant, and 20/400 cases (5.0%) of administration to an individual with immune anti-D. Other cases included anti-D Ig administration to D-positive individuals (16/400, 4.0%), and incorrect dose (9/400, 2.3%). In 2 cases there were errors in administration of anti-D Ig post transfusion of a D-positive component to a D-negative individual; In 1 case anti-D Ig was not appropriate due to the age of the patient and in the other an incorrect dose was administered.

Deaths n=0

There were no deaths reported during 2020 related to anti-D Ig errors.

Major morbidity n=0

No cases resulting in major morbidity were reported in 2020. However, it should be noted that the impact of the errors reported in this category, in particular late or omitted anti-D Ig may not be fully realised at the time of reporting. All cases of immune anti-D identified in pregnancy and reported to SHOT are discussed in Chapter 25, Immune Anti-D in pregnancy. In 16 cases where immune anti-D was detected during pregnancy errors were noted in RAADP provision, in 15 cases no RAADP had been given and in 1 case RAADP was delayed.

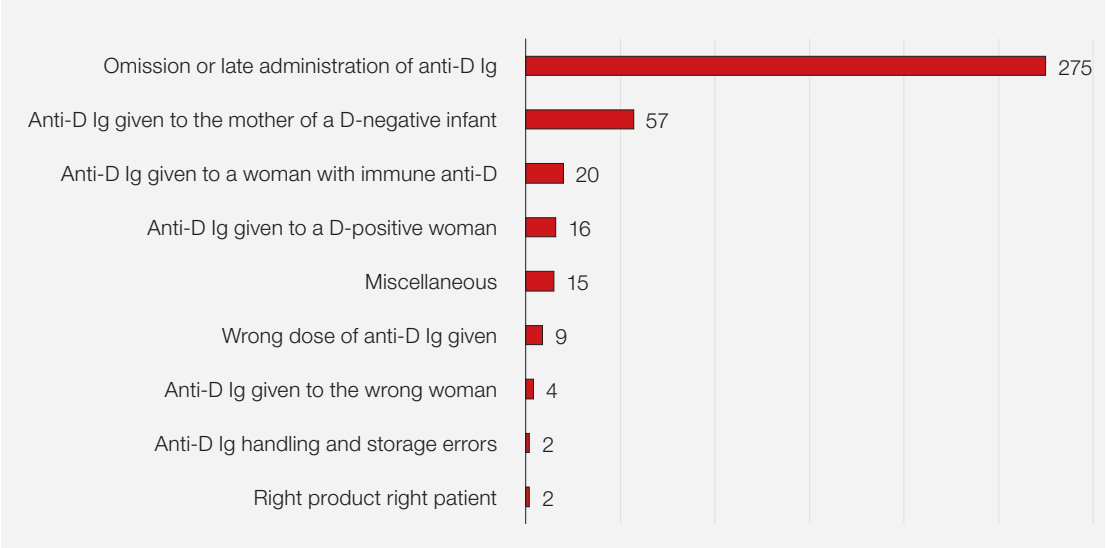
Overview of cases

There were 197/400 (49.3%) errors that occurred in either the community or outpatient settings. These largely involved late administration or omission of RAADP, 89/197 (45.2%), suggesting that the planning and processes for routine outpatient reviews could be improved. Errors occurring in the hospital ward setting accounted for 126/400 (31.5%) cases and 65/400 (16.3%) in the laboratory. Most errors in the ward setting related to failure to administer anti-D Ig (63/126, 50.0%), and 22 (17.5%) cases related to late administration of RAADP. Most laboratory errors related to failures in cffDNA processes (24/65, 36.9%), 16 (66.7%) of these resulted from apparent error in prediction of the fetal D-type by the testing laboratory.

There were 8/400 (2.0%) reported cases of transcription errors when documenting D status in the handheld

records, which were then used to inform treatment decisions. On each occasion the correct results were available electronically and if accessed, which should be policy, would have prevented the errors.

Figure 9.1: Distribution of anti-D Ig related error reports in 2020 (n=400)



Omission or late administration of anti-D Ig n=275

Omission or late administration continues to be the highest source of errors relating to the administration of anti-D Ig (275/400, 68.8%), with 136/275 (49.5%) relating to RAADP. In 139/275 cases (50.5%) there was failure to give anti-D Ig following a PSE (including post-delivery), mostly due to patients being discharged before administration (63/139, 45.3%) and 35/139 (25.2%) resulting from incorrect decisions in anti-D Ig administration. Last year's Annual SHOT Report made suggestions for how midwifery units could address omissions and delays in administration, specifically the provision of RAADP during pregnancy, administration post-delivery and administration after a PSE.

BSH guidelines for the use of anti-D immunoglobulin for the prevention of haemolytic disease of the fetus and newborn (BSH Qureshi et al. 2014) and NICE guidance (NG140 and NG126) should be reflected in local policies.

Case 9.1: Confusion caused by labelling of a cord blood sample

A midwife contacted the laboratory to enquire if a D-negative patient had received any anti-D Ig. According to the LIMS the named patient had not had a post-delivery sample, or request for a Kleihauer. There was also no record of the baby or that the cord blood sample had been received. On investigation by the laboratory, a sample for a baby with same date of birth and corresponding address to the mother was located, however the baby did not have the same surname and so had not been associated with the mother in question.

Case 9.2: Late administration of anti-D Ig post-delivery of twin infants

One infant tested D-positive to a D-negative mother. However only one cord sample was sent to the laboratory at the time of delivery, which tested D-negative. There was no indication of a twin delivery therefore anti-D Ig was not issued to the patient. Anti-D Ig was administered day 7 post-delivery.

Inappropriate administration of anti-D Ig

Case 9.3: Anti-D Ig given to woman who had pre-existing anti-D antibodies

A woman was referred to the fetal medicine institute for invasive sickle cell testing of fetus. The presence of alloimmune anti-D antibodies was not adequately identified by the referring hospital report. Although written in the blood transfusion report, it was embedded in a paragraph of text and difficult to identify. When the appointment was made the clerical team created a new record, although the woman had an existing record in the system (Failure to follow correct process of creating records by the administration team). A G&S sample was taken pre-administration of anti-D Ig, but

the midwives did not wait for the result to come back (usual practice) and issued anti-D Ig from the stock on the ward. The failsafe of a midwife checking the previous reports before issuing the anti-D Ig did not happen because the woman had two files and the report had been scanned into the wrong file. The research fellow did not identify that the patient had anti-D antibodies from the G&S report and prescribed anti D Ig. A second research fellow realised that the patient had alloimmune anti-D antibodies and alerted the consultant and fetal medicine midwives. A second failsafe, writing all procedures including blood group and virology, on a white board in the midwives' office had not happened because the member of staff responsible had been delayed due to a train strike.

Cell-free fetal deoxyribonucleic acid (cffDNA) n=47

High-throughput NIPT for fetal D genotype, also known as cffDNA for D testing uses a real-time quantitative PCR method for identifying fetal D genotype from fetal DNA in the plasma of D-negative women. The IBGRL at NHSBT offers a UKAS accredited fetal D screening service to all customers in the UK and Ireland. The test predicts fetal D status with high accuracy from a sample of maternal blood and will improve care for D-negative women by reducing the need to administer a blood product to healthy pregnant women.

IBGRL have optimised and automated the testing technology applied to pregnancies at risk of HDFN to enable high-throughput fetal D screening of all D-negative pregnant women, who have not formed immune anti-D or anti-G to guide antenatal anti-D Ig prophylaxis. The service aims to report 98% of samples within 10 business days of receiving the sample (further details in the link provided under references). High-throughput NIPT for fetal D genotype is recommended by the NICE as a cost-effective option to guide antenatal prophylaxis with anti-D Ig. Tools to put this NICE guidance into practice are available https://www.nice.org.uk/guidance/dg25.

The benefits of using high-throughput NIPT for fetal D genotype to guide antenatal prophylactic treatment with anti-D Ig as per the NICE guidance include:

- Preventing unnecessary administration of anti-D Ig and associated risk for D-negative mothers when the fetal D type is predicted as D-negative
- Reducing the number of antenatal anti-D Ig prophylactic clinic appointments needed, and the amount of anti-D Ig used
- Increasing the availability of anti-D Ig for use after PSE in pregnancy when the NIPT result for fetal D genotype is positive or unknown
- Reducing the anxiety associated with potentially sensitising events for D-negative women when the NIPT result for fetal D genotype is negative
- Providing information to allow D-negative women to make an informed decision about whether to have treatment with anti-D Ig

The test is highly accurate and can be performed from 11^{+2} weeks gestation. The assay has a false positive rate of up to 2%, where fetuses predicted to be D-positive will in fact be found to be D-negative at birth. The false D-negative predictive rate for fetal D screening is 0.1% according to the literature. At present IBGRL has a false negative prediction rate of 0.08%. It is also important to note that for NIPT, IBGRL requires only one sample and does not require or test a second sample from the patient at the same point in time. This is a routine test and samples are expected to be taken in a controlled environment by trained staff to avoid wrong blood in tube incidents.

A total of 47/400 (11.8%) cases were reported relating to cffDNA. In 16/47 (34.0%) staff acted on the cffDNA results and anti-D Ig was given or omitted because the cffDNA assay predicted an incorrect D type. In 8/16 (50.0%) of these cases the fetal D-type was predicted D-positive but cord sample tested was D-negative, and in 8/16 (50.0%) the fetal D-type was predicted negative but cord sample tested D-positive. All these cases were referred to IBGRL for investigation. In 22/47 (46.8%) cases anti-D Ig or RAADP was administered to a woman with a fetus predicted to be D-negative by cffDNA testing as a result of failure to check the fetal D screening results.

Other errors included:

- Failure to order anti-D Ig or RAADP when cffDNA results indicated a D-positive fetus (n=3)
- Delay in entering cffDNA results into the LIMS (n=1)
- Misinterpretation of cffDNA results (n=1)
- Incorrect advice (n=1)
- A cord sample WBIT (n=1)
- Patient insistence on receiving anti-D Ig despite cffDNA predicting a D-negative fetus (n=1)
- Manual transcription of results (n=1)

SHOT encourages further reporting of discrepant cffDNA results.

NHS Blood and Transplant FAQ's from September 2018 state: *'The fetal RHD screen has been set up to be highly sensitive for detection of fetal RHD, thus avoiding false negative results as in such cases anti-D Ig will not be given. The false negative rate in this case is 0.1% i.e. highly accurate. The false positive prediction is up to 2% although this is dependent on the ethnicity of the population.'*

False positive results may occur as a result of rare silent or variant Rh genes or weak D alleles, vanishing twin, or extraneous low-level DNA contamination of the sample. Where a fetal D-positive result has been reported but the cord blood tests D-negative, this should be reported to the testing laboratory and SHOT. Investigations at the local level could include WBIT (mother or cord) and weak D (cord sample), although this is not included in current guidelines. All cases of apparent false negative cffDNA results should be reported to the testing laboratory, along with blood samples from mother and baby. They should also be reported to SHOT. Local investigations should include WBIT (cord sample) and anti-D Ig prophylaxis should be given as appropriate.

Case 9.4: Apparent false positive cffDNA D-type due to vanishing twin syndrome

A cffDNA result issued by the NHSBT reference laboratory for a D-negative pregnant lady, predicted the fetus to be D-positive. Prophylactic anti-D Ig was given to the patient based on the cffDNA result. A cord sample taken at delivery grouped as D-negative. The laboratory confirmed the cord sample as fetal by performing an alkali denaturation test. It was not possible to obtain repeat samples for testing as mum and baby has been discharged. The NHSBT reference laboratory was notified. Further hospital investigation indicated that the incorrect predicted cffDNA result could possibly be due to the 'vanishing twin syndrome' as the patient had IUD of a twin on the first scan during the pregnancy at 16^{+5} weeks. It was unknown to be a twin pregnancy until the fetus had died. The cffDNA test was performed at 21 weeks.

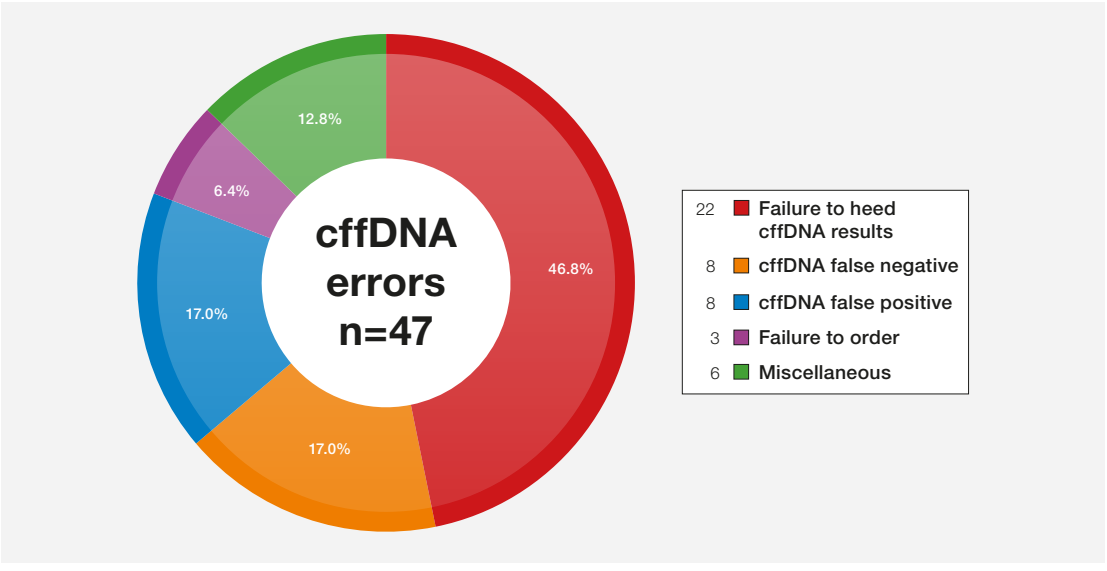


Figure 9.2: Errors relating to cffDNA in 2020 (n=47)

Near miss cases n=35

There were 35 near miss anti-D Ig errors in 2020. The largest sub-category of reports was those preventing late or omitted anti-D Ig,16/35 (45.7%). Most of the near misses were errors in the laboratory, 20/35 (57.1%), with 14 clinical errors, and 1 miscellaneous error.

Conclusion

Omission or late administration of anti-D Ig accounts for most errors in this category. Administration of RAADP at the recommended gestation period is critical in reducing risk of immunisation to the D antigen (see Chapter 25, Immune Anti-D in Pregnancy).

SHOT recommend that gynaecology, early pregnancy units and maternity units review their procedures to ensure that care pathways reflect the environment that care is being delivered in and subsequently avoid omissions or late administration of anti-D Ig and RAADP. As the uptake of NIPT for fetal D increases laboratories and maternity units need to ensure that processes are in place for checking the cffDNA result prior to issue and administration of anti-D Ig or RAADP. There also needs to be awareness of the sensitivity and specificity of the assay and the actions to be taken in the event of discrepant results when cord blood samples are tested.

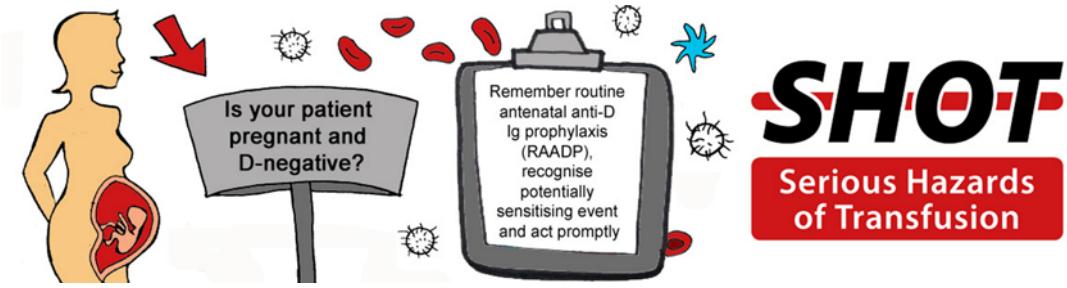
Recommended resources

Anti-D Immunoglobulin (Ig) Administration to avoid sensitisation in pregnancy - an aide memoire SHOT 2020
https://www.shotuk.org/resources/current-resources/

SHOT Bite No 2: Anti-D Ig Administration
https://www.shotuk.org/resources/current-resources/shot-bites/

Blood assist App to cover anti-D following transfusion
Apple (https://apps.apple.com/gb/app/blood-assist/id1550911130)
Google play (https://play.google.com/store/apps/details?id=uk.nhsbt.bloodassist)
Web based (www.bloodassist.co.uk)

NHSBT FAQ document
https://nhsbtdbe.blob.core.windows.net/umbraco-assets-corp/12552/fetal-rhd-screen-questions-answers.pdf



References

BSH Qureshi H, Massey E, Kirwan D, et al. BCSH guideline for the use of anti-D immunoglobulin for the prevention of haemolytic disease of the fetus and newborn. Transfus Med 2014;**24(1)**:8-20. https://doi.org/10.1111/tme.12091 [accessed 28 April 2021].

NHSBT FAQ's (September 2018) https://nhsbtdbe.blob.core.windows.net/umbraco-assets-corp/12552/fetal-rhd-screen-questions-answers.pdf [accessed 10/06/2021].

NICE Guidance: Routine antenatal anti-D prophylaxis for women who are rhesus D negative 2008 WBIT https://www.nice.org.uk/guidance/ta156/chapter/1-Guidance [accessed 10/06/2021].

NICE Guidance: High-throughput non-invasive prenatal testing for fetal RHD genotype 2016 https://www.nice.org.uk/guidance/dg25 [accessed 10/06/2021].

10 Incorrect Blood Component Transfused (IBCT) n=323

Authors: Victoria Tuckley, Simon Carter-Graham, Emma Milser, Jennifer Davies and Shruthi Narayan

Definitions:

Wrong component transfused (WCT)

Where a patient was transfused with a blood component of an incorrect blood group, or which was intended for another patient and was incompatible with the recipient, which was intended for another recipient but happened to be compatible with the recipient, or which was other than that prescribed e.g. platelets instead of red cells.

Specific requirements not met (SRNM)

Where a patient was transfused with a blood component that did not meet their specific requirements, for example irradiated components, human leucocyte antigen (HLA)-matched platelets when indicated, antigen-negative red cell units for a patient with known antibodies, red cells of extended phenotype for a patient with a specific clinical condition (e.g. haemoglobinopathy), or a component with a neonatal specification where indicated. (This does not include cases where a clinical decision was taken to knowingly transfuse components not meeting the specification in view of clinical urgency).

Key SHOT messages

- The person carrying out the bedside checks must only deal with one transfusion at a time, they must not check two transfusions simultaneously
- If during the administration step the person is distracted the process must be started again from the beginning
- It is essential that staff members are adequately trained and competency-assessed before they are expected to perform any task without supervision
- A robust checking process at the administration step immediately prior to transfusion remains a critical step to support prevention of transfusion of ABO-incompatible blood components
- Paediatric specifications must be clearly documented in standard operating procedures and rules in laboratory information management systems (LIMS) applied
- Distractions are dangerous – where these are flagged in incident investigation, attempts should be made to rectify working conditions and reduce distractions
- For further laboratory key messages and recommendations please see Chapter 15, Laboratory Errors

Abbreviations used in this chapter

ABOi	ABO-incompatible
BMS	Biomedical scientist
BSH	British Society for Haematology
CCP	COVID-19 convalescent plasma
CMV	Cytomegalovirus
FFP	Fresh frozen plasma
Hb	Haemoglobin
HDU	High dependency unit
HLA	Human leucocyte antigen
HSCT	Haemopoietic stem cell transplant
HSE	Handling and storage errors
HT	High titre
IBCT	Incorrect blood component transfused
ID	Identification
IT	Information technology
ICU	Intensive care unit
LIMS	Laboratory information management system
MAU	Medical admissions unit
NHS	National Health Service
NM	Near miss
SRNM	Specific requirements not met
WCT	Wrong component transfused

Recommendations

- Laboratory information management system (LIMS) rules for compatibility should be reviewed (including for group changes in transplant) and where possible a stop function should be implemented for ABO-incompatible red cells

Action: Laboratory managers and transfusion information technology (IT) specialists

- It is essential that safety critical steps should be protected from distraction (e.g. by implementing a physical cue such as tabard or armband)
- Distractions are inevitable when staff are working alone, conditions for lone working should be examined to reduce distraction where possible

Action: Laboratory and ward managers

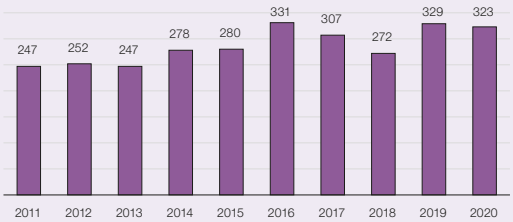
- Redeployment/surge nursing to areas where transfusion is required should be accompanied by training and competency-assessment

Action: Ward managers and education/training staff

Headline data 2020

Number of reports n=323
Deaths n=0
Major morbidity n=6

IBCT reports by year



Demographic data

Male n=162
Female n=148
Unknown n=13

Adults n=261
Paediatric n=44
Unknown n=18

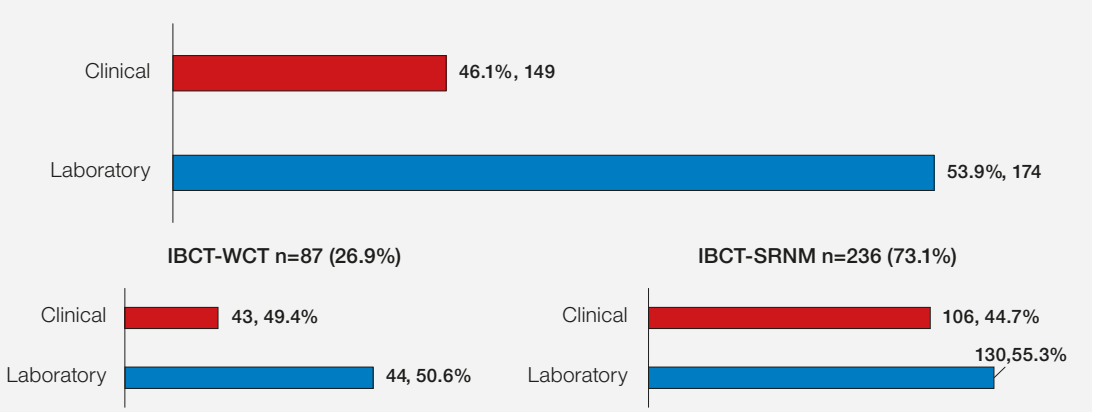
Blood component data

Red cells n=260
Platelets n=31
Plasma n=15
Multiple Components n=12
Granulocytes n=1
Unknown n=4

Introduction

IBCT events have the potential to cause major morbidity in patients and are often due to multiple errors in the transfusion process. Whilst the number of reports in most SHOT categories has decreased this year, IBCT events have not changed significantly. Figure 10.1 provides an overview of reports submitted to SHOT in 2020 where an incorrect blood component was transfused. This category includes instances where wrong components were transfused, and/or specific requirements were missed. The BSH guidelines for use of irradiated components were updated in 2020 (BSH Foukaneli et al. 2020).

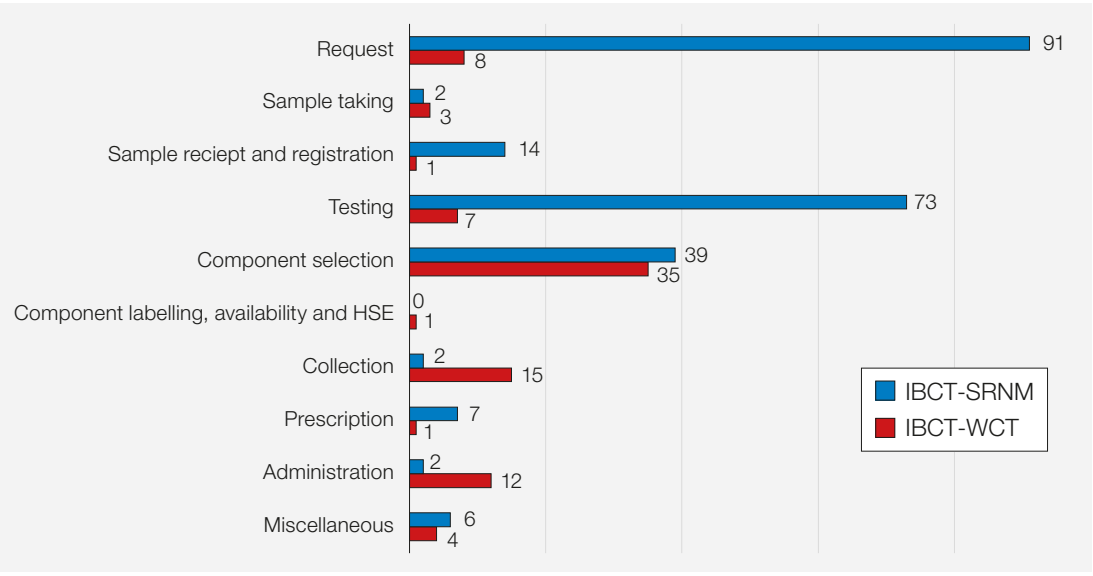
Figure 10.1: Overview of reports where an incorrect blood component was transfused in 2020 (n=323)



IBCT-WCT=incorrect blood component transfused-wrong component transfused; IBCT-SRNM=IBCT-specific requirements not met

IBCT (WCT and SRNM) errors commonly occurred at the request step, 99/323 (30.7%) and the testing step 80/323 (24.8%) as shown in Figure 10.2. Component selection 35/87 (40.2%), collection 15/87 (17.2%) and administration errors 12/87 (13.8%) continue to account for most IBCT-WCT reports.

Figure 10.2: Total incorrect blood component transfused errors categorised by the step where the error occurred (n=323)



IBCT-WCT=incorrect blood component transfused-wrong component transfused; IBCT-SRNM=IBCT-specific requirements not met; HSE=handling and storage errors

Deaths n=0

There were 11 deaths reported in the IBCT category (5 with clinical errors and 6 with laboratory errors), however none of the deaths were directly attributable to the transfusion (imputability 0 excluded or unlikely). Nine deaths occurred in the IBCT-WCT category (1 paediatric patient and 8 adults) and two in the IBCT-SRNM category (both adults). All deaths were attributed to the patients underlying conditions.

Major morbidity n=6

There were 5 cases of major morbidity which occurred in the laboratory and resulted in sensitisation to the K antigen in patients of childbearing potential (imputability not stated). These are discussed further in Chapter 15, Laboratory Errors. There was 1 clinical case which involved an ABOi transfusion (Case 5 in Table 10.1) and can be found in the supplementary information on the SHOT website (https://www.shotuk.org/shot-reports/report-summary-and-supplement-2020/).

ABO-incompatible (ABOi) transfusions n=9

This is an NHS Never Event (NHS England 2018), Wales (NHS Wales 2018) and Northern Ireland. In Scotland these cases would be reported as Red Incidents through the Scottish National Blood Transfusion Service. ABOi transfusions have the potential to cause severe clinical consequences including patient death.

In total there were 7 ABOi red cell transfusions (all clinical errors) and 2 ABOi plasma component transfusions, 1 of FFP and 1 of CCP (both laboratory errors). Table 10.1 provides an overview of each case.

All these cases are listed in Table 10.1 and are discussed in detail in the online supplementary material for this chapter (https://www.shotuk.org/shot-reports/report-summary-and-supplement-2020/). A couple of illustrative cases have been included below.

Case 10.1: Dealing with two units of blood for two different patients at the same time (Case 6 in Table 10.1)

A patient in his 30s with oesophageal varices was having an endoscopy as an out-patient. Some bleeding was identified, and he was found to have deranged clotting and a Hb of 91g/L. He was admitted to the ICU for monitoring and treatment. The unit was treating patients with COVID-19. There were two patients (one located within the 'hot' zone and the other within the 'cold' zone) and the porters had been asked to collect their blood units at the same time. Both units were collected and delivered to the 'hot' zone. The temporary agency nurse covering the shift set up the first unit and it was transfused to the patient quickly as he was actively bleeding. The second unit was then set up for the same patient and administered. Soon into the transfusion, the patient complained of intense back pain, melaena and shivering. It was then identified that the unit intended for another patient had been set up and was immediately stopped. Further information provided with the report alluded to poor lighting in the work environment as also being contributory.

A temporary agency nurse may be less likely to be fully aware of the organisation's transfusion policy. There was poor communication between the agency nurse and permanent staff. They did not realise that the blood was intended for another patient because they did not check the details at several points before giving it to the patient. The agency nurse assumed that another nurse had checked the unit so did not check it themselves.

In addition, certain work conditions were also identified as being contributory. The bedside light above the patient's bed was not working making it difficult to see clearly. Prior to the incident the department had been relocated to a new area to increase bed capacity due to the COVID-19 pandemic. The requirement for putting on and taking off personal protective equipment on a frequent basis was time-consuming and the additional time staff spent outside the clinical area collecting medication, other equipment or disposables when needed increased the pressure on the staff.

Case 10.2: Distraction during bedside checks (Case 7 in Table 10.1)

Patient 1 was a gentleman in his 80s who had recently had surgery for a fractured neck of femur but did not require a blood transfusion. The nurse was dealing with Patient 2 in the next bed who did require a transfusion. The appropriate checks were made on the blood prescription, the unit of blood and the patient ID using a bedside checklist. Before the transfusion could commence Patient 1, who was being cared for by an aspirant nurse, became acutely unwell and required the assistance of the nurse. When Patient 1 was stable the nurse preceded to connect the unit of red cells for Patient 2 to Patient 1, without restarting the checking process, and commenced the transfusion. The error was noted at a handover meeting approximately 15 minutes later, by this time Patient 1 had received approximately 15mL of the unit prescribed to Patient 2. This patient went on to have a delayed haemolytic transfusion reaction, and the patient subsequently recovered.*

The nurse was distracted by a sick patient during the administration part of the transfusion process and consequently failed to follow the organisation's administration policy by completing the final bedside identification checks without interruption.

The ward was busy and there were higher numbers of unqualified staff than usual requiring support. Safe staffing levels for the ward were usually six qualified nurses and four nursing assistants for a day shift. This shift was staffed with four Band 5 qualified nurses, three Band 2 nursing assistants, three unqualified aspirant nurses and one student nurse all requiring supervision and support.

**Aspirant nurses were introduced nationally as a rapid response to staffing concerns during the first wave of the COVID-19 pandemic. This role enabled student nurses in the final 6 months of their training programme to be employed as Band 4 nurses to use the skills and experience they had attained whilst they were supported to complete their training, through observational assessment of the use of their knowledge and skills in practice. Although these nurses could manage the care of a group of patients under the supervision of a registered nurse, they were not able to administer medication or blood components.*

Commentary

In the clinical ABOi reports there were 2 cases where the administering nurse was dealing with two different units of blood for two different patients simultaneously. This dramatically increases the risk of error. Four transfusions were carried out using a two-person independent check and three using a one-person check.

In 1 case the transfusion went ahead despite the patient not wearing an ID wristband. The BSH guideline (BSH Robinson et al. 2018) states that a patient identification band (or risk-assessed equivalent), including the core identifiers (first name, last name, date of birth and unique patient identification number), **must** be worn by all patients receiving a blood transfusion.

The remaining ABOi cases are described in full in the supplementary information on the SHOT website (https://www.shotuk.org/shot-reports/report-summary-and-supplement-2020/).

Investigating these incidents, including WBIT, using human factors principles will help identify the causal and contributory factors; and will inform the corrective and preventive actions to improve patient safety. This year one of the ABOi cases has been worked through using the new SHOT human factors investigation tool (HFIT) (incorporating the Yorkshire Contributory Factors Framework) and the Systems Engineering Initiative for Patient Safety (SEIPS) model to illustrate the benefits of applying human factors principles and systems thinking to incident investigations- both these re-worked investigation reports can be accessed online (https://www.shotuk.org/shot-reports/report-summary-and-supplement-2020/).

Figure 10.3: Clinical ABOi red cell cases (n=7)

ABOi=ABO-incompatible

Note: case numbers refer to the cases in Table 10.1

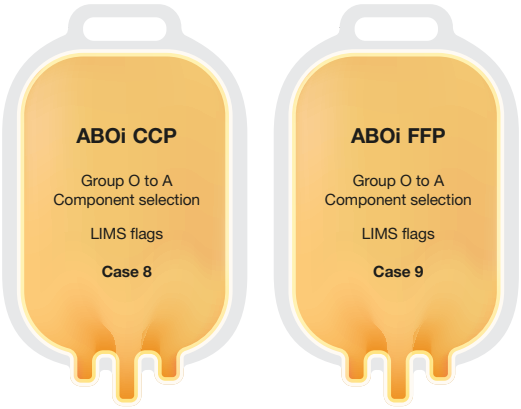


Figure 10.4: Laboratory ABOi cases (n=2)

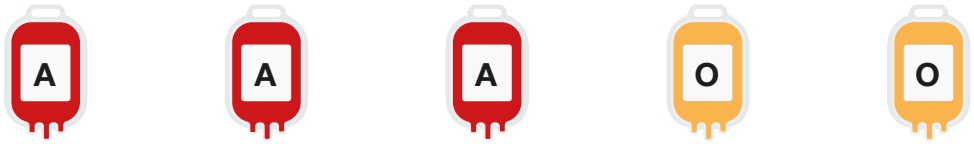
ABOi=ABO-incompatible; CCP=COVID-19 convalescent plasma; FFP=fresh frozen plasma; LIMS=laboratory information management system

Note: case numbers refer to the cases in Table 10.1

Both laboratory ABOi cases involved inappropriately overriding LIMS flags which should act as safety mechanisms. These cases are discussed further in Chapter 15, Laboratory Errors (Cases 15.4 and 15.5).

Table 10.1: ABO-incompatible transfusions key information (n=9)

Blood group of component issued				
Case number	**Case 1**	**Case 2**	**Case 3**	**Case 4**
Component transfused	Red cells group A	Red cells group AB	Red cells group A	Red cells group A
Patient Group	Group B	Group O	Group O	Group O
Volume transfused	<0.1mL	approx 50mL	<50mL	3mL
Primary error	Administration	Collection	Collection	Administration
When was error detected	Immediately after starting transfusion	Acute adverse reaction in patient	Patient informed staff	Patient informed staff
Patient impact	No clinical reaction	Minor or moderate morbidity	Minor or moderate morbidity	No clinical reaction
Urgency	Routine	Routine	Routine	Routine
In hours (8am–8pm) **Out-of-hours** (8pm–12 pm or 12pm–8am)	In hours	In hours	Out-of-hours	In hours
MHP	No	No	No	No
Department	Haematology day care unit	Urology ward	MAU	Haematology out-patients
Adult/paediatric	Adult	Adult	Adult	Adult
Administration checklist available	Yes (electronic)	Yes (electronic)	Not used at this hospital	Yes (electronic)
Patient ID	1-person check	2-person dependent check	1- person check	2-person dependent check
Root cause	Bedside checks not carried out	Failure to follow transfusion policy	Bedside checks not carried out	Bedside checks not carried out
Contributing factors	Nurse was dealing with 2 units for 2 different patients at the same time	The use of a single folder, holding every patient's sticky identification labels presents an unnecessary risk	2 patients with same surname Bedside check not carried out properly Several admissions at the same time	2 units for 2 different patients were checked against the electronic prescription Patient ID band missing Checks made away from the bedside
What controls are in place that should have prevented this	Bedside checklist Patient ID band	Transfusion policy	Positive patient ID	Positive patient ID



Case 5	Case 6	Case 7	Case 8	Case 9
Red cells group A	Red cells group A	Red cells group A	FFP group O	CCP group O
Group O	Group O	Group O	Group A	Group A
Unknown	1 unit	approx 15mL	2 units	1 unit
Administration	Administration	Administration	Component selection	Component selection
Acute adverse reaction in patient	Acute adverse reaction in patient	At handover meeting 15 minutes into transfusion	After the transfusion	After the transfusion (upon investigation of HSE NM with previous ABOi unit)
Major morbidity - admitted to HDU overnight	Minor or moderate morbidity	No clinical reaction	No clinical reaction	No clinical reaction
Routine	Urgent	Routine	Urgent	Routine
Out-of-hours	Out-of-hours	In hours	Out-of-hours	Out-of-hours
No	No	No	Code red trauma TX pre-hospital	No
Surgical ward	ICU	Trauma/orthopaedic ward	Laboratory	Laboratory
Adult	Adult	Adult	Adult	Adult
Yes (paper)	Yes	Yes (paper)	Yes	Yes
1-person check	2-person independent check	2-person independent check	1-person check (no info on manual v electronic)	2-person independent check
Failure to follow transfusion policy Lapse of concentration at the point of printing the blood request forms from the computer	Several breaches of transfusion policy Bedside checks not carried out properly	Bedside checks not carried out due to distraction of another unwell patient	Slip in attention by BMS due to distraction	Incorrect assumption by BMS that group O high titre negative was appropriate due to lack of group A in stock
2 patients requiring transfusion at the same time Checks made away from the bedside	Workload and staffing issues	Both nurses' competency training not up to date Higher number of unqualified staff requiring support due to COVID-19	Manual edit of group to O as unable to resolve, flag added for universal products Lone working	New clinical trial. Assumptions about rarity of component and availability Lone working Lack of training for clinical staff on CCP Confusion over standard operating procedure differences
Positive patient ID Bedside checklist Competency training	Positive patient ID Bedside checklist	Competency training	Warning flag in place to use universal products that was easily overridden Component labelling check Laboratory and clinical knowledge of ABO-compatibility	Warning flag not heeded BMS knowledge of ABO-compatibility

Clinical IBCT errors n=149

There were 149 cases reported in 2020 which is an increase from 131 in the 2019 Annual SHOT Report.

The COVID-19 pandemic was cited to have contributed to the errors in 4/149 (2.7%) of clinical events.

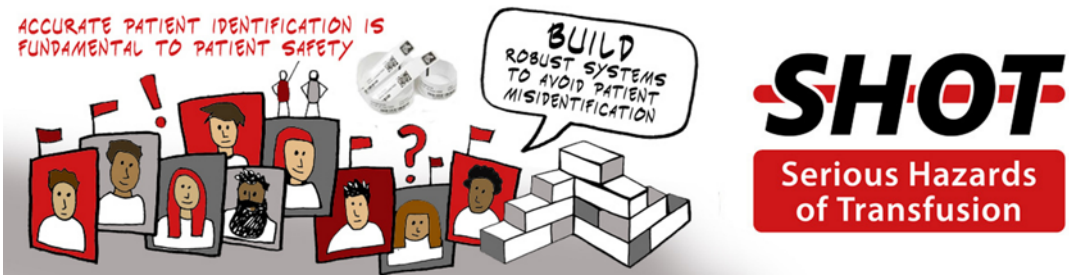
Clinical WCT events n=43

This is an increase in cases from 29 in the 2019 Annual SHOT Report.

The majority of WCT errors, 15/43 (34.9%), occurred at the point of collection of the component from the storage area, where the wrong unit was selected for the patient. Whilst the primary error occurred at collection for these incidents, there were additional missed opportunities to detect and rectify the error prior to administration had the pre-administration checklist been applied or used correctly. There were 12/43 (27.9%) cases where the bedside checks were not carried out correctly such as a failure to positively identify the patient or where the patient was not wearing an ID wristband. There was an error in the request in 8/43 (18.6%) of cases, 4/43 (9.3%) were miscellaneous errors including a case where the patient details were crossed out on the tracer tag and then handwritten and given to another patient. Blood sample errors accounted for 3/43 (7.0%) and 1/43 (2.3%) was a prescription error. Figures 10.5 a and b show the clinical WCT errors according to transfusion step and categories.

The trend for not using a bedside checklist continues despite repeated SHOT recommendations and the CAS alert: 'Safe Transfusion Practice: Use a bedside checklist' (Department of Health 2017). In 6/12 (50.0%) of these cases where a checklist was not used, the organisation had no plans to use or implement the use of such a checklist.

It is important to note that in 3/43 (7.0%) cases there were extra pressures on the staff involved due to re-deployment of staff, more staff requiring supervision and concerns over contamination of documentation in relation to COVID-19.



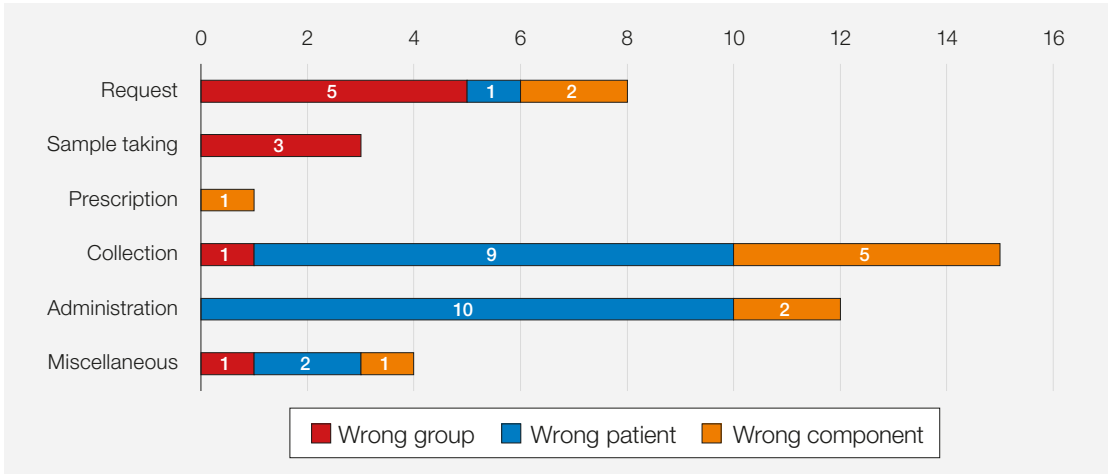


Figure 10.5a: Categorisation of clinical WCT errors by transfusion step where the primary error occurred (n=43)

Note: 'Miscellaneous' cases include: a WBIT where the patient was clerked with another patient's details, an adult unit administered to a neonate where this was a conscious decision made by the doctor due to volume requirements, a patient who was wearing another patient's ID band, and patient details on a compatibility label manually changed by clinical staff

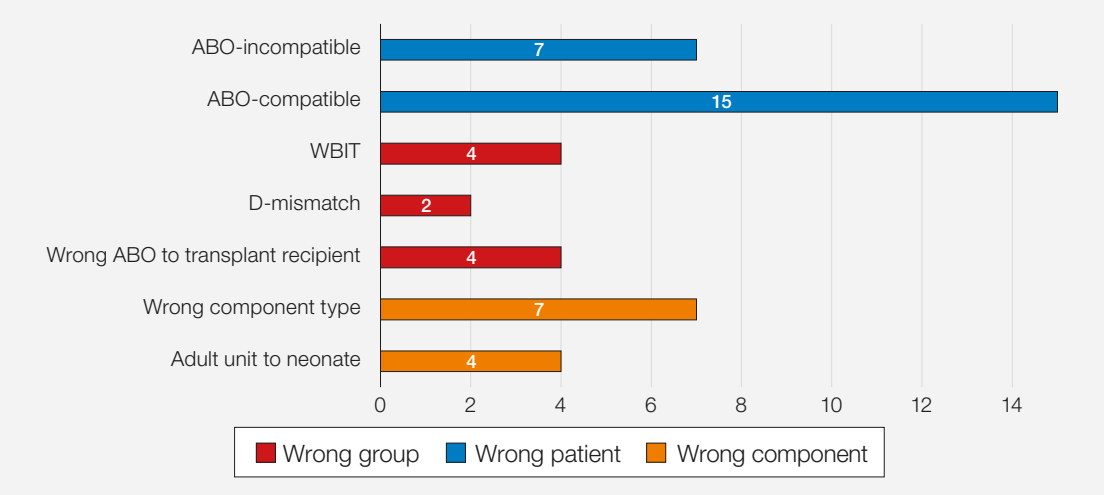


Figure 10.5b: Categorisation of clinical WCT errors by sub-category (n=43)

Note: Wrong blood in tube (WBIT) events which resulted in ABO/D compatible blood transfusions

Clinical IBCT-SRNM events n=106

This is a slight increase from the 102 events in the 2019 Annual SHOT Report.

There were 82/106 (77.4%) reports where there was a failure to adhere to the requirements for irradiated components, in each case this was not recorded on the request. Interestingly in 21/82 (25.6%) of these cases the patient had a previous diagnosis of Hodgkin's lymphoma which was either not on the patient's records or not communicated to the laboratory team. Reasons for these failures included lack of knowledge of the requirement, poor communication through shared care and clinical electronic systems not being updated.

There were 9/106 (8.5%) cases where the requirement for CMV-negative components was missed. An incorrect phenotype was transfused in 6/106 (5.7%) cases, 3 of these cases involved patients with sickle cell disease where the diagnosis was not conveyed to the laboratory. In 5/106 (4.7%) cases a blood warmer was not used when required. Other cases included 2 invalid samples, 1 incomplete testing and 1 not pathogen-inactivated.

The point in the ten-step transfusion process at which the error occurred was 91/106 (85.8%) at the request stage, at prescription in 7/106 (6.6%), and 2/106 (1.9%) each at administration, collection, sampling and miscellaneous.

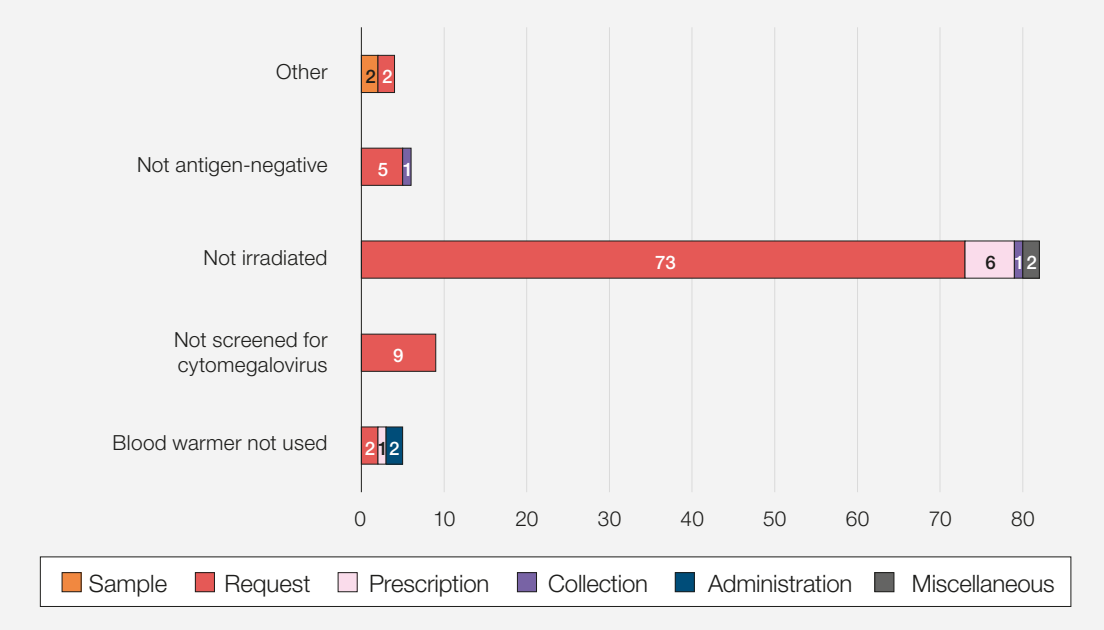


Figure 10.6: Clinical errors resulting in IBCT-SRNM categorised by patient impact and stage the error occurred (n=106)

Laboratory errors n=174

There has been a slight decrease in laboratory errors, however IBCT-WCT have remained relatively unchanged at 44, compared to 41 in 2019. IBCT-SRNM have decreased by 17.2% to 130 from 157 in 2019. When compared to the proportion of work conducted during core hours, a relatively high proportion of IBCT-WCT errors occurred when the member of staff was lone working, 15/44 (34.1%), however this was only 31/130 (23.8%) in IBCT-SRNM. The information regarding lone working was not available in 44/174 (25.3%) of IBCT errors.

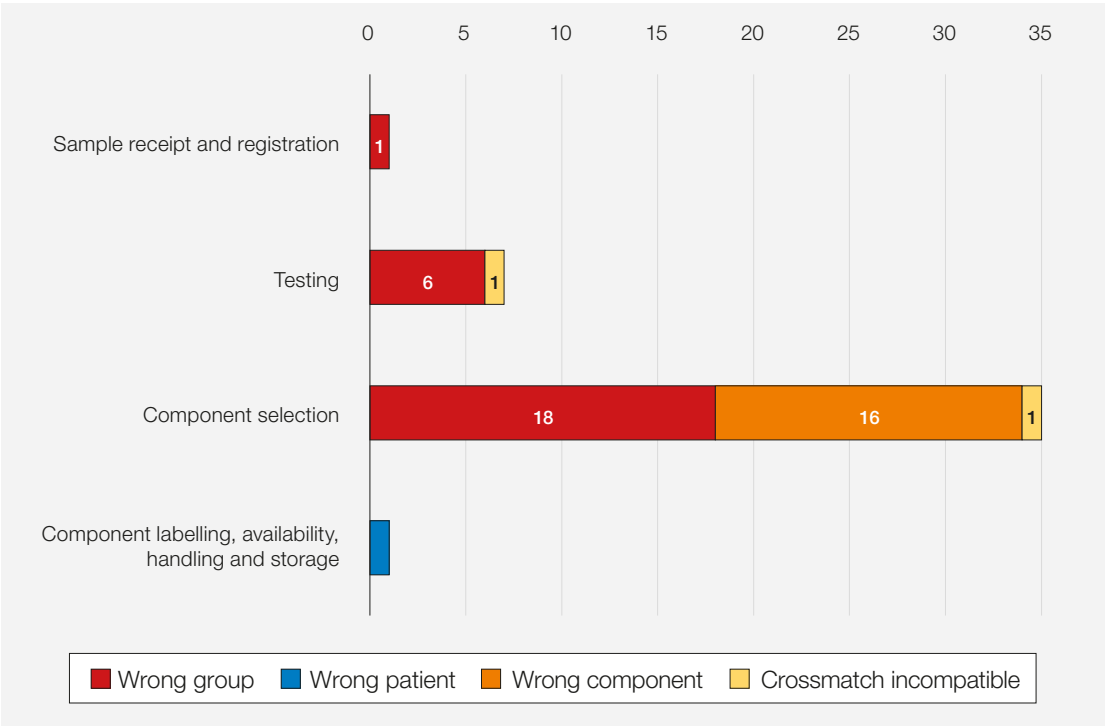
Laboratory IBCT-WCT events n=44

IBCT-WCT events are occurring consistently at the component selection step, 35/44 (79.5%). The highest number of IBCT-WCT events involved administration of the wrong component 16/44 (36.4%), which is an increase from 9/41 (22.0%) in 2019. These were mostly transfusion of adult units to neonates 9/16 (56.3%), and 1 case of neonatal red cell split packs being supplied to a child leading to undertransfusion. Nine of these cases were reported from a single site due to a lookback exercise, where the LIMS rules incorrectly mandated adult units for all patients >4 months old, misleading staff and resulting in infants under 1 year being supplied with adult units contradictory to BSH guidance (BSH New et al. 2016). However, in 2 cases adult units were supplied to infants <4 months old. This illustrates how a poorly configured LIMS system that does not reflect national guidance has the potential to cause patient harm. It also highlights that staff knowledge is a key aspect of transfusion safety. Staff should have the appropriate knowledge, or know where to find relevant information, to make informed decisions and identify when errors may have occurred. This is of particular importance during IT downtime events. These cases are also discussed in Chapter 23, Paediatric Cases. Figures 10.7a and b show the laboratory WCT errors according to transfusion step and sub-categories.

Learning points

- Transfusion management should ensure that policies and staff are kept up to date with national guidance, including the age specific requirements for all blood components
- Staff should use their professional knowledge and be empowered to challenge when they think the IT system, or an SOP is incorrect or requires amendments

Figure 10.7a: Laboratory WCT errors by transfusion step where the primary error occurred (n=44)



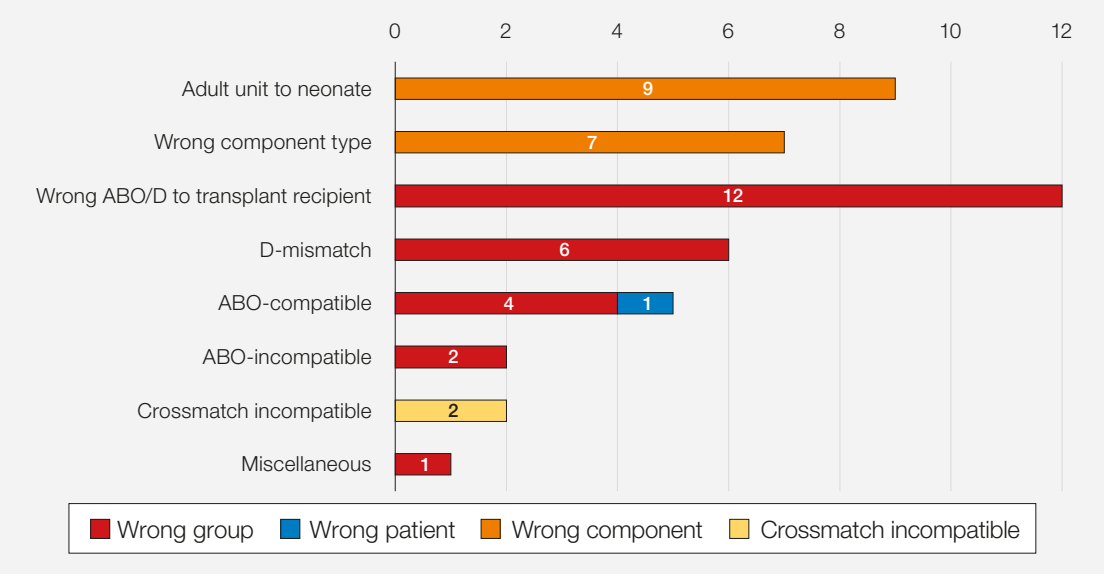


Figure 10.7b: Laboratory WCT errors by category (n=44)

Note: Case classified as 'Miscellaneous' involved communication errors between the issuing laboratory and the laboratory who routinely treated this patient.

Of the cases of D-mismatch, 4/6 (66.7%) were reported in individuals of childbearing potential – however no case of sensitisation to the D antigen were reported.

Cases of incorrect ABO/D group being given to solid organ and HSCT patients persist. These were mostly component selection errors 9/12 (75.0%) and in 5/9 (55.6%) the correct information was available in the LIMS or an alert/flag was overridden. The 2019 Annual SHOT Report (Chapter 14, Laboratory Errors) discusses the importance of designing systems to minimise alert fatigue (Narayan et al. 2020). These messages remain pertinent.

Laboratory IBCT-SRNM events n=130

Laboratory IBCT-SRNM are discussed in more detail in Chapter 15, Laboratory Errors. Most laboratory IBCT-SRNM events are the result of incomplete testing 40/130 (30.8%), followed by inappropriate use of electronic issue 23/130 (17.7%) (Figure 10.8).

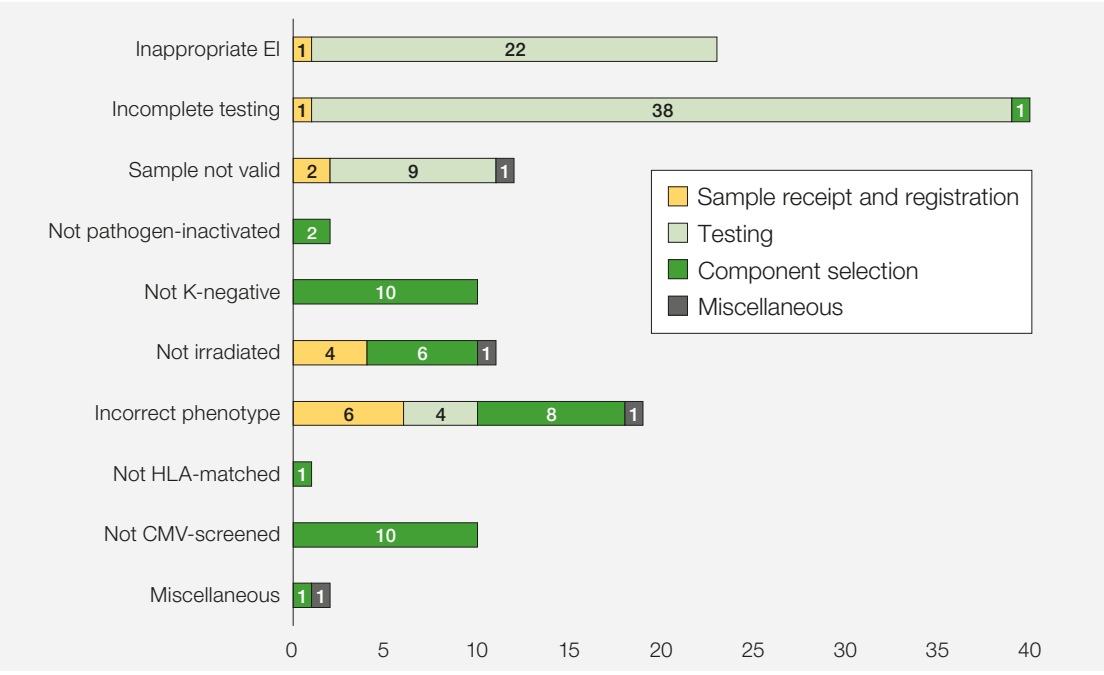
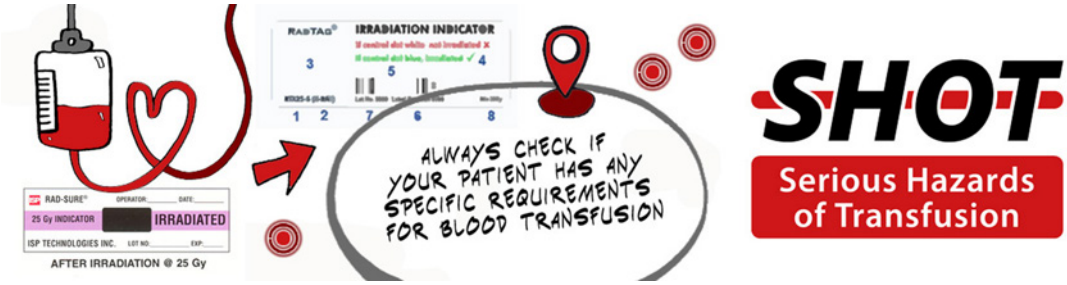


Figure 10.8: Laboratory errors resulting in IBCT-SRNM (n=130)

CMV=cytomegalovirus; HLA=human leucocyte antigen

Where the primary error occurred at the testing stage, the majority of incomplete testing cases were due to incomplete antibody identification 16/38 (42.1%). Most of these cases 9/16 (56.3%) occurred during routine hours, 5/16 (31.3%) occurred out-of-hours and this information was not available in 2/16 (12.5%). Procedures were not followed in 12/16 (75.0%), were followed but the antibody was masked in 1/16 (6.2%) and this information was not available in 3/16 (18.8%).

This is another example of how LIMS should be used to enhance safety of transfusions. They should not allow unchallenged issue of components when test results are outstanding, alerts should be raised which require rationale to be provided, and are accessible for future reference.



Case 10.3: Transfusion of antigen-positive blood due to misidentification of alloantibodies in non-ideal working conditions

A male patient in his 50s undergoing chemotherapy required a red cell transfusion. The antibody identification panel showed a historical anti-C, however a newly presenting anti-Fy^b was missed and an appropriate antigen-negative unit was not selected. The BMS performing the panel was rushing to avoid leaving unfinished work for the next shift. They failed to perform full antibody exclusions on the panel and relied on previous history to guide decision making. The unit was crossmatch-compatible by indirect antibody test and the mistake was detected 4 days later when panel results were second checked by a senior BMS.

It is vital that every antibody identification panel is fully interpreted, and no assumptions based on previous results are made. Staff should also not begin tasks if they cannot be completed safely before shift handover. The pressures of workload were recognised in the investigation, however it is concerning to see that the investigator had noted 'excuses of busyness and distraction cannot be used continually as defence for incidents in blood transfusion'. This suggests that underlying system issues, such as staffing and workload, are not being addressed appropriately to avoid future errors. This may itself contribute to staff members feeling pressure to cut corners and not mention any potential errors for fear of blame. Workload pressures also seem evident as it took 4 days for the panel to be second checked. Laboratories are busy workplaces. Whilst laboratory staff must be equipped to prioritise and be aware of their own working limits, if multiple errors are highlighting excessive workload and distraction these factors should be investigated and if necessary, procedures and capacity plans adjusted considering these risks.

Learning point

- All essential testing should be resolved prior to issue of blood components. If the antibody identification is yet to be completed then concessionary release should be considered to avoid transfusion delays

A total of 17/38 (44.7%) incomplete testing errors occurred during urgent (12) or emergency (5) situations. In these situations, it may not be possible to complete all required testing prior to release of blood components. These components will be less safe than if testing was completed, therefore it is essential that the decision to issue components with incomplete testing is a conscious decision which is made after approval for concessionary release by haematology doctors or within local procedures.

Learning point

- In complex situations advice should be sought from senior laboratory staff and haematology doctors, and rationale for concessionary release recorded according to local procedure

Near miss IBCT cases n=178 (107 clinical, 71 laboratory)

Definition

A 'near miss' event refers to any error which if undetected, could result in the determination of a wrong blood group or transfusion.

There was a total of 20 NM ABOi transfusions in 2020, 1 less than in the 2019 Annual SHOT Report. Of these, 16/20 (80.0%) originated in the clinical area and 4/20 (20.0%) in the laboratory.

Clinical NM IBCT-WCT n=88

As in 2019 the most common error in this category was at the collection stage of the process with 54/88 (61.4%) of reports, 33/54 (61.1%) of these errors being identified on administration at the beside with the use of a checklist;19/33 (57.5%) with an electronic bedside check and 14/33 (42.5%) with manual bedside check. A total of 25/88 (28.4%) errors occurred at the administration stage of the transfusion process where there had been an attempt to give the component to the wrong patient. In 21/25 (84.0%) of these cases the error was identified by an electronic system alert and 4/25 (16.0%) by nurses identifying the error during the final bedside check.

Clinical NM IBCT-SRNM n=19

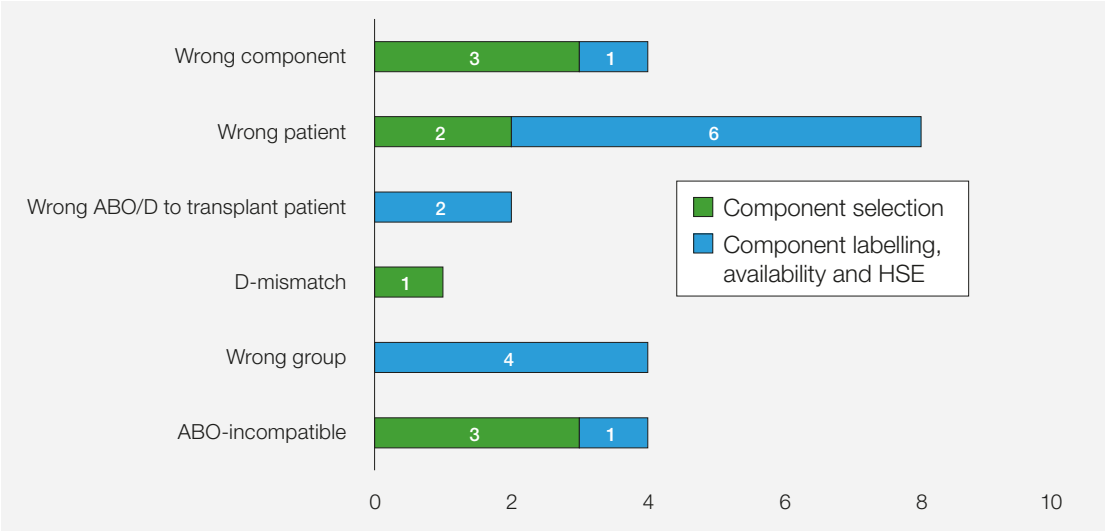
These potential errors were identified by vigilant nurses who noticed the specific requirements were not present prior to the transfusion taking place. There were 15/19 (78.9%) of NM events where the patient could have potentially received non-irradiated components. The majority 13/15 (86.7%) of errors had been made at the request stage. As with previous years the most common reason for these errors was poor communication where the clinical area had not informed the laboratory of specific requirements.

Laboratory NM IBCT-WCT n=23, IBCT-SRNM n=48

The highest proportion of laboratory NM-IBCT events occurred at the component selection step, 47/71 (66.2%). A number of NM IBCT-WCT errors 8/23 (34.8%) had the potential to result in blood being administered to the wrong patient and were mostly component labelling errors, 6/8 (75.0%). NM IBCT-WCT errors were mostly detected at the pre-administration bedside check 15/23 (65.2%).

Most NM IBCT-SRNM were detected at the pre-administration bedside check 26/48 (54.2%). In others the error was detected by chance. The highest proportion of laboratory NM IBCT-SRNM events involved patients requiring irradiated blood, 25/48 (52.1%).

Figure 10.9: Laboratory near miss IBCT-WCT events categorised by error and step in the transfusion process (n=23)



HSE = handling and storage errors

Conclusion

This year has seen an alarming rise in ABOi blood transfusions. The key themes highlighted in these cases have safety implications throughout the transfusion chain and healthcare in general. It is fortuitous that no patients died due to these errors. Three patients did suffer adverse reactions, 1 of which resulted in major morbidity and admission overnight to the HDU. The importance of accurate positive patient identification at the patient's side cannot be underestimated and a lack of compliance with this fundamental step can be taken as an indicator of a struggling healthcare system or poor safety culture. Distractions in healthcare can have disastrous consequences, these are even more of a danger in unfamiliar circumstances. Procedures should be clear to follow and contain all relevant information, and if staff do not feel they are able to safely follow these procedures these concerns should be escalated immediately. Training is essential in all healthcare settings; this should be tailored for the role and enough time allowed for this to be meaningful. Where bank, agency, locum, or redeployed staff are involved in transfusion they must receive the same level of training and competency assessment as substantive staff. If this is not possible or has not been completed staff should receive appropriate supervision and should not work alone. It is surprising that only 1 ABOi case mentioned the pressures of COVID-19 and it may be reasonable to assume that a stretched and exhausted workforce was also contributory in some of these cases.

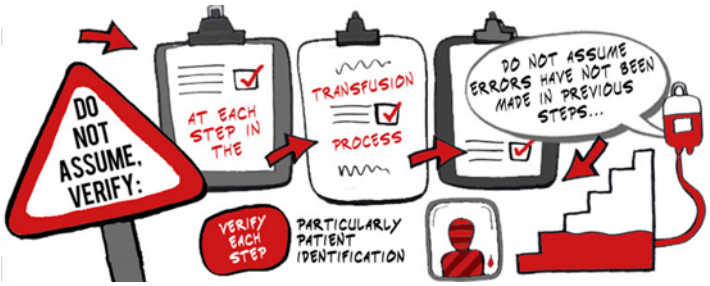
Recommended resources

The BSH guidance for the use of irradiated blood components was updated in 2020. All who prescribe blood components should be familiar with this guidance
https://onlinelibrary.wiley.com/doi/full/10.1111/bjh.17015

SHOT safe transfusion checklist
https://www.shotuk.org/resources/current-resources/

ABO-incompatible transfusion events 2010-2019 video
https://www.shotuk.org/resources/current-resources/videos/

SHOT Bite No. 17 Near Miss
https://www.shotuk.org/resources/current-resources/shot-bites/



SHOT
Serious Hazards of Transfusion

References

BSH Foukaneli T, Kerr P, Bolton-Maggs PHB, et al. Guidelines on the use of irradiated blood components. *Br J Haematol* 2020;**191(5)**:704-724. https://doi.org/10.1111/bjh.17015 [accessed 28 April 2021].

BSH New HV, Berryman J, Bolton-Maggs PHB, et al. Guidelines on transfusion for fetuses, neonates and older children. *Br J Haematol*. 2016;175(5):784-828.

BSH Robinson S, Harris A, Atkinson S, et al. The administration of blood components: a British Society for Haematology Guideline. *Transfus Med* 2018;**28(1)**:3-21. http://onlinelibrary.wiley.com/doi/10.1111/tme.12481/full [accessed 25 March 2021].

Narayan S (Ed), Poles D, et al. on behalf of the Serious Hazards of Transfusion (SHOT) Steering Group. The 2019 Annual SHOT Report (2020). https://www.shotuk.org/shot-reports/ [accessed 30 April 2021].

NHS England. Never Events list (2018). https://www.england.nhs.uk/wp-content/uploads/2020/11/2018-Never-Events-List-updated-February-2021.pdf [accessed 30 April 2021].

NHS Wales. Never Events List 2018 and Assurance Review Process (2018). http://www.patientsafety.wales.nhs.uk/sitesplus/documents/1104/WHC%202018%2012%20Never%20Events%20List%202018%2029-3-18.pdf [accessed 30 April 2021].

11 Handling and Storage Errors (HSE) n=278

Authors: Heather Clarke and Victoria Tuckley

Definition:

All reported episodes in which a patient was transfused with a blood component or plasma product intended for the patient, but in which, during the transfusion process, the handling and storage may have rendered the component less safe for transfusion.

Key SHOT messages

- In progress or planned transfusions must be included in patient handover procedures to prevent handling and storage errors (HSE). This must include information on the transfusion duration and monitoring required

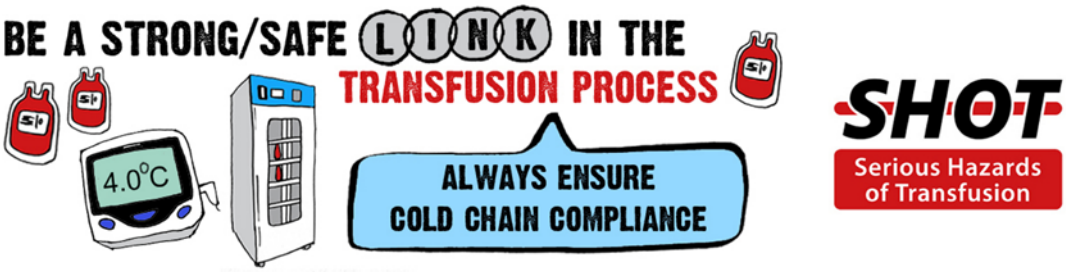
Abbreviations used in this chapter

HSE	Handling and storage error	**NM**	Near Miss

Recommendations

- Education for clinical staff should include information on the appropriate rates of transfusion and should consider variations required for individual patient needs. Where an infusion pump is used, procedures must be in place to ensure the correct rate is achieved
- Wherever possible cold chain compliance should be controlled by laboratory information management systems and/or electronic blood tracking systems. Laboratory procedures should be in place for the accurate return of components back into stock, including information about cold chain compliance

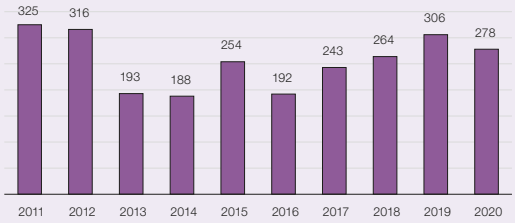
Action: Clinical education teams, laboratory management



Headline data 2020

Number of reports n=278
Deaths n=0
Major morbidity n=0

HSE reports by year



Demographic data

Male n=135
Female n=104
Unknown n=39

Adults n=231
Paediatric n=14
Unknown n=33

Blood component data

Red cells n=233
Platelets n=18
Plasma n=20
Multiple Components n=3
Other n=2
Unknown n=2

Introduction

There were 278 cases reported in 2020. HSE errors accounted for 306/3397 (9.0%) reports in 2019 (Narayan et al. 2020) and for 278/3214 (8.6%) in 2020. The reduction in total number of HSE may be attributed to the reduction in transfusions taking place during the first wave of the COVID-19 pandemic. Clinical errors accounted for 185/278 (66.5%) and laboratory errors for 90/278 (32.4%). The distribution of clinical and laboratory errors is illustrated in Figure 11.1.

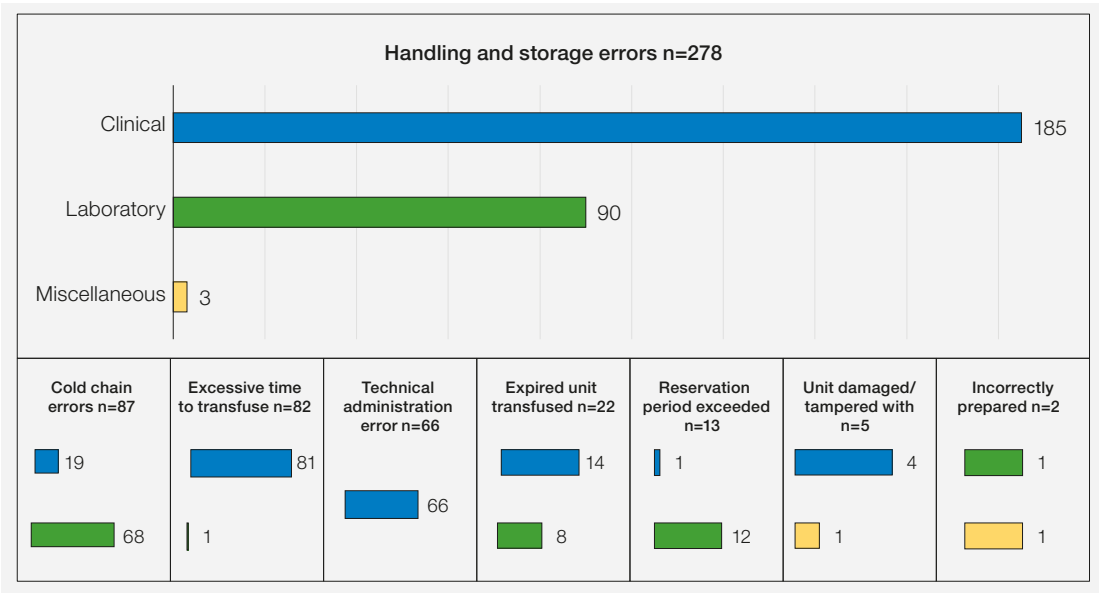


Figure 11.1: Breakdown of 2020 handling and storage error reports (n=278)

The top graph shows an overview of the HSE errors. These are broken down into specific groups of errors in the bottom graph. One case categorised as 'miscellaneous' is not displayed by error in the bottom graphs as it did not fit into any of the categories.

Deaths n=0

There were 19 deaths reported in 2020, but only 1 that related to errors associated with HSE (imputability 1 – possibly related), in which a patient was transfused a unit of red cells over 6 hours and subsequently developed transfusion-associated circulatory overload. This death is not counted in the HSE data but is included in Chapter 18b, Transfusion-Associated Circulatory Overload (TACO).

Major morbidity n=0

There was 1 HSE case reported in 2020 that resulted in major morbidity, but this was unrelated to the transfusion.

Clinical errors

The number of clinical errors remains consistent with previous years, however there has been a 25.8% decrease in technical administration errors (66/185 in 2020 and 89/199 in 2019) and a slight increase (3.8%) in excessive time to transfuse errors (81/185 in 2020 and 78/199 in 2019). Excessive time to transfuse errors include all cases where components have been transfused beyond the recommended time duration. Technical administration errors have been further categorised below in Table 11.1.

Table 11.1: Clinical technical administration errors (n=66)

Technical administration error	Number of cases
Administration pump error	45
Giving set error	15
Inappropriate rate	3
Same venous access used	2
Other	1
Total	**66**

Note: The case included as 'other' contained insufficient information about the technical administration error to categorise.

There were 82 errors relating to excessive time to transfuse, 81 clinical errors and 1 case where the laboratory staff gave inappropriate advice on the transfusion duration. Excessive time to transfuse errors mostly occurred during routine hours (08:00-20:00) 58/82 (70.7%), and surprisingly 22/82 (26.8%) occurred with urgent requests. In both these situations there should be sufficient staff available for patient monitoring. In 32/82 cases (39.0%) no incident investigation was performed, with the most common reason given being that the error was not serious enough to warrant further investigation. This lack of investigation may indicate why the problem is persisting and increasing. Most excessive time to transfuse errors are detected by transfusion practitioners 29/82 (35.4%) or laboratory staff 12/82 (14.6%) showing the error is not always recognised by the clinical staff providing the patients care, and there is likely to be a high level of under-reporting.

There may be a degree of under-reporting in the category of 'expired unit transfused'. SHOT strongly encourage all actions are taken to provide a component which will not expire during the transfusion period. The expiry date represents the latest point in time that the component has been deemed safe for transfusion. A number of systemic factors often contribute to a component being transfused past its expiry, such as staff shortages and gaps in communication. These should be explored and addressed to ensure safe practices.

Case 11.1: Red cells transfused after the units had expired

Two units of red cells due to expire at midnight that day were issued to a patient for a top up transfusion. The units were placed in the issue refrigerator ready for collection. The first unit was collected at 22:00 and the second unit was collected at 06:10 the next day, which was over 6 hours past the midnight expiry. It also transpired that transfusion of the first unit was not completed until after the unit had expired. On investigation the expiration date was highlighted on the blood collection slip and both units were collected by the same healthcare assistant, administered by the same nurse, and both failed to notice the expiry date of the units at collection and pre-administration checks. The laboratory reacted quickly in creating corrective and preventative actions to avoid this happening again and now have a new procedure in place. Any units issued to a patient that expire at midnight on the day of issue are now kept within the laboratory awaiting collection, thus ensuring that they will not be transfused past expiry.

As part of pre-administration checks, components must be inspected to ensure that they have not expired or will not expire during the period of transfusion.

Laboratory errors

In most HSE categories the numbers remain consistent with previous Annual SHOT Reports; however, there has been a decrease in the number of laboratory errors from the 2019 Annual SHOT Report, 90 errors in 2020 compared to 107 in 2019. There was 1 case of excessive time to transfuse which was attributed to laboratory practice. The laboratory gave incorrect advice to the clinical area when asked about continuing a platelet transfusion that had been stopped as the patient needed re-cannulation. This resulted in the unit being transfused nearly 5 hours after collection from the laboratory.

Most laboratory HSE errors involved cold chain errors, 68/90 (75.6%) reports in 2020. The largest cause of cold chain errors identified was refrigerator/equipment failure 33/68 (48.5%) of which 5 involved failures of temperature monitoring processes. Inappropriate return to stock errors accounted for 20/68 (29.4%) of which 5 involved failures in electronic blood tracking systems. Other errors included incomplete cold chain 10/68 (14.7%) and transport and delivery 4/68 (5.9%). In one case cryoprecipitate was inappropriately stored.

Case 11.2: Blood storage refrigerator out of temperature for 2 hours due to failure to respond to temperature monitoring system alerts

A blood storage refrigerator core temperature exceeded its high limit for almost 2 hours. The temperature monitoring service called the laboratory mobile phone as per standard procedure, but the laboratory did not answer as the phone battery was dead and the charger for the phone had gone missing. The caller left a voicemail on the mobile phone and emailed the site lead as per instructions. The site lead missed the email and only found the alarm alert 2 days later whilst clearing another alarm received that day. Three patients were transfused a total of five units of red cells that were out of temperature control for 1.5 hours. Another three units, that were also in the blood refrigerator at that time, had to be wasted. The clinical teams looking after the 3 patients who were transfused were informed and no adverse reactions or harm were reported.

Temperature monitoring systems must have a robust process for escalation of alarms that does not rely on emails and messages left on answering machines. Laboratory management must ensure that reliable communication channels are available at all times. It is important that all staff are aware of the need to act on temperature monitoring alerts in a timely manner to ensure that any equipment problems are picked up and acted upon as quickly as possible. This should prevent wastage and transfusion of potentially unsafe blood components. The laboratory must also have a robust process in place, for staff, so that alerts are picked up as soon as possible and must include clear guidance of what, when and how to escalate.

Emergency preparedness

In 2021, SHOT issued 'SHOT Safety Notice 01: Emergency preparedness in the transfusion laboratory in case of total power outage'. This is based on a handling and storage error reported which occurred during a major power outage and involved thawing of fresh frozen plasma in a non-standard manner. There are many points of merit to be acknowledged in this case, and many learning points about ensuring safety of components during extreme circumstances. This case is included as part of online supplementary material for Chapter 6, Acknowledging Continuing Excellence in Transfusion (ACE). The safety notice can be found in current resources on the SHOT website (see recommended resources at the end of this chapter) and the case has been detailed in the supplementary material (https://www.shotuk.org/shot-reports/report-summary-and-supplement-2020/).

Learning points

- Components must not be transfused past the expiry date. Transfusions should not commence if they cannot be safely completed prior to their expiry
- All staff involved in the transfusion process must be aware of the need for accurate cold chain compliance and the correct storage for blood components

Near miss HSE cases n=129

There were 129 near miss HSE cases which is a 21.3% reduction in the number of cases reported in 2019 (n=164), 105/129 (81.4%) originated in the clinical area and 24/129 (18.6%) in the laboratory. The near miss HSE cases primarily involved cold chain errors 59/129 (45.7%) followed by 39/129 (30.2%) cases of incorrect storage of units and 19/129 (14.7%) cases where expired units were almost transfused to patients. Near miss events outnumber actual errors relating to inappropriate storage (13/278, 4.7%). This suggests that most staff are aware of correct component storage and vigilant clinical staff are returning components to the laboratory when they are outside of appropriate conditions.

Conclusion

By working collaboratively, staff in the laboratory and clinical area can ensure the safety of the blood components that are transfused. Staff need to be aware of the correct rate and duration of transfusions. Other factors, such as staffing levels and appropriate working conditions to ensure safe patient monitoring should be addressed.

SHOT reinforces that all staff who participate in the handling and storage of blood components should adhere to correct procedures in accordance with local transfusion policies. Transfusion policies should be easy to access and contain useful information based on the most current published guidance available (BSH Robinson et al. 2018). By embedding these policies in working practice, safer patient care overall can be achieved.

Recommended resources

Blood Assist - a blood administration safety app developed by the Patient Blood Management team at NHS Blood and Transplant.
Apple (https://apps.apple.com/gb/app/blood-assist/id1550911130)
Google play (https://play.google.com/store/apps/details?id=uk.nhsbt.bloodassist)
Web based (www.bloodassist.co.uk)

SHOT Safety Notice 01: Emergency preparedness in the transfusion laboratory in case of total power outage
https://www.shotuk.org/resources/current-resources/

References

BSH Robinson S, Harris A, Atkinson S, et al. The administration of blood components: a British Society for Haematology Guideline. *Transfus Med* 2018;**28(1)**:3-21. http://onlinelibrary.wiley.com/doi/10.1111/tme.12481/full [accessed 25 March 2021].

Narayan S (Ed), Poles D, et al. on behalf of the Serious Hazards of Transfusion (SHOT) Steering Group. The 2019 Annual SHOT Report (2020). https://www.shotuk.org/shot-reports/ [accessed 27 April 2021].

Avoidable, Delayed or Under/Overtransfusion (ADU) and Incidents Related to Prothrombin Complex Concentrate (PCC) n=285

12

Authors: Paula Bolton-Maggs and Simon Carter-Graham

Key SHOT messages

- The increase in reports of delayed transfusion is of concern
- Poor communication is a major cause of delays
- Major haemorrhage events should be audited, protocols reviewed, and drills used to embed in practice
- Gaps in staff knowledge and training need to be addressed so that haematinic deficiencies are recognised and treated appropriately

Abbreviations used in this chapter

AAA	Abdominal aortic aneurysm
ADU	Avoidable, delayed or under/overtransfusion
AIHA	Autoimmune haemolytic anaemia
BMS	Biomedical scientist
BP	Blood pressure
BSH	British Society for Haematology
CMV	Cytomegalovirus
ERCP	Endoscopic retrograde cholangiopancreatography
ED	Emergency department
FBC	Full blood count
FFP	Fresh frozen plasma
GI	Gastrointestinal
Hb	Haemoglobin
HSE	Handling and storage errors
ICH	Intracranial haemorrhage
ICU	Intensive care unit
INR	International normalised ratio
IV	Intravenous
LIMS	Laboratory information management system
MCV	Mean cell volume
MH	Major haemorrhage
MHP	Major haemorrhage protocol
MHRA	Medicines and Healthcare products Regulatory Agency
NCA	National comparative audit
NPSA	National Patient Safety Agency
PCC	Prothrombin complex concentrate
RECOVERY	Randomised Evaluation of COVID-19 Therapy
SOP	Standard operating procedure
TACO	Transfusion-associated circulatory overload

Recommendation

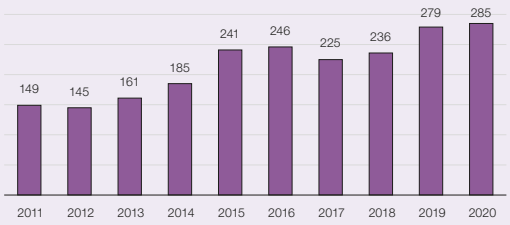
- Problems arising during major haemorrhage indicate a continuing need for review of major haemorrhage protocols (MHP) and regular drills. This has increasing importance with fragmentation of clinical care and management by multiple teams

Action: Medical directors and hospital transfusion teams

Headline data 2020

Number of reports n=285
Deaths n=13
Major morbidity n=6

ADU reports by year



Demographic data

Male n=130
Female n=147
Unknown n=8

Adults n=244
Paediatric n=35
Unknown n=6

Blood component data

Red cells n=201
Platelets n=29
Plasma n=22
Multiple Components n=14
PCC n=17
Unknown n=2

Overview of ADU cases

- **Delayed transfusions n=133**
- **Avoidable transfusions n=110**
- **Under or overtransfusion n=25**
- **Cases related to PCC n=17 (9 in 2019)**

Near miss cases n=21 (not included in the total above)

There were 12 near miss avoidable transfusions including 2 patients nearly given O D-negative units (when crossmatched or group-specific units were available) in the context of major haemorrhage activations. There was 1 near miss delay, 1 PCC nearly given to wrong patient, 6 potential overtransfusions (4 in children; 1 adult female with iron deficiency and 1 patient who had altered the request form themselves from 'group and screen' to 'transfuse 2 units') and 1 undertransfusion of platelets to a child.

Deaths n=13

There were 12 deaths related to delays: 1 definitely related, 3 probably related and 8 possibly related to the delayed transfusion.

One death was possibly related to undertransfusion.

Major morbidity n=6

These were all related to delays in transfusion.

Delayed transfusion

The increase in reports of delayed transfusion, with 12 deaths (2 in 2019), is of concern. Bleeding that is not visible (e.g. GI, ruptured ectopic pregnancy) is more likely to be associated with delayed recognition. Two deaths occurred in infants after elective biopsy. Massive blood loss can occur very quickly in obstetrics and some surgical procedures, so MH procedures need to be slick and efficient. This requires preparedness and practice.

Issues with MH procedures n=41

- Delays were reported for 26 cases of MH, 25 where the MHP was activated and 1 in a child where it was not
- Avoidable transfusions were reported in 11 cases of MH, 9 potentially avoidable use of group O D-negative red cells, and transfusion of red cells to 2 Jehovah's Witnesses
- Overtransfusion was reported in 4 cases of MH, with post-transfusion Hb levels ranging from 173 to 202g/L

Learning points

- Major haemorrhage protocols (MHP) need to be practical and work efficiently. All cases of activation should be reviewed to learn from each event
- The MHP may vary between hospitals and between departments, e.g. ratios of red cells to plasma may be different for obstetric haemorrhage compared with trauma. Staff need to be aware of local protocols and know how to access components in an emergency

MHP Drills

It is difficult to perform drills with all relevant staff at the same time; some hospitals have used simulation suites to set up a mock emergency and this can be used to drill all parts of the activation process such as taking blood samples. Some also recommend activation of the cardiac arrest call at the same time to alert other senior staff who can assist, particularly in wards or areas of the hospital where haemorrhage activations are rare. It is important to include laboratory staff in these drills, for example to see how long it actually takes to get components from the laboratory to the emergency department. A suggested audit is to walk around wards and simply ask staff of all grades if they know where their protocol is and how to activate it. In one hospital this resulted in placing laminated protocols on each resuscitation trolley on wards as this was the one place that gets checked daily and that staff run for when a patient is very unwell.

MHP Audit

Audit of activations can be very useful. The following questions can be included in audit templates: What can be learned or improved? Positive aspects of the management of a major haemorrhage are important; what went well and why?

Conclusion

Delays in transfusion are associated with about a quarter of all deaths reported to SHOT. These should be preventable.

Recommended resources

NICE. Acute upper gastrointestinal bleeding in over 16s: management. Clinical Guideline 141 (2012).
https://www.nice.org.uk/guidance/CG141/chapter/1-Guidance#timing-of-endoscopy

NICE. Major trauma: assessment and initial management. Clinical Guideline 39 (2016).
https://www.nice.org.uk/guidance/ng39

North West Regional Transfusion Committee Steering Group Major Haemorrhage Guidelines Group. Toolkit for the Management of Major Haemorrhage.
https://www.transfusionguidelines.org/uk-transfusion-committees/regional-transfusion-committees/north-west/policies/massive-haemorrhage-toolkit

SHOT educational video about transfusion delays in major haemorrhage can be accessed at this link
https://www.shotuk.org/resources/current-resources/videos/

12a Delayed Transfusions n=133

Definition:

Where a transfusion of a blood or blood component was clinically indicated but was not undertaken or was significantly delayed or non-availability of blood components led to a delay with impact on patient care (not restricted to emergency transfusion).

Key SHOT messages

- Serial delays at different transfusion steps are cumulative and can result in harm or death
- Good communication between clinical and laboratory staff is essential
- Many different groups of staff will be involved in the management of major haemorrhage; ensure the learning is done involving teams
- Patient transfer between departments and clinical teams is associated with delays in transfusion
- A haematologist should be contacted at the earliest opportunity for advice about patients with irregular antibodies and can enable timely concessionary release
- Gastrointestinal bleeding can be deceptive, the severity is often masked, diagnosis may be delayed; hypotension and tachycardia are important clinical signals
- Elderly patients are often on anticoagulants exacerbating the severity of bleeding
- Obstetric haemorrhage can be rapid and massive; it is vital that major haemorrhage protocols work smoothly and quickly. Training and drills are essential
- Staff should be familiar with local protocols. In the event of major haemorrhage all the necessary components may not be available at the same time. Red cells should be quickly available but fresh frozen plasma and cryoprecipitate take time to thaw; platelets may have to be sourced off site

Recommendations

- Clinical staff involved in frontline care must be trained to recognise major blood loss early and know when to activate/trigger the local major haemorrhage protocol and take prompt and appropriate action (NCA 2018)
- Major haemorrhage protocols should be regularly reviewed and practiced with drills particularly in areas of greatest risk, i.e. emergency departments, obstetrics, and operating theatres
- Transfusion laboratories should ensure they have a robust procedure for concessionary release to avoid deaths from bleeding or anaemia
- Ensure that all communication channels function well particularly the correct pathway for activation, including means of contacting porters and transfusion laboratory staff
- Major haemorrhage activations should be regularly audited to ensure lessons are learned

Action: Hospital transfusion teams

Abbreviations used in this chapter

HDFN	Haemolytic Disease of the Fetus and Newborn	**NW**	North West
NICE	National Institute for Health and Care Excellence	**NWRTC**	North West Regional Transfusion Committee

Introduction

The number of reports of delayed transfusion has increased in 2020 (133 compared with 129 in 2019) with 12 deaths (3 in 2019, 1 of these was due to delay in PCC administration) and 6 cases of major morbidity. The reports illustrate many problems with communication and delayed recognition of the severity of haemorrhage. Overall, transfusion was urgent or emergency in 80/133 (60.2%).

Delays were associated with the MHP in 25/133 (18.8%) with features as described in previous years (poor communication, lack of knowledge and failure to follow the correct procedure). There were 4 cases of major obstetric haemorrhage. The principles described in the BSH guidelines (Hunt et al. 2015) should be followed. Several useful resources are available, including the North West RTC toolkit (NW RTC Steering Group 2013) and NICE guidance (links are provided in the recommended resources section). A recent comprehensive protocol has been published from Canada (Callum et al. 2021).

The NCA of major haemorrhage (826 cases) reported that 28% were associated with surgery, 21% with obstetrics, 20% with GI bleeding and 17% with trauma (NCA 2018). This recommended that 'clinical teams must be trained to recognise major blood loss early, and to know when to activate and stand down the major haemorrhage protocol'. In some cases reported to SHOT, recognition of bleeding severity was delayed, particularly when 'concealed' with catastrophic outcomes.

The increase in both total number of reported delays and deaths is of concern. Recurring themes over these 10 years include delayed recognition of serious bleeding, use of the wrong activation phrase when contacting switchboard, bleep failures (laboratory and porters), sample mislabelling, and failure to follow the MHP. Serial delays occur during transfer of patients between departments and teams. Poor communication is a major problem (see below). In major haemorrhages every minute counts and delays should be avoided. Patients should not die from bleeding.

Components may not all be available at once. Delays may be reduced when staff know how to access the emergency group O D-negative and D-positive red cells. These should be available within minutes. In hospitals that do not keep pre-thawed FFP (the majority), the thawing process can take up to 40 minutes. Platelets are usually required later in the treatment of major bleeding; they may or may not be available on site.

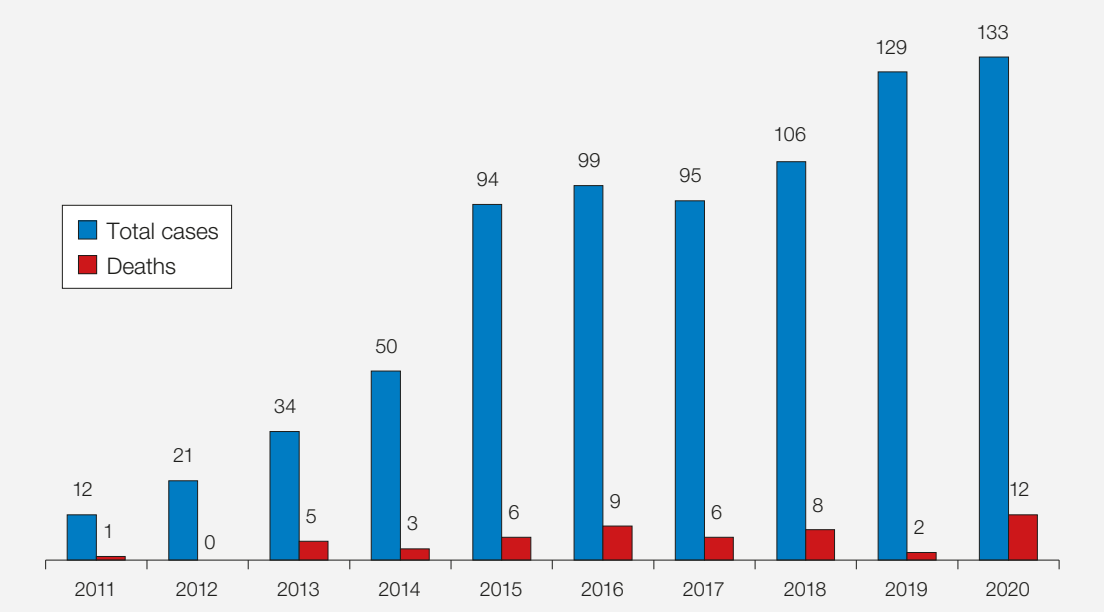


Figure 12a.1: Delayed transfusion reports and deaths by year 2011 to 2020 (n=773, deaths n=52)

Deaths n=12 (2 in 2019)

Imputability: one death was 'definitely' related (imputability 3), 3 'probably' related (imputability 2) and 8 'possibly' related (imputability 1) to the delay in transfusion.

Two infants died from haemorrhage after elective biopsy (liver biopsy and rectal biopsy). This is a very rare complication. In both cases there was delayed recognition of the severity of haemorrhage and delay in activating the major haemorrhage procedures. These are described in Chapter 23, Paediatric Cases.

Four deaths in elderly patients were associated with GI bleeding; 3 of these patients were on anticoagulants for atrial fibrillation.

Case 12a.1: Death from GI bleeding with serial delays and miscommunications

An elderly woman on anticoagulants was admitted with a history of melaena. She was pale with hypotension, blood pressure 88/55mmHg, and tachycardia, and was assessed within 3 minutes of arrival. She was noted to be in shock from blood loss. Her Hb on the blood gas machine on admission was 41.8g/L. The MHP was not activated. Transfusion was delayed for almost 7 hours from admission and she died shortly after it was started.

The investigation noted that:

- There was no clear line of responsibility for delivering care and limited resources in the ambulance bay. A hospital pre-alert would have resulted in a 'fast-track' to resuscitation
- There was failure to escalate due to poor communication when the patient was moved from the ambulance bay to resuscitation, and a lack of communication between doctors and nurses in the resuscitation area
- Computer blood prescribing was noted to be complex and 'a common source of clinical error'
- The medical consultant was working in an unfamiliar and understaffed environment with an unfamiliar clinical condition with staff he did not know
- Handover to the registrar resulted in decisions being made without seeing the patient
- Mandatory transfusion training for medical staff should take place

Case 12a.2: Death related to GI haemorrhage with multiple points of delay

An elderly man had a prolonged admission for renal problems. His anticoagulant for atrial fibrillation and omeprazole were discontinued. Two months later after successful treatment he was awaiting discharge. His anticoagulant had been restarted. Unexpectedly he developed large volume melaena. A group and screen sample taken at 10:01 was received in the laboratory at 13:15 (portering delays) but not processed due to incorrect labelling. The clinical team did not know this due to the LIMS not interacting with the patient information system. The FBC sample was clotted, requiring repeat. At 16:26 Hb 66g/L was noted and transfusion of two units requested. The repeat sample for transfusion was delivered to the laboratory at 17:09 (diagnosis anaemia rather than GI bleeding) requesting blood for 20:00. However, at 19:00 he had a large rectal bleed and died.

The review concluded that:

- There were significant delays in obtaining a valid Hb in a patient with GI bleeding together with mislabelling and rejection of the transfusion sample
- There was failure to recognise the signs: the patient had a sustained tachycardia but maintained normal BP. 'Clinicians should be aware of potential need for urgent transfusion and resuscitation in a bleeding patient with tachycardia, even if the BP is within normal limits'

Case 12a.3: Delayed transfusion despite severe anaemia and GI bleeding

An elderly woman presented to the ED with lethargy and a history of dark stools. She was taking apixaban for atrial fibrillation. Her Hb was 36g/L. Two units of blood were prescribed but not ordered from the laboratory. There was delayed medical review. She had a massive GI bleed after transfer to the ward and died without transfusion after a 9-hour delay.

Learning points

- Gastrointestinal (GI) bleeding can be difficult to recognise and assess, and can be particularly severe in elderly patients on anticoagulants
- Where it is recognised that a patient requires urgent transfusion, delays must be avoided. Every effort must be made to ensure prompt transfusions, which should be commenced without waiting for transfer of patients to other departments

Major morbidity n=6

A patient suffered serious bleeding after a total hip replacement requiring inter-hospital transfer, and transfusion was delayed.

Two patients with GI bleeding suffered delay:

- A patient had a 45-minute delay in provision of components after the MHP was called because there were no trained staff able to collect these (in the operating theatre and out-of-hours). Hypovolaemic shock resulted and the patient required admission to the ICU
- A patient with Hb 41g/L had a 7-hour delay before transfusion and suffered cardiac arrest but survived

Case 12a.4: Ruptured ectopic pregnancy with delayed diagnosis

A young woman presented with vaginal bleeding and three syncopal episodes at 17:45. Her BP 62/30 improved with fluids to 95/53mmHg. She was referred to gynaecology who were unable to review her in the ED, so she was transferred to the ward at 20:15. The diagnosis of ruptured ectopic pregnancy was then considered but not escalated. She became increasingly hypotensive over the next 2 hours with tachycardia and Hb 51g/L on venous gas. When taken to surgery at 23:55 she was haemodynamically unstable, systolic BP 45mmHg, tachycardia of 160bpm. It took more than 1.5 hours to stabilise her and secure venous access. The estimated blood loss was 5-6L. She was admitted to ICU and made a full recovery. The review noted that there had been failure to recognise how sick she was and there was delayed MHP activation.

Two delays resulting in major morbidity occurred as a result of antibodies (see Case 12a.6).

Delays related to presence of antibodies n=8

In 8 cases transfusions were delayed for between 9 and 36 hours due to difficulty in crossmatching. These patients were seriously ill; three died and two suffered myocardial ischaemia due to delay. One death was possibly related to the delay. Three patients had AIHA with severe anaemia and 5 others had antibodies detected on screening. Delays occurred due to the need to send samples to external specialist laboratories for investigation and crossmatch. Poor communication was a notable feature.

Case 12a.5: Death related to failure to transfuse in timely manner in a patient with AIHA

An elderly man with chronic lymphocytic leukaemia complicated by autoimmune haemolysis (diagnosed in 2015) was on a small dose of prednisolone. He was recently noted to have critical aortic stenosis and presented with shortness of breath, dizziness, and blackouts. His Hb was 76g/L and red cells were requested. Transfusion was delayed. Due to a positive antibody screen (AIHA) the blood had to be crossmatched at the specialist red cell immunohaematology laboratory. The correct procedure was not followed exacerbating the delay. The urgency of transfusion was not communicated to the referral service. The next day was a bank holiday. The samples arrived out-of-hours (could be 2 hours by taxi but took longer as sent using a Blood Service driver). The local hospital made available the least incompatible units (ABO Rh-compatible and Kell-negative). Over the course of the next day the Hb result of 59g/L was delayed as samples were marked 'routine', the blood was not given, the patient deteriorated and died. The units were available from the Blood Service within 4 hours of the discussion about urgency. The available local hospital units were 'not

collected as the ward environment was considered too unsafe to give a transfusion' because of high level of patients needing intense input. The transfusion laboratory was understaffed.

Multiple factors contributed to the delay in this case, for example, poor communication, deviation from correct procedures, inadequate staffing in the laboratory and clinical area, all of which could be prevented.

Case 12a.6: Newly diagnosed autoimmune haemolysis results in delayed transfusion

A patient with chronic lymphocytic leukaemia developed severe anaemia (Hb 53g/L) due to new autoimmune haemolysis. Blood samples were obtained at 19:00. A 20-hour delay in obtaining red cells resulted because the samples needed to be sent out to a specialist laboratory. There was poor communication with failure to escalate to haematology consultants and misunderstanding about the concessionary release policy. The patient sustained myocardial ischaemia due to the anaemia (major morbidity).

Case 12a.7: A dangerous antibody in pregnancy

An anti-K antibody in a pregnant woman found at booking (at about 12 weeks) was not reported in a timely manner and was noted by the midwife 4 weeks later when the titre was 1 in 512. This delay impacted referral to the fetal medicine unit. Serial intrauterine transfusions were required starting at about 18 weeks for anaemia.

The antibody result should have been communicated immediately by the laboratory staff to the relevant teams as this is a well-recognised cause of fetal anaemia. The clinical team have a responsibility to follow up the results of blood tests in a timely manner and take appropriate actions.

Case 12a.8: Delay in providing blood for neonatal exchange transfusion due to multiple factors

A neonate with HDFN required an exchange transfusion. Blood was requested from the Blood Service but was not received within the expected timeframe (2.5 hours). When blood was finally delivered 4.5 hours from order time, there were further delays in the hospital laboratory due to problems with the maternal sample and staff misunderstanding of results.

Learning points

- Patients with autoimmune haemolytic anaemia or irregular antibodies are more difficult to crossmatch. Timely and clear laboratory to clinician communication is essential
- Procedures should be in place for concessionary release of red cells for patients with atypical antibodies in an emergency, including early involvement of a haematologist
- Maternal antibodies can cause serious harm to the fetus during pregnancy. Where these are detected and deemed to be clinically significant, appropriate timely actions must be taken to reduce the potential of such harm. When there is doubt or confusion regarding antenatal testing, immune prophylaxis or referral to the fetal medicine unit, laboratory or transfusion medicine experts must be contacted for additional guidance
- Neonatal exchange transfusion for HDFN is an emergency and delays must be avoided to prevent adverse outcome

Concessionary release

In situations of emergency haemorrhage or severe anaemia with haemolysis, blood components that do not meet patient specific requirements may need to be released from the laboratory. This is generally termed concessionary release (BSH Milkins et al. 2013).

Laboratories should have robust procedures for concessionary release of components in these situations that ensure the clinical team treating the patient are aware of the potential risks of transfusion and can balance them against the risk of blood loss. This should include, as a minimum release of:

- D-positive red blood cells for D-negative patients of childbearing potential (risk of production of anti-D that can cause HDFN in future pregnancies)
- Antigen-positive red cells for a patient with clinically significant atypical red cell antibodies (very small risk of delayed transfusion reaction)
- ABO/Rh/K matched red cells to patients with AIHA without exclusion of alloantibodies (very small risk of delayed transfusion reaction)
- Components that do not have specific requirements such as CMV-screened negative or irradiated (very small risk of patient developing CMV infection or transfusion-associated graft versus host disease)

The involvement of a consultant haematologist at the earliest opportunity is vital for concessionary release but should not delay provision of components in massive haemorrhage. If not contactable at the time of the event consultant haematologists must be made aware that a concessionary release has been completed so that the patient can receive appropriate follow up. Use of a script within the concessionary release form that covers the potential risks can help to guide conversations between the laboratory and clinical teams and support the safe provision of blood components. Concessionary release events should be reported, monitored and subject to trend analysis in accordance with local protocols. The patient should not die from bleeding or anaemia.

Near miss case n=1

A woman for an elective caesarean section with high risk of bleeding was not eligible for electronic issue. Prior to the operation the transfusion laboratory was contacted, and a two-unit crossmatch requested. The BMS confirmed that they had an appropriate sample and would do it straight away. The operation proceeded uneventfully but as the patient was returned to recovery (1 hour 15 minutes later) a BMS telephoned to request another sample before crossmatch could go ahead as the sample they had was no longer valid. No blood had been required during surgery, but none would have been available.

The investigation noted a shortage of trained staff in the transfusion department and that there was miscommunication between the different BMS. The BMS who took the first call did what he thought was right but had not been trained in crossmatching and the provision of blood and other components.

Main factors leading to delay

Multiple factors often contribute to delayed transfusion, particularly communication failures. These were primary in 37 reports but contributory in a further 34, altogether cited in 71 reports of delays. The correct procedures were not followed in 55 (43 clinical and 12 laboratory).

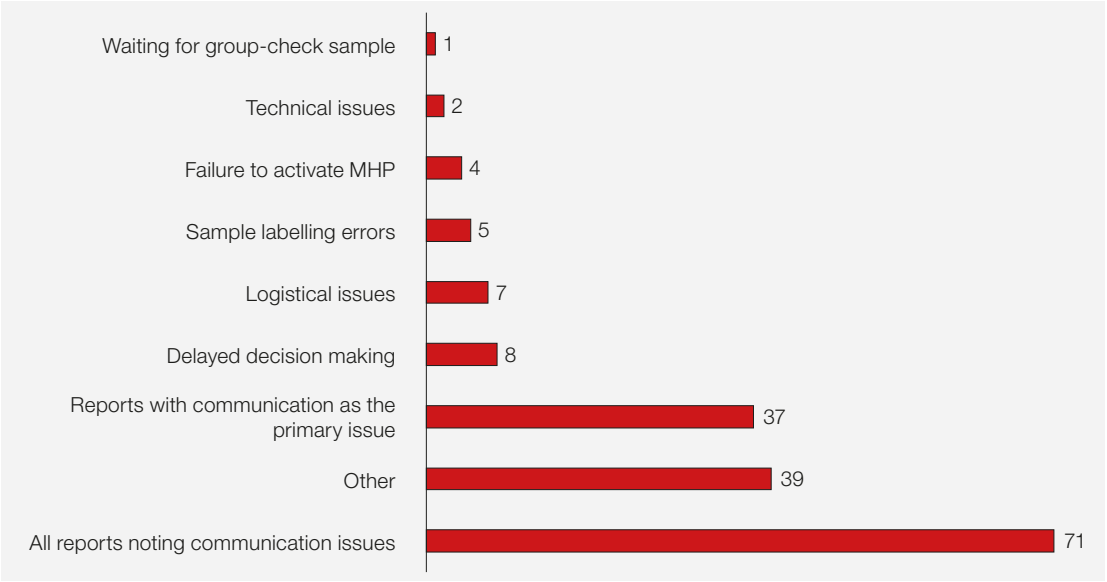


Figure 12a.2: Errors contributing to delayed transfusion

Conclusion

The number of reported delayed transfusions continues to increase each year. The deaths related to this should be preventable with improved communication and attention to the correct activation and actions in the MHP. More than 10 years on from the NPSA rapid response report it is disappointing to see many instances of MHP delays with poor communication. Delays in recognition and treatment of GI bleeding are reported year on year. The safety of patients is compromised by these factors and likely compounded by staff shortages and challenges over the past year.

SHOT
Serious Hazards of Transfusion

References

BSH Hunt BJ, Allard S, Keeling D, et al. A practical guideline for the haematological management of major haemorrhage *Br J Haematol* 2015;**170(6)**:788-803.

BSH Milkins C, Berryman J, Cantwell C, et al. Guidelines for pre-transfusion compatibility procedures in blood transfusion laboratories. *Transfus Med* 2013;**23(1)**:3-35. http://onlinelibrary.wiley.com/doi/10.1111/j.1365-3148.2012.01199.x/full [accessed 25th March 2021].

Callum J, Petrosoniak A and Haas B. What's in the name – why "Massive Hemorrhage Protocol" and not "Massive Transfusion Protocol"? The 7 Ts of Massive Hemorrhage Protocols. 2021 https://emergencymedicinecases.com/7-ts-massive-hemorrhage-protocols/?start=true [accessed 27 April 2021].

National Patient Safety Agency. Rapid Response Report 2010. (NPSA/2010/RRR017) https://www.transfusionguidelines.org/document-library/documents/npsa-rapid-response-report-the-transfusion-of-blood-and-blood-components-in-an-emergency-21-october-2010-pdf-100kb [accessed 07 June 2021]

NW RTC Steering Group Major Haemorrhage Guidelines Group. Toolkit for the Management of Major Haemorrhage. https://www.transfusionguidelines.org/uk-transfusion-committees/regional-transfusion-committees/north-west/policies/massive-haemorrhage-toolkit [accessed 27 April 2021].

NCA. National comparative audit of major haemorrhage. 2018. https://nhsbtdbe.blob.core.windows.net/umbraco-assets-corp/19130/2018-major-haemorrhage-audit-full-report.pdf [accessed 27 April 2021].

Avoidable Transfusions n=110

12b

Definition:

Where the intended transfusion is carried out, and the blood component itself is suitable for transfusion and compatible with the patient, but where the decision leading to the transfusion is flawed.

Key SHOT messages

- Inappropriate management of haematinic deficiency continues and indicates an ongoing need for better education of medical and nursing staff
- Group O D-negative units are a precious resource and D-positive units may be used in an emergency in women over 50 and men over 18 years of age
- Unexpected low platelet counts should trigger careful review of the blood count and diagnosis before prescribing platelets

Abbreviations used in this chapter

AoMRC Academy of Medical Royal Colleges

NBTC National Blood Transfusion Committee

Recommendation

- Hospitals should review their use of O D-negative units and ensure that group O D-positive units are used when possible in emergencies in older patients as advised by guidelines (NBTC 2019)

Action: Hospital transfusion committees

Introduction

The number of avoidable transfusions has increased compared to the previous year. The causes are similar and are discussed below. Where recorded, 48 red cell transfusions were considered to be indicated by BSH guidelines. These included 19 where group O D-negative unit transfusion could have been avoided, and 2 Jehovah's Witnesses. Overall, 46 avoidable transfusions were not in line with BSH guidelines.

Deaths n=0

Major morbidity n=0

Avoidable transfusion of red cells

Key features are considered below.

Haematinic deficiency n=8

Eight patients with B12 (n=3) or iron deficiency (n=5) received unnecessary transfusions. A woman with B12 deficiency was given five units of red cells (Case 12b.1). An elderly man under regular follow up with a history of autoimmune haemolysis was found to be anaemic at a clinic visit so transfusion was arranged; however, the blood findings suggested a diagnosis of iron deficiency on this occasion.

Case 12b.1: Inappropriate management of anaemia

A woman in her 60s with minimal symptoms was found to have Hb 62g/L. She was transfused with three units of red cells without checking the Hb until afterwards when it was 103g/L. She was then found to have B12 deficiency. Three days later when Hb was 89g/L she was given another unit, and a further unit the next day when Hb was 94g/L.

Correct practice for any case of anaemia is to review the MCV on the presenting blood count and to check the haematinics. A raised MCV is a characteristic feature of B12 and/or folate deficiency. While she might have warranted transfusion of a single unit there was no reason to continue to a total of five. The bone marrow responds rapidly to replacement with the missing vitamin. Excessive transfusion can be dangerous in haematinic deficiency. This case (discovered by audit) suggests a lack of knowledge about anaemia and its causes.

Avoidable use of group O D-negative red cells n=25

There were 25 reports of avoidable use of O D-negative red cells; 9 were associated with MH procedures. Four patients had crossmatched units available and the other 5 could have received group-specific units. More than half the individuals could have received group O D-positive red cells, 15/25 (60.0%). This included 9 men (age range 54 to 74 years) and 6 women over the age of 50 years. The 2018 NCA of major haemorrhage procedures (NCA 2018a) showed that 36/67 (54%) males and 22/26 (85%) females over the age of 50 were transfused with group O D-negative red blood cells where group O D-positive could have been given. Group O D-negative blood is a scarce resource, and hospitals should review their local practices in accordance with national guidelines (NBTC 2019).

The NCA of group O D-negative use showed that 6% were transfused in an emergency to females aged over 50 years and males. At that time (NCA 2018b) 31% of sites did not have a policy to provide O D-positive red cells in an emergency to unknown males and females aged over 50 years. If this policy had been applied to all potential recipients in this audit, transfusion of 10% (504/4970) of O D-negative red cells during the audit period could have been avoided.

Case 12b.2: Get the blood sample details right first time – potentially avoidable use of O D-negative blood at delivery

The initial sample from a woman's booking visit to the antenatal clinic was successfully grouped without incident (A D-positive), however a subsequent sample taken 6 months later gave a different result (O D-positive). This discrepancy was flagged on the analyser but was not acted on correctly by the member of staff processing the samples, instead the result was amended manually and transmitted. Three weeks later the group was again O D-positive but was now flagged as a wrong blood in tube. The next grouping sample was clotted. The fifth sample was taken when the woman was in the delivery suite. By now there were two records of A D-positive and two that were O D-positive. Emergency O D-negative blood was issued as the blood grouping results did not match either of the previous results. Neither the acceptance of the discrepant result on the analyser or its subsequent amendment on the LIMS were in accordance with laboratory SOP.

Further information was provided in the investigation report submitted by the reporter. It stated that the provider of LIMS systems was subsequently contacted, and a call logged to investigate whether it would be possible to limit access to the grouping results editor function to higher level staff. On this occasion the member of staff had used this function instead of following documented laboratory procedures. LIMS access rights could not be restricted.

Case 12b.3: Avoidable transfusion of group O D-negative units in an emergency

The MHP had been activated for a patient on the obstetric delivery unit. The porter arrived in the

laboratory to collect the shock pack. The BMS selected a bag containing two units of red cells from the refrigerator, signed them out and handed them to the porter. They were transfused and retrospectively assigned to the patient. This occurred towards the end of a shift. When the next BMS on duty came to replace the shock pack they noticed that although the O D-positive units were signed out and allocated, the O D-negative shock pack was actually given to the porter and had been transfused. The patient's group was O D-positive, this had been checked before the shock pack was collected and was the reason the BMS intended to give the O D-positive units instead of the O D-negative units. On realising the mistake, the BMS allocated the correct units to the patient.

Avoidable transfusion of platelets n=9

Nine cases were reported:

- In 5 cases, patients had spurious low platelet counts due to platelet clumping. A blood film should be examined before issuing the result
- In 1 case the count was low due to a partial clot in the sample which had not been detected in the blood count sample but was noted in the biochemistry samples
- In 3 cases platelets were not necessary (a young woman presenting with immune thrombocytopenia for which platelet transfusions are the wrong treatment; platelets were requested only for standby at caesarean section for another woman but were given). In the 3rd case platelets were transfused in excess of requirements (an elderly woman with lymphoma receiving cover for hip replacement following fractured neck of femur)

Learning points

- An unexpected low platelet count should prompt review of the sample for clots
- Laboratories should explore rules and algorithms within analyser, middleware or laboratory information management systems that can be used to suppress reporting of platelet counts below the lower limits of normal in the presence of analyser flags indicating clumping. The presence of platelet clumps can then be verified by reviewing a blood film and confirmation of a normal platelet count using a sample taken in a citrate tube

Avoidable transfusion of FFP n=4 or cryoprecipitate n=2

- An elderly man on apixaban for atrial fibrillation required a laparotomy. Advice was sought from a haematologist who recommended PCC, but the patient received two units of FFP
- A young woman with liver failure received a single unit of FFP to cover drain insertion but this was not indicated
- Two other patients received FFP which was not indicated
- Medical staff wrongly prescribed cryoprecipitate as part of fluid replacement for plasmapheresis
- Communication confusion resulted in inappropriate transfusion of cryoprecipitate to cover emergency laparotomy. Four units of cryoprecipitate were erroneously ordered, issued from the lab, prescribed and administered by the theatre team when only one unit was originally intended to be transfused to ensure safe fibrinogen levels. Communication was further impacted by a hyperdynamic situation in a busy theatre during the pandemic, compounded by use of wireless telephones with unreliable reception

Near miss cases n=12

An overview of these 12 cases are detailed here:

- In 2 cases, inappropriate transfusion of red cells was avoided by repeat testing in the laboratory when initial analyser results were erroneous

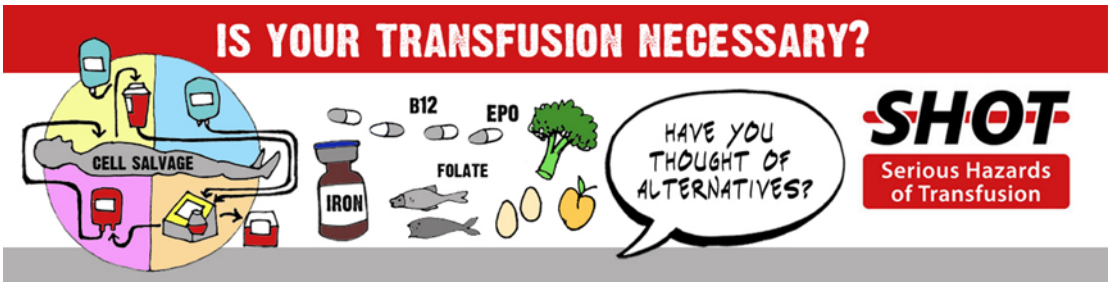
- Six transfusions were avoided because staff recognised that the low Hb results were probably wrong and repeated them
- Transfusion of an additional unit was avoided when staff realised the transfusion was complete, but the second unit had not been recorded on the prescription chart
- There were 2 cases related to miscommunication during MHP activations
- One patient was nearly transfused convalescent plasma for COVID-19 instead of the monoclonal antibody treatment to which they had been randomised

Conclusion

Avoidable transfusions continue to be reported to SHOT and the causes for these remain similar year on year. Transfusions are a valuable and scarce resource and every effort must be made to avoid unnecessary transfusions. This also will help ensure that patients are not put at unnecessary risk of exposure to blood components. Clinicians should be familiar with the 'Choosing Wisely' recommendations for transfusion and ensure that medical and nursing staff receive appropriate education and training about anaemia and its management. Haematinic deficiencies can be detected before severe anaemia develops and primary care teams can help address this before patients are admitted with severe symptomatic anaemia. The Evidence-Based Interventions Proposed List 2, drafted by the independent Expert Advisory Committee to the Evidence-Based Intervention programme and endorsed by the Academy of Medical Royal Colleges (AoMRC 2020) supports the use of red cell transfusions only where indicated and then in single units, unless there are exceptional circumstances. While transfusions are safe there are inherent risks and unnecessary transfusions must be avoided wherever possible.

Recommended Resources

O D-negative red cell tool kit
https://hospital.blood.co.uk/patient-services/patient-blood-management/o-d-negative-red-cell-toolkit/



References

AoMRC (2020). Evidence-based interventions List 2. https://www.aomrc.org.uk/wp-content/uploads/2020/12/EBI_list2_proposals_1220.pdf [accessed 29 April 2021].

NBTC. National Blood Transfusion Committee Responses and Recommendations – Appropriate use of group O D negative red cells 2019. https://www.transfusionguidelines.org/uk-transfusion-committees/national-blood-transfusion-committee/responses-and-recommendations [accessed 28 April 2021].

NCA 2018a. National Comparative Audit of major haemorrhage https://nhsbtdbe.blob.core.windows.net/umbraco-assets-corp/19130/2018-major-haemorrhage-audit-full-report.pdf [accessed 27 April 2021].

NCA 2018b. National Comparative Audit of group O D-negative red cells https://hospital.blood.co.uk/audits/national-comparative-audit/medical-audits/2018-survey-of-group-o-d-negative-red-cell-use/ [accessed 27 April 2021].

Royal College of Pathologists. Recommendations for transfusion medicine. 2019. https://www.rcpath.org/profession/patient-safety-and-quality-improvement/patient-safety-resources/choosing-wisely/recommendations-for-transfusion-medicine.html [accessed 27 April 2021].

Under or Overtransfusion n=25

12c

Definition:

A dose/rate inappropriate for the patient's needs, excluding those cases which result in transfusion-associated circulatory overload (TACO). Infusion pump errors leading to under or over transfusion (if it did not lead to under/over transfusion then it is reportable under handling and storage errors (HSE)).

Key SHOT messages

- In the setting of major haemorrhage, it can be difficult to estimate the quantity of blood lost and the effect of fluid resuscitation
- During the management of haemorrhage regular monitoring of haemoglobin and other parameters is recommended
- Point-of-care testing should be quality assured with oversight from the laboratory, and dubious results confirmed by standard laboratory tests
- Errors continue to be made in paediatric prescribing
- A Blood Assist app is now available (developed by the NHS Blood and Transplant Patient Blood Management team) which gives information for all aspects of blood transfusion (see recommended resources)

Abbreviations used in this chapter

JPAC Joint United Kingdom (UK) Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee

Recommendation

- In instances where allogeneic blood components and cell salvage have been used, regular checks of haemoglobin (quality assured point-of-care tests or standard laboratory tests) should take place to avoid over or undertransfusion
- All staff responsible for authorisation of blood component transfusion must be aware of the different component indications and the appropriate dose calculations for fresh frozen plasma and cryoprecipitate for all age groups

Action: Hospital transfusion committees

Introduction

Quantitative transfusion errors leading to overtransfusion are made mostly in paediatric patients due to errors in calculation or pump setting. Overtransfusion and undertransfusion are both risks in major haemorrhage where it can be difficult to assess the balance of gain versus loss.

Deaths n=1

Two deaths were reported in patients who were overtransfused. Both occurred in the management of ruptured AAA with major blood loss during surgery. One death was 'possibly related' to the overtransfusion but the other was unrelated. This is a serious condition with a high mortality rate.

Case 12c.1: Overtransfusion in a case of AAA (1)

A man in his 80s collapsed at home. He was found to have a ruptured AAA and proceeded to surgery receiving a total of more than 3L of red cells and cell salvage material.

The postoperative Hb was 202g/L. He died later the same day (death 'possibly related' to transfusion).

Case 12c.2: Overtransfusion in a case of AAA (2)

This case was associated with estimated blood loss of more than 10L and a postoperative Hb 181g/L. The review (death unrelated to transfusion) noted that reliance was placed on Hb estimation from serial blood gases and formal laboratory tests (FBC, clotting screen and fibrinogen) were not undertaken until the patient was admitted to the ICU postoperatively.

Overtransfusion might have been avoided if near patient testing had been supplemented by formal laboratory blood tests during surgery. However, the case review noted that 'the patient was cardiovascularly unstable with catastrophic blood loss and corresponding aggressive fluid replacement which meant that accurate assessment of fluid balance would have been challenging whatever means of assessment were used'.

Regular monitoring of Hb and coagulation during major haemorrhage is recommended in the Transfusion Handbook (JPAC 2013, link to relevant web page is included in the references and has been updated in April 2020) and BSH guidelines (BSH Hunt et al. 2015).

Major morbidity n=0

There were no cases where major morbidity resulted from over or undertransfusion.

Overtransfusion n=18

Two patients in the RECOVERY trial received excess doses of convalescent plasma for COVID-19 infection by mistake. They were each transfused four units instead of two. Patients randomised to receive convalescent plasma were to be given a single unit on day 1 and if tolerated, then also on day 2 as per the trial protocol. In these cases, the prescriptions had been written as recurring daily, and the error was only identified after four units had been administered. All transfusion decisions should be reassessed regularly, and the appropriateness of subsequent transfusions evaluated.

Other cases:

Case 12c.3: Unexpected complication of pregnancy

A woman in her 30s was found to have an unexpected placenta praevia at caesarean section and suffered major haemorrhage. She received massive transfusion of red cells, plasma, platelets, and cell salvage. Her preoperative Hb was 123g/L and postoperative was 173g/L indicating that she had received more red cells than she needed.

In the setting of massive bleeding, it can be difficult to estimate the losses as indicated in the two cases of AAA described above. This hospital is considering introduction of thromboelastography in the management of major haemorrhage.

Case 12c.4: Hb not checked between transfused units

A woman in her 90s presented with breathlessness due to heart failure and was transfused two units of red cells on the basis of Hb 56g/L. Her Hb was not checked between units and post transfusion was 160g/L suggesting the first result had been incorrect. In addition, the pre-transfusion Hb result of 140g/L on the blood gas machine was not noticed. Fortunately, she did not experience worsening heart failure as a result.

Case 12c.5: An excess of platelet transfusions

A young man with leukaemia and history of retinal haemorrhages received excessive doses of platelets (three units). the decision to transfuse had been made taking into account a historical note in the patient's medical records that the platelet target should be 50x10^9/L. The patient was known to have poor increments to transfused platelets. When the case was reviewed after all the three units were given it was noted that these units were avoidable as the patient platelet count was acceptable and the retinal haemorrhages had occurred several days previously so the platelet target was no longer required. This advice had not been updated in a timely manner in the patient's records.

Case 12c.6: Second unit of red cells transfused without authorisation or clinical need

An elderly woman with pelvic fractures following a fall received a unit of red cells with post-transfusion Hb 85g/L. A second unit was subsequently transfused that was not indicated or prescribed due to miscommunication during handover. The nurse administering the second unit saw that there was another unit available for the patient but did not check the medical notes or blood prescription prior to administering the second unit.

Paediatrics n=9

Nine children age range 10 days to 15 years (6 were aged 2 years or less) received excess volumes. Two cases related to platelets, 1 to FFP and 6 to red cells. Prescription errors were made in 3 cases.

Undertransfusion n=7

Red cells n=4

- One premature infant received 7mL instead of 12mL due to problems with the infusion pump and giving set
- Three patients did not receive the intended quantity of red cells, 1 due to clamping the line shut during transfer, 1 due to the pump alarming and the other because the rate was inappropriately slow (3mL/hour)

Plasma components n=3

One report identified two adults who received inappropriately low doses of FFP because they were prescribed as 10mL/kg instead of units. The doses had been calculated by a consultant haematologist. The nursing staff misunderstood the prescription and, in each case, gave only a single unit. BSH guidelines (BSH Green et al. 2018) note that there is no good evidence for what the dose should be, but a starting dose of 15mL/kg is suggested prior to an invasive procedure. The internal review recommended that the calculated dose is converted to units of FFP to avoid confusion.

An additional patient should have received three units of FFP prior to ERCP but only received one. No bleeding complications were reported.

A patient with hepatic encephalopathy received a single pool of cryoprecipitate rather than the two indicated as a standard adult dose. Following this treatment, the fibrinogen was below 1g/L.

Learning points

- Volume errors are most often made in paediatric transfusion
- Fresh frozen plasma should be given in accordance with national and local guidelines
- The standard adult dose of cryoprecipitate is two pools, each adult pool is made up of five single components
- Those authorising/prescribing need to know the appropriate doses for adults and how to calculate for children

Near miss cases n=7

Six patients avoided overtransfusions (4 children) and 1 infant was nearly undertransfused.

- In 1 case a parent of a regularly transfused child noticed that an inappropriate dose of red cells had been prescribed
- One regularly transfused adult changed the request from 'group and screen' to 'crossmatch two units'. This individual was aware that there were often delays as the crossmatch needed to be done at a specialist laboratory and was trying to avoid delay
- An elderly patient with iron deficiency anaemia (Hb 55g/L) was prescribed 1134mL of red cells by a doctor. This was noted and challenged by the BMS
- Three children had inappropriately large amounts prescribed. The FFP prescription for a 1-year-old was calculated as 100mL/kg instead of 10mL/kg. A second child was also prescribed an incorrect amount of FFP. Another excessive dose of red cells was prescribed based on the weight of the wrong patient
- The ward requested a paediatric platelet pack for a 3-year-old. The laboratory staff queried the volume required but this information was not supplied. The unit supplied was 80mL when the unit arrived at the ward the nursing staff noted that the volume was insufficient.

Conclusion

It is difficult to assess the amount of blood lost in severe major bleeding such as AAA and obstetric emergencies. Clinical staff should do their best to continuously evaluate the balance using quality-assured near patient testing (blood gas analysers, thromboelastography) and regular samples sent to the main laboratory. Paediatric patients continue to be at risk of miscalculation and wrong settings on intravenous pumps. All staff responsible for transfusion should understand the different components and their appropriate dose schedules.

Recommended resource

Blood Assist - a blood administration safety app developed by the Patient Blood Management team at NHS Blood and Transplant.
Apple (https://apps.apple.com/gb/app/blood-assist/id1550911130)
Google play (https://play.google.com/store/apps/details?id=uk.nhsbt.bloodassist)
Web based (www.bloodassist.co.uk)

References

BSH Green L, Bolton-Maggs P, Beattie C, et al. British Society for Haematology Guidelines on the spectrum of fresh frozen plasma and cryoprecipitate products: their handling and use in various patient groups in the absence of major bleeding. *Br J Haematol* 2018;**181(1)**:54-67.

BSH Hunt BJ, Allard S, Keeling D, et al. A practical guideline for the haematological management of major haemorrhage. *Br J Haematol* 2015;**170(6)**:788-803.

JPAC. 7.3: Transfusion management of major haemorrhage. 2013. https://www.transfusionguidelines.org/transfusion-handbook/7-effective-transfusion-in-surgery-and-critical-care/7-3-transfusion-management-of-major-haemorrhage [accessed 28 April 2021].

RECOVERY trial. 2021 https://www.recoverytrial.net/ [accessed 27 April 2021].

Incidents Related to Prothrombin Complex Concentrate (PCC) n=17

12d

Definition:

Hospitals are asked to report any issues with prescription and administration of prothrombin complex concentrate. This include delays in administration, inappropriate prescription, or problems with administration. (Allergic reactions should be reported to the MHRA via the Yellow Card scheme)

Key SHOT messages

- Prothrombin complex concentrate (PCC) administration is an emergency treatment and should be started within an hour of the decision being made and before the patient is transferred to other wards or departments
- Emergency departments should ensure they have clear instructions for PCC administration
- Medical and nursing staff working in emergency departments should be trained in the prescription and administration of PCC

Recommendations

- Emergency departments should ensure they have a protocol for prothrombin complex concentrates (PCC) use with clear instructions for dose and administration, and ensure that staff are appropriately trained in their use
- Use of PCC should be regularly audited for timeliness and appropriateness

Action: Medical directors of acute Trusts/Health Boards

Introduction

These incidents occurred in an elderly population (age range 61 to 97 years, median age 82 years), who often have multiple comorbidities. There were 11/17 reports of delayed infusion, 1 inappropriate treatment to a patient receiving heparin and 3 cases where the patient received less than was prescribed. In another case PCC was administered to the correct patient but labelled with an incorrect surname (right product right patient), and in the final case PCC was issued incorrectly by the pharmacy. An electronic prescription was received, and a new pharmacist issued PCC from stores (which were held for the laboratory), when it should only have been issued from the laboratory. The dose issued was also incorrect.

Deaths n=0

Although 4 patients died, none were related to the PCC incidents.

Major morbidity n=0

There were no complications causing major harm related to these PCC incidents.

Delays n=11

Delays were caused by poor communication, transfer of patients between departments or setting inappropriately long infusion times. Treatment with PCC for anticoagulant reversal is an emergency and should take place within an hour of the treatment decision. Two studies from teaching hospitals (one unpublished) demonstrated the median time to administration was 5-6 hours (Toth et al. 2013). In the Toth study the mean time to PCC for ICH was 3 hours and the mortality from ICH was 22.3%, a reminder of the serious nature of this disease.

Case 12d.1: Three cases of suspected ICH with delayed infusion

- *In a patient on warfarin with a head injury, there was a 4-hour delay while the patient was moved between departments and the prescription was lost*
- *Following a head injury in a patient on apixaban for atrial fibrillation the infusion was set to run at 1mL/hour instead of 1mL/minute. This was recognised after running for 16 hours*
- *A man in his 80s with suspected ICH had delayed administration because each vial was collected separately from the transfusion laboratory rather than all collected together*

Additional factors included unfamiliarity of staff with PCC prescription and administration, the use of infusion pumps calibrated in mL/hour, verbal instructions, and rearrangement of the ED due to COVID-19.

Learning points

- Medical staff working in emergency departments and medical/surgical admissions units should be trained in the indications and ordering of prothrombin complex concentrate (PCC) so that it can be administered without delay for anticoagulant reversal in the face of major haemorrhage
- PCC should be easily accessible, and consideration given to keeping a stock in the emergency department (but this blood product must be fully traceable)
- Where use of PCC is indicated immediate reversal of anticoagulant should take place (and certainly within an hour) especially in cases of suspected intracranial haemorrhage

Comment

Could delays be reduced by using a fixed PCC dose? What is the evidence for fixed dose PCC for warfarin reversal?

Delay in administration of PCC is potentially life-threatening. The mortality related to ICH is high, nearly 34% in the USA (Sweidan et al. 2020). PCC should be kept in the ED with a simple dosing structure independent of the degree of abnormality of the INR (Toth et al. 2013). PCC are blood products and must be traceable, so that the batch number must be recorded in the patient record and transfusion laboratory.

There are no UK guidelines recommending fixed dose protocols, but several papers in the literature support this with variable evidence. Many are not very robust studies (retrospective case series, observational studies) and do not always give the clinical outcome, although clearly demonstrating that the INR can be rapidly reduced. The use of fixed dose may also have financial benefit.

The reported fixed dose was usually either 1000 or 1500IU (some used 2000IU). Some patients needed additional doses to achieve the INR goal. The higher the INR and the heavier the patient, the more likely it is that additional doses will be required. A literature review up to 2018 (Schwebach et al. 2019) noted that patients with a high INR or ICH may need higher doses. A randomised controlled trial is underway to assess the standard variable dose regimen compared with a fixed dose of 1000IU in patients on vitamin K antagonists with extracranial bleeding, and the protocol has been published (Abdoellakhan et al. 2018).

The Oxford University Hospitals NHS Foundation Trust use a simplified and standardised weight-based protocol, Table 12d.1(Oxford University Hospitals 2017). The Royal Devon and Exeter NHS Foundation

Trust use a fixed dose protocol (1000IU), with an additional dose (500IU) given if indicated (Davies et al. 2020). However, it is crucial that treatment is 'immediate' for ICH (NICE 2015). The American College of Cardiology consensus guidelines for anticoagulant reversal include a fixed dose option of 1000IU and 1500IU for ICH (Tomaselli et al. 2020). The use of a fixed dose of PCC simplifies management and can reduce the time to treatment which is an advantage and is easier to organise. Although studies show good reduction of the INR after fixed doses for warfarin reversal, currently there is no clear published evidence of benefit to morbidity or mortality. Whatever dose is given the INR should be checked 15-30 minutes after the dose to confirm the reduction in INR and may guide the need for additional doses. The effect of the PCC will wane and therefore the INR should be repeated over the next few days to confirm satisfactory correction.

The patient on warfarin should always also receive IV vitamin K urgently which will generate increased synthesis of factors 2, 7, 9 and 10 within a few hours providing a longer lasting correction.

PCC may also be used for selected direct oral anticoagulants. The evidence has been reviewed recently (Sweidan et al. 2020). Canadian authors recommend that for a patient on dabigatran consider the specific reversal agent idarucizumab 5g. For a patient on a Xa inhibitor (apixaban, rivaroxaban), give PCC 2000IU; if significant bleeding persists after 1 hour, a second dose of 2000IU of PCC should be considered; while not approved in Canada, a specific reversal agent to Xa inhibitors, andexanet alfa, has also been used in these situations as a continuous infusion (Callum et al. 2021). Reversal of oral anticoagulation in patients with ICH has recently been reviewed noting the importance of rapid treatment (Kuramatsu et al. 2019).

Weight	Dose of PCC
Less than 60kg	1500IU
60-75kg	2000IU
76-90kg	2500IU
Greater than 90kg	3000IU

PCC= prothrombin complex concentrate

Table 12d.1: Warfarin reversal in haemorrhage: dose of PCC (Oxford regimen)

Near miss cases n=1

PCC was requested and issued for the wrong patient. The doctor used an addressograph label from another patient who had been in the same area of the ED earlier whose paperwork had not been fully cleared. The telephoned order should be made from the patient's prescription. The error was discovered at the bedside pre-administration check. Staff went to the correct patient but observed that the product was labelled with the wrong patient's details.

Conclusion

PCC is an important treatment for immediate reversal of vitamin K antagonists and some other oral anticoagulants and should be given immediately after a decision is made. All clinical staff involved in the acute care of patients with suspected serious haemorrhage, particularly ICH, who are eligible for reversal should ensure that they know how to obtain and how to administer PCC. Delay can contribute to death.

References

Abdoellakhan RA, Khorsand N, Van Hest RM, et al. Randomised controlled trial protocol to evaluate a fixed dose prothrombin complex concentrate against the variable dose in vitamin K antagonist related bleeding (PROPER3). *BMJ Open* 2018;**8(3)**:e020764.

Callum J, Petrosoniak A and Haas B. What's in the name – why "Massive Hemorrhage Protocol" and not "Massive Transfusion Protocol"? The 7 Ts of Massive Hemorrhage Protocols. 2021. https://emergencymedicinecases.com/7-ts-massive-hemorrhage-protocols/?start=true [accessed 27 April 2021].

Davies J, Sansom V, Piper J et al. Fixed dose prothrombin complex concentrate for direct oral anticoagulant and warfarin reversal: a rapid and effective solution. *Br J Haematol* 2020;**189(S1)**:271. https://onlinelibrary.wiley.com/doi/10.1111/bjh.16638 [accessed 28 April 2021].

Kuramatsu JB, Sembill JA and Huttner HB. Reversal of oral anticoagulation in patients with acute intracerebral hemorrhage. *Crit Care* 2019;**23(1)**:206-214.

NICE (2015) Guideline NG 24 Blood transfusion. Prothrombin complex concentrate. Thresholds and targets. https://www.nice.org.uk/guidance/ng24/chapter/Recommendations#prothrombin-complex-concentrate-2 [accessed 28 April 2021].

Oxford University Hospitals. Oxford Haemophilia and Thrombosis Centre Protocols for Outpatient Oral Anticoagulation with Vitamin K Antagonists. 2017. https://www.ouh.nhs.uk/services/referrals/specialist-medicine/documents/anticoagulant-protocols.pdf [accessed 28 April 2021].

Schwebach A, Waybright RA and Johnson TJ. Fixed-Dose Four-Factor Prothrombin Complex Concentrate for Vitamin K Antagonist Reversal: Does One Dose Fit All? *Pharmacotherapy* 2019;**39(5)**:599-608.

Sweidan AJ, Singh NK, Conovaloff JL, et al. Coagulopathy reversal in intracerebral haemorrhage. *Stroke Vasc Neurol* 2020;**5(1)**:29-33.

Tomaselli GF, Mahaffer KW, Cuker A, et al. ACC Expert Consensus Decision Pathway on Management of Bleeding in Patients on Oral Anticoagulants A Report of the American College of Cardiology Solution Set Oversight Committee. *J Am Coll Cardiol* 2020;**76(5)**:594-622. https://doi.org/10.1016/j.jacc.2020.04.053 [accessed 28 April 2021].

Toth P, van Veen JJ, Robinson K et al. Real world usage of PCC to "rapidly" correct warfarin induced coagulopathy. *Blood Transfus* 2013;**11(4)**:500-505.

Near Miss (NM) Reporting n=1130

13

Author: Shruthi Narayan and Debbi Poles

Definition:

A 'near miss' event refers to any error which if undetected, could result in the determination of a wrong blood group or transfusion of an incorrect component, but was recognised before the transfusion took place.

Abbreviations used in this chapter

cffDNA	Cell-free fetal deoxyribonucleic acid	**NM**	Near miss
HSIB	Healthcare Safety Investigation Branch	**PAS**	Patient Administration System
ID	Identification	**WBIT**	Wrong blood in tube
Ig	Immunoglobulin		

Near miss events account for the largest proportion of the events/reactions reported to SHOT (1130/3214, 35.2%) however for the third year in a row, the number of reports included has decreased, n=1314 in 2019, and n=1451 in 2018. The overall percentage of NM compared to total SHOT reports is also decreasing, with 2020 being the lowest percentage in the last 10 years.

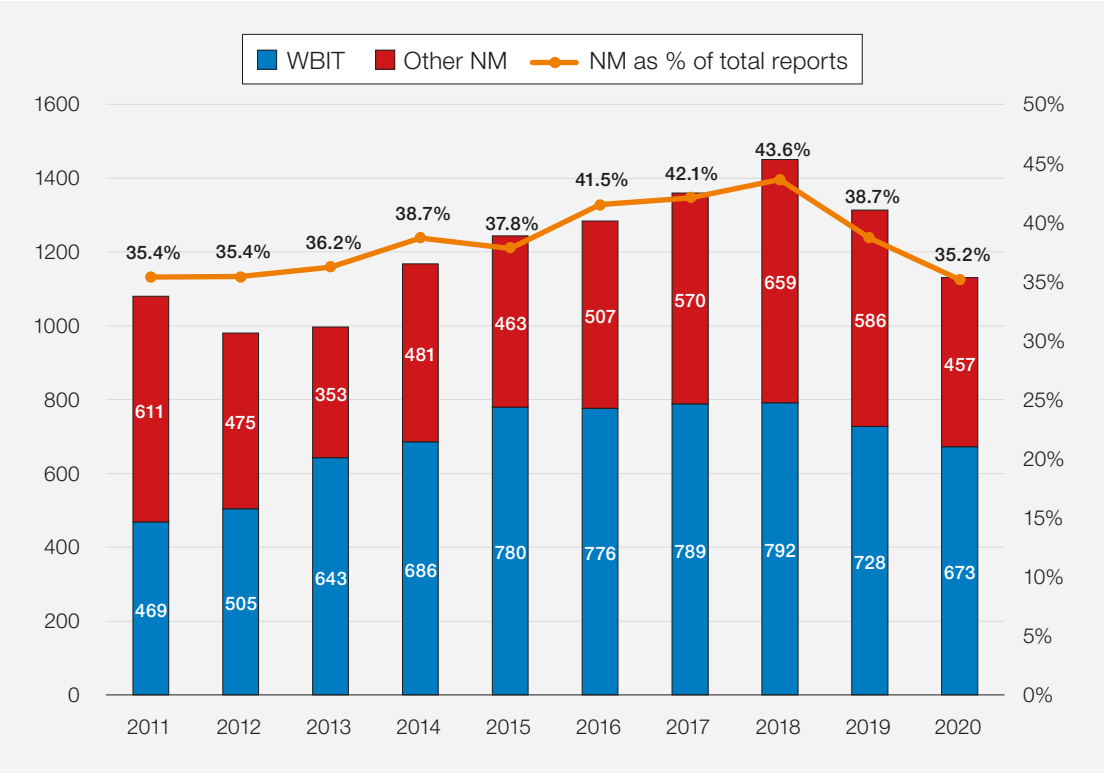


Figure 13.1: A decade of near miss and WBIT reports 2011-2020

WBIT= wrong blood in tube; NM= near miss

Near misses may occur many times before an actual harmful incident. Many avoidable events including deaths have a history of related NM preceding them. They represent 'error prone situations' that can impact other patients and staff. To truly improve patient safety, all healthcare organisations must recognise NM as valuable learning and improvement opportunities. Staff should not be falsely reassured by NM because no harm occurs and should not mistakenly conclude that the system of care is safe. Investigating NM and looking into correctable systemic factors will help improve patient safety. In a culture committed to improving safety, NM are 'free lessons'. The goal of any reporting system is to identify and address any root causes or contributory factors of incidents (not merely logging the events) and this can be achieved by NM. There are many more NM events than there are actual adverse events. Thus, the emphasis on reporting adverse events results in a small database with insufficient data for analysis.

By reporting near misses, we can have a large database for analysis. Staff should be encouraged and applauded for picking up NM and reporting them. Each time that a staff member ignores or fails to report a NM situation, the likelihood of a subsequent serious incident increases. It is important that the learning from investigating NM informs improvement activities and is shared widely.

Discussion of near miss errors in other categories

Near miss cases have been reviewed and discussed in each relevant chapter for this Annual SHOT Report, and Table 13.1 shows the chapters that include near miss events according to SHOT definitions.

Table 13.1: Categorisation of all near misses according to SHOT definitions (n=1130)

SHOT Reporting Categories		Discussed in chapter	Number of cases	Percentage of cases
Incorrect blood component transfused (IBCT)	Wrong component transfused (WCT)	Chapter 10	111	9.8%
	Wrong blood in tube (WBIT)	Chapter 13a	673	59.6%
	Specific requirements not met (SRNM)	Chapter 10	67	5.9%
Handling and storage errors (HSE)		Chapter 11	129	11.4%
Right blood right patient (RBRP)		Chapter 14	93	8.2%
Adverse events related to anti-D Ig (Anti-D Ig)		Chapter 9	35	3.1%
Avoidable, delayed or under/overtransfusion (ADU)		Chapter 12	21	1.9%
Miscellaneous		N/A	1	0.1%
Total		-	**1130**	**100%**

WBIT incidents continue to be the largest subset of near miss cases, 673/1130 (59.6%) of all near miss events and as such are analysed and reported separately in this chapter.

Near Miss – Wrong Blood in Tube (WBIT) n=673

13a

Authors: Paula Bolton-Maggs and Pamela Diamond

Definition:

- **Blood is taken from the wrong patient and is labelled with the intended patient's details**
- **Blood is taken from the intended patient, but labelled with another patient's details**

Key SHOT messages

- The number of errors in blood sampling in maternity departments is of concern and needs to be addressed with midwives and other obstetric staff. These samples may be taken in the community setting, or in hospital clinics and wards
- The presence of a historical group resulted in detection of many wrong blood in tube (WBIT) events in the laboratory and demonstrates the value of the two-sample rule
- Near miss events matter: they provide an opportunity to learn and avoid serious and potentially life-threatening events, particularly ABO-incompatible transfusion

Recommendations

- As recommended in the 2017 Annual SHOT Report, 'all available information technology (IT) systems to support transfusion practice should be considered and these systems implemented to their full functionality. Electronic blood management systems should be considered in all clinical settings where transfusion takes place. This is no longer an innovative approach to safe transfusion practice; it is the standard that all should aim for'
- Near miss incidents should be fully investigated as the learning may prevent serious events in future

Action: Chief executives, medical directors

- The Royal College of Midwives should reinforce the importance of adherence to local practices for correct patient identification and sample labelling to avoid potentially serious outcomes for patients. The same standards should be applied whether in the patient's home, a community setting or hospital clinic

Action: Royal College of Midwives

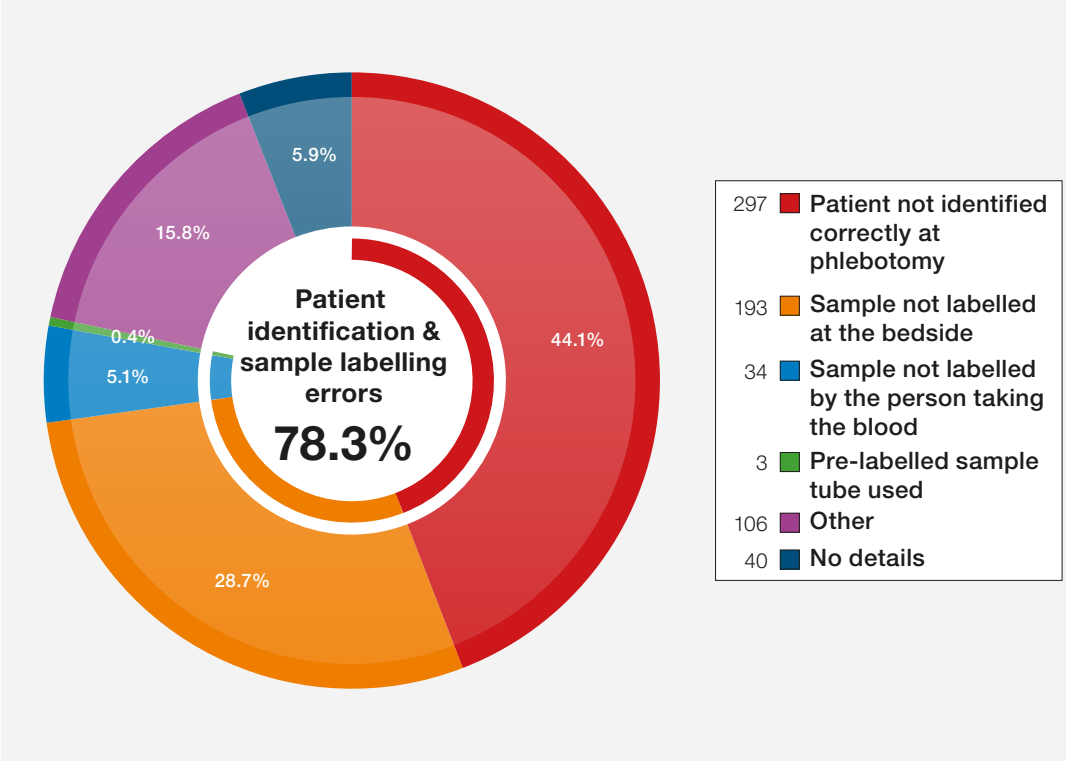
Introduction

WBIT samples remain a cause for concern. In 2020, 673 were reported which is a decrease from 728 in 2019. These comprise the majority of near miss reports, 673/1130 (59.6%). A third of reports originated in maternity care, 233/673 (34.6%), and are considered in a subsection below. Four incidents of wrong component transfused were reported as a result of WBIT events, fortunately with no harm. These are described in Chapter 10, Incorrect Blood Component Transfused (IBCT).

What errors lead to WBIT?

Figure 13a.1 shows that the majority of WBIT errors are made due to the patient not being identified correctly at phlebotomy or the sample being labelled away from the patient. These two factors were identified in the inaugural Annual SHOT Report (SHOT, 1998) when it was first noted that wrong transfusion was responsible for most reported incidents. The recommendation was made in 1998 to ensure correct patient identification by asking the patient to state their name and date of birth, and that samples should be labelled at the bedside at the time of sampling. This should be a single uninterrupted procedure. Failure to do this has resulted in incompatible transfusions and death. This recommendation remains central for safe transfusion.

Figure 13a.1: Primary errors leading to WBIT (n=673)



Other causes of WBIT were recorded including patients having similar names, errors at initial registration in the PAS and in one case a midwife changed the patient surname on the form as it was believed that the patient had changed her name. A patient was identified by review of the notes at the bedside, others (n=3) were booked incorrectly into a clinic or on admission. In another case, sample labels were used from a patient who had attended earlier in the day. One patient was misidentified by the police who had taken the information from a 'friend' and another patient had deliberately given the wrong details in the emergency department after a stabbing.

It is notable that there were often serial errors. In 635/673 (94.4%) reports where the primary error was recorded there was at least one additional error in 418/635 (65.8%).

Case 13a.1: Misidentification of an adult triplet

A woman attended the early pregnancy unit wearing a facemask (COVID-19 precautions). The midwife asked for her name, first line of address and date of birth. Blood samples were taken but allocated to the wrong patient record. She was one of triplets with the same date of birth, family name and address. The first name was misheard but very similar to the others, differing only by a letter. The patient was concerned that this might have happened and clarified her name when the results were telephoned. The triplets were advised for any hospital attendance always to ensure they were identified in addition by their middle names which were different.

Case 13a.2: Patient identification errors by three different members of staff

Before admission, a ward clerk updated a patient name for a child <5 years of age (Patient 1) from 'baby' to a name already belonging to another patient (Patient 2). On admission no ID band was put on, Nurse 1 sampled the patient without positive identification and labelled the sample using patient notes. This sample from Patient 1 (labelled with Patient 2 details) was rejected due to an insufficient amount of blood in the sample tube. Nurse 2 (without required competency for transfusion) took another sample again without positive ID from Patient 1 (labelled with Patient 2 details) labelling it away from the bedside using the request form and prescription chart. This sample was also rejected as there was no signature to confirm the patient had been identified. A blood group request was made on the computer with Patient 2's details, further samples were taken from Patient 1 and accepted by the transfusion laboratory. The blood group result was entered on Patient 2's record (sample was from Patient 1). A request was made for platelets using the correct details for Patient 1, but the laboratory staff now asked for blood samples as they did not have a confirmed group. The ward staff knew their patient had several blood samples taken earlier and the nurse was asked to confirm the ID of the patient she had sampled. She then confirmed with the mother that this was Patient 1 who had been misidentified as Patient 2. Platelets were transfused with delay while the child was admitted to the high dependency unit and an ID band was applied.

Most near miss WBIT incidents are detected in the laboratory, either during testing or at authorisation of results: Figure 13a.2.

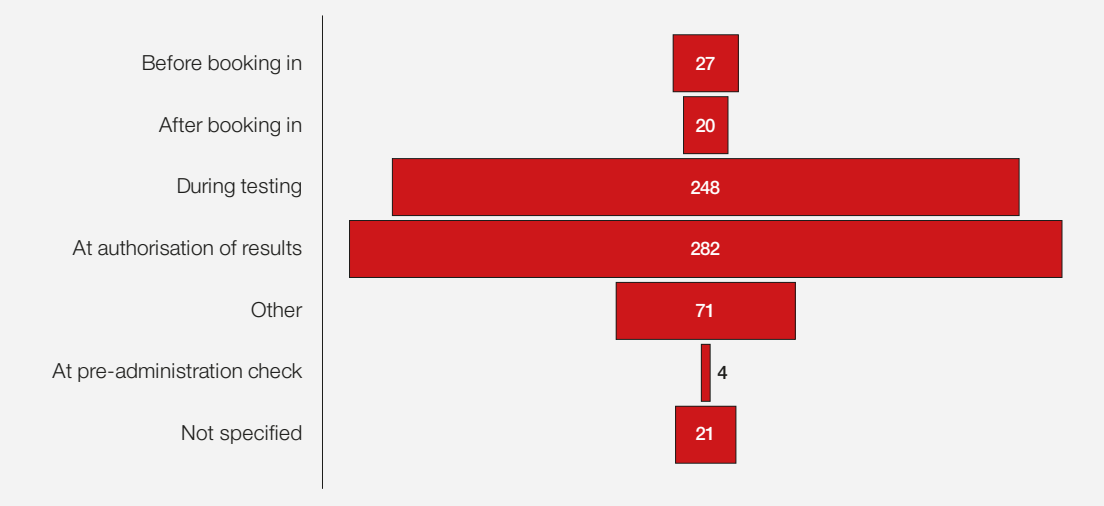


Figure 13a.2: Point in the process where the error was detected (n=673)

ABO-incompatibility

If the WBIT remains undetected there is potential for transfusion of incompatible components. In 555 cases blood group data were provided. Had these patients required red cell transfusions, 239/555 (43.1%) would have been ABO-incompatible with a risk of serious harm or death.

		Blood group of the component that might have been transfused as a result of the WBIT					
		A	B	AB	O	Compatible	Incompatible
Patient blood group	A	54	37	15	115	169	52
	B	30	9	5	47	56	35
	AB	3	8	0	10	21	0
	O	112	34	6	70	70	152
	Totals	**199**	**88**	**26**	**242**	**316**	**239**

Table 13a.1: Blood groups and potential red cell incompatibility of WBIT (n=555)

Who takes the samples?

There is paucity of information at a national level regarding the staff groups involved in taking transfusion samples. Previous Annual SHOT Reports have included data of staff groups involved in transfusion sampling provided by the Oxford Hospitals group for illustration, but this may not be truly representative across all NHS Trusts and Health Boards. This year, data is also included from the Southampton Hospitals. Understanding patterns of errors in different clinical situations will help identify targeted interventions to improve practice. British Society for Haematology guidelines (BSH Robinson, 2018) must be followed to ensure safe practice. Further details with information from Oxford and Southampton can be seen in the supplementary material that can be accessed online at this link (https://www.shotuk.org/shot-reports/report-summary-and-supplement-2020/).

Review of maternity cases n=233

The majority of near miss WBIT cases from maternity reported to SHOT in 2020 were taken by midwives 169/233 (72.5%). Healthcare assistants were responsible in 22, 17 were taken by medical staff and 5 by phlebotomists. Most were taken in hospital but 8 were taken at home and 14 in community clinics (3 of these in general practice surgeries). Eighteen cases related to infants from birth to 3 days of age. These numbers reflect the importance and diversity of midwives' practice. More work needs to be done to emphasise the importance of correct patient identification and sample labelling in the community and antenatal setting to improve patient safety.

Errors in labelling of cord blood samples have arisen when the placenta is removed from the mother's side and sampled elsewhere with inadequate identification. In 1 case the WBIT was then identified when the adult was found to have a group that differed from that recorded at birth 20 years before.

Potential for adverse incidents as a result of WBIT leading to wrongly recorded red cell D-type

There were 51 women whose correct group was D-negative but were grouped as D-positive. These women might have missed anti-D Ig prophylaxis. Wrong D-types in samples from infants of D-negative mothers also have potential for errors with anti-D Ig. There were 28 cases where a mother or baby was recorded as D-negative whose true group was D-positive. Three of these were errors related to mislabelling of mother and cord blood samples.

Case 13a.3: A D-negative mother apparently had a D-negative baby

An antenatal cffDNA test predicted the baby would be D-positive. Cord blood testing showed the infant to be D-negative. Laboratory testing of the paired samples showed that maternal blood was present in both mother and 'cord' sample bottles. Repeat sampling from the baby confirmed the group as D-positive. The reporter noted: 'There have been several WBIT errors from midwives and the transfusion practitioners have been taken off the training programme for face-to-face sessions so there is a reminder about sample labelling to be included in the drills and skills'.

Case 13a.4: A mother identifies that her baby cannot be D-positive

Blood was taken from a neonate for grouping as the mother was known to be D-negative. The baby's sample grouped as B D-positive. The mother was informed of her requirement for anti-D Ig, but she informed the staff that the child's father was also D-negative. The baby was bled again twice and grouped as A D-negative on both occasions.

Learning points

- Wrong blood in tube is a particular risk in midwifery. Steps in positive patient identification and safe sample labelling must be followed whether in a hospital, general practitioner clinic, or in a patient's home
- Methods for blood sampling from pregnant individuals should be reviewed to ensure safe practice at all steps. The standard for identification and labelling should be adhered to, whatever the setting
- If the placenta is moved to another room prior to taking the cord blood sample, ensure it is correctly identified

Conclusion

The investigation of near miss events provides important opportunities for learning. These reviews can identify all contributory factors which can inform which corrective actions can then be taken. The number of near miss WBIT from maternity departments has been highlighted in this year's Annual SHOT Report. The HSIB published a report about a WBIT full blood count sample from a maternity unit where there was no patient harm (HSIB 2019). This illustrated many reasons why these errors can occur ('work as done' may not reflect 'work as imagined' in protocols) and recommended the use of electronic systems for patient identification and blood sample labelling. Additional recommendations for organisations from the HSIB report include human factors training, adequate staffing, provision of appropriate equipment and reduction in distractions.

There is clear evidence that WBIT errors can be reduced by using electronic patient identification systems (Kaufman et al. 2019, Murphy et al. 2019). In the Kaufman study the incidence of WBIT was 1:3046 by manual labelling methods (16 sites, >1.6 million samples) and was much lower at 1:14,606 for 4 sites (>0.5 million samples) using electronic systems ($p < 0.0001$). They also reported that WBIT rates were high among mislabelled (rejected) samples, confirming that rejecting samples with even minor labelling errors helps mitigate the risk of ABO-incompatible transfusions. This is further evidence for the introduction of electronic sample labelling systems in transfusion to increase safety as has been previously recommended by SHOT.

References

BSH Robinson S, Harris A, Atkinson S, et al. The administration of blood components: a British Society for Haematology Guideline. *Transfus Med* 2018;**28(1)**:3-21. http://onlinelibrary.wiley.com/doi/10.1111/tme.12481/full [accessed 25 March 2021].

HSIB. Wrong patient details on blood sample. 2019. https://www.hsib.org.uk/documents/147/hsib_report_wrong_patient_details_blood_sample.pdf [accessed 28 April 2021].

Kaufman RM, Dinh A, Cohn CS, et al. Electronic patient identification for sample labeling reduces wrong blood in tube errors. *Transfusion* 2019;**59(3)**:972-980.

Love L, et al. The SHOT Annual Report 1996/1997 (1998). www.shotuk.org/shot-reports/ [accessed 06 June 2021].

Murphy MF, Addison J, Poles D, et al. Electronic identification systems reduce the number of wrong components transfused. *Transfusion* 2019;**59(12)**:3601-3607. https://onlinelibrary.wiley.com/doi/10.1111/trf.15537 [accessed 28 April 2021].

14 Right Blood Right Patient (RBRP) n=207

Authors: Terrie Perry and Victoria Tuckley

Definition:

Incidents where a patient was transfused correctly despite one or more serious errors that in other circumstances might have led to an incorrect blood component transfused (IBCT).

Key SHOT messages

- Staff must utilise a pre-administration bedside checklist as recommended by the Department of Health in 2017. It is concerning that some sites are yet to implement these or are not consistently using them
- Accurate patient identification must be adhered to throughout the transfusion process
- The laboratory exit check (Narayan et al. 2020) is a useful guide for laboratory staff issuing blood components and may reduce component labelling errors
- Collection of blood components is a critical step in the transfusion process and robust procedures should be in place to ensure that necessary checks are made (Narayan et al. 2020)

Abbreviations used in this chapter

BSH	British Society for Haematology	**IT**	Information technology
CAS	Central alerting system	**LIMS**	Laboratory information management system
DOB	Date of birth	**PID**	Patient identification
ED	Emergency department	**RBRP**	Right Blood Right Patient
IBCT	Incorrect blood component transfused	**SOP**	Standard operating procedure
ID	Identification		

Recommendations

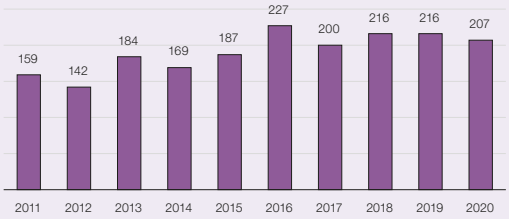
- The PLEDGE aide memoire detailed in the chapter could be incorporated in blood component collection procedures
- Regular audit of blood collection and administration could help identify potential errors and identify opportunities for learning

Action: Hospital transfusion teams

Headline data 2020

Number of reports n=207
Deaths n=0
Major morbidity n=0

RBRP reports by year



Demographic data

Male n=92
Female n=104
Unknown n=11

Adults n=181
Paediatric n=15
Unknown n=11

Blood component data

Red cells n=161
Platelets n=17
Plasma n=10
Multiple Components n=19
Other n=0

Introduction

There were 207 cases reported in 2020, slightly lower than the 216 in 2019. Clinical errors accounted for 142/207 (68.6%), and laboratory errors 65/207 (31.4%). Transposed compatibility tags were implicated in 62 cases and 21 cases mentioned wrong names, transposed names, wrong DOB on component documentation. Pressures due to COVID-19 were mentioned in 15 reports, mainly related to reduced staffing and organisational/workspace reconfiguration.

Deaths n=0

There were 13 deaths in this patient group, none related to the transfusion.

Major morbidity n=0

No patient suffered major morbidity as a result of these errors.

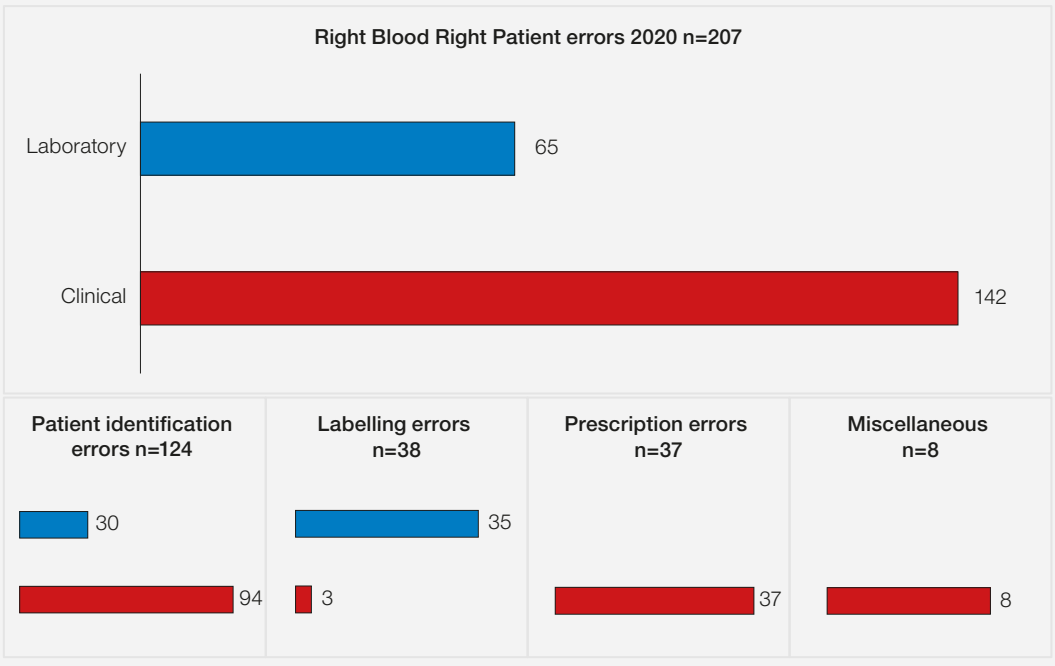
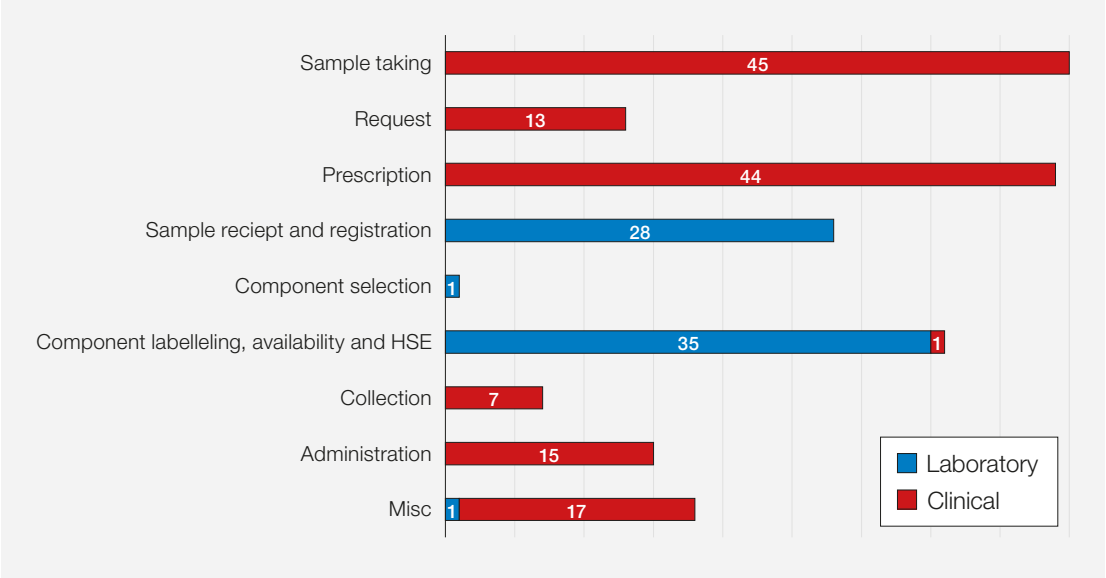


Figure 14.1: Breakdown of 2020 RBRP reports (n=207)

Sampling errors accounted for 45/207 (21.7%). Errors in prescribing accounted for 44/207 (21.3%) of which 32/44 (72.7%) involved an error in prescribing the components correctly, and 12/44 (27.3%) PID errors on prescriptions (Figure 14.2).

Figure 14.2: RBRP classified by the transfusion step in which the primary error occurred (n=207)

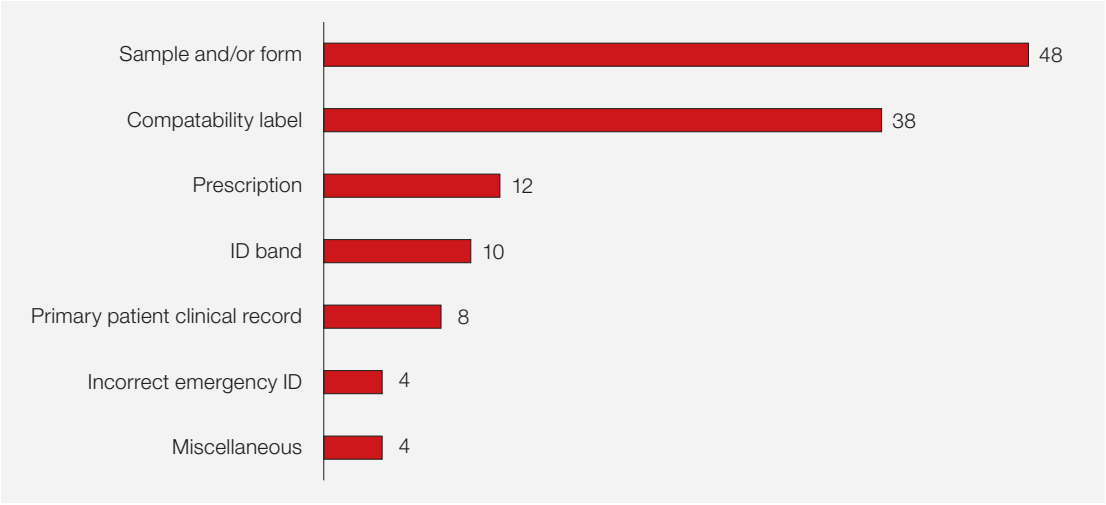


HSE=handling and storage errors

Patient identification (PID) errors n=124

PID errors 124/207 (59.9%) occurred in all parts of the transfusion process. These included patient details wrongly transcribed onto request forms and sample tubes, and laboratory staff not entering data correctly onto the LIMS during the booking in process (Figure 14.3).

Figure 14.3: Details of patient identification errors (n=124)



ID= identification

Most transfusion samples are labelled correctly. SHOT data demonstrate that many RBRP errors occur at the sample labelling step. Many RBRP investigations only address laboratory errors at sample receipt and registration, but this may not be the primary cause. Reporters should look back to the original error (the oversight at sample taking, and why this occurred) to help identify the primary cause and prevent these errors recurring.

Case 14.1: Incorrectly labelled emergency components transfused due to clerical error

During core hours a major haemorrhage protocol was pre-activated on unknown Patient 1 (a male

in his 50s) who was issued with the next emergency ID (ID X) on the list of ID used for unknown patients. This was not entered onto the system immediately as the member of staff was not aware of the full procedure but was trying to help. Before Patient 1's arrival in the ED, an unknown Patient 2 was issued with ID X and this was entered on the system. When Patient 1 arrived, a new ID had to be issued (ID Y) but the required blood components had been issued using ID X. The error was recognised but the patient was peri-arrest and medical staff felt that the delay caused by re-labelling would be detrimental to the patient's outcome.

There should be a clear, defined procedure for allocation of emergency identifiers in all hospitals. For hospitals in England, this should be in accordance with patient safety alert NHS/PSA/RE/2018/008 'Safer temporary identification criteria for unknown or unidentified patients' (NHSI 2018). All staff members involved in clerking patients should be competent in this procedure. Whilst the instinct to help is commendable, all members of hospital staff should be aware of their limits of responsibility.

Case 14.2: Patient 2 appears to have had Patient 1's unit of red cells

Two patients on the same ward were to receive blood. Patient 1 was prescribed two units on the transfusion documentation but only one was recorded as given. Patient 2 was prescribed one unit on the transfusion documentation, but it was recorded that two had been given. The second unit documented as given to Patient 2 was one issued for Patient 1. A two-person independent checklist was completed but the compatibility tag was applied to the transfusion documentation retrospectively away from the bedside at the nurses' station. This was a documentation error; the patients did receive the correct units.

Checking and completion of the transfusion documentation must occur at the time of transfusion at the patient side.

Pre-administration checklists

The CAS alert: 'Safe Transfusion Practice: Use a bedside checklist' (Department of Health 2017) was issued in response to SHOT recommendations. A pre-administration checklist was used in 131/207 (63.3%) RBRP cases. In 26/207 (12.5%) cases a checklist was available but not used. In 30/207 (14.5%) cases no bedside check was available, and only half of these reports stated an intention to implement one (Figure 14.4) however, some sites were represented more than once. Pre-administration checklists help guide safe transfusion and must be used prior to every component transfusion. They are of particular use for inexperienced staff and conversely for extremely experienced staff who may fail to identify errors due to cognitive bias.

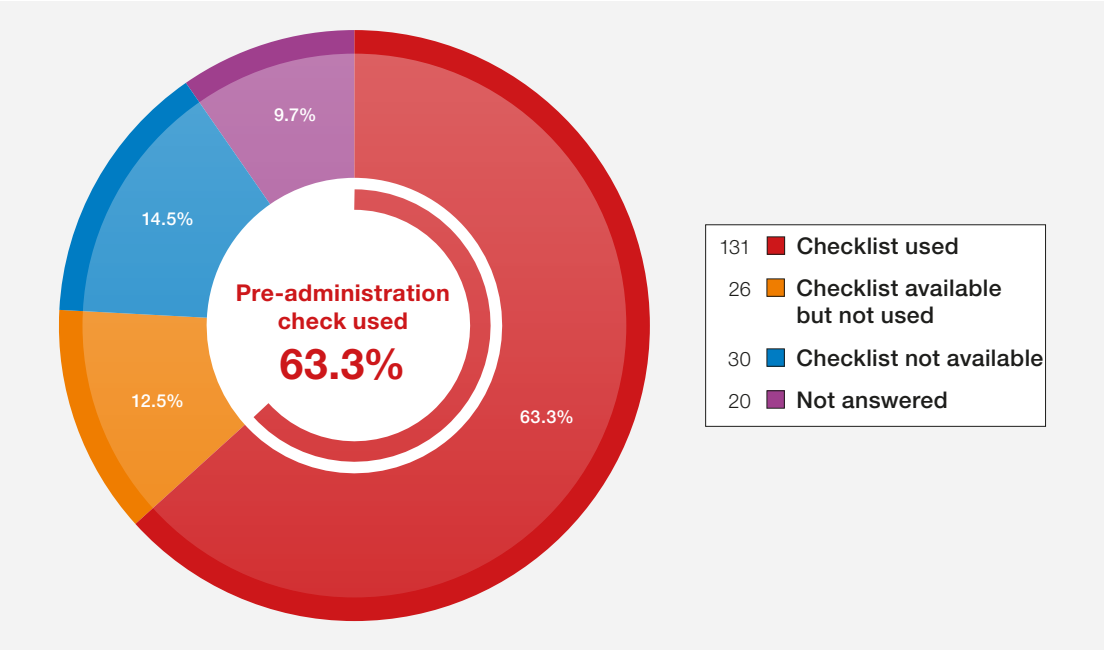
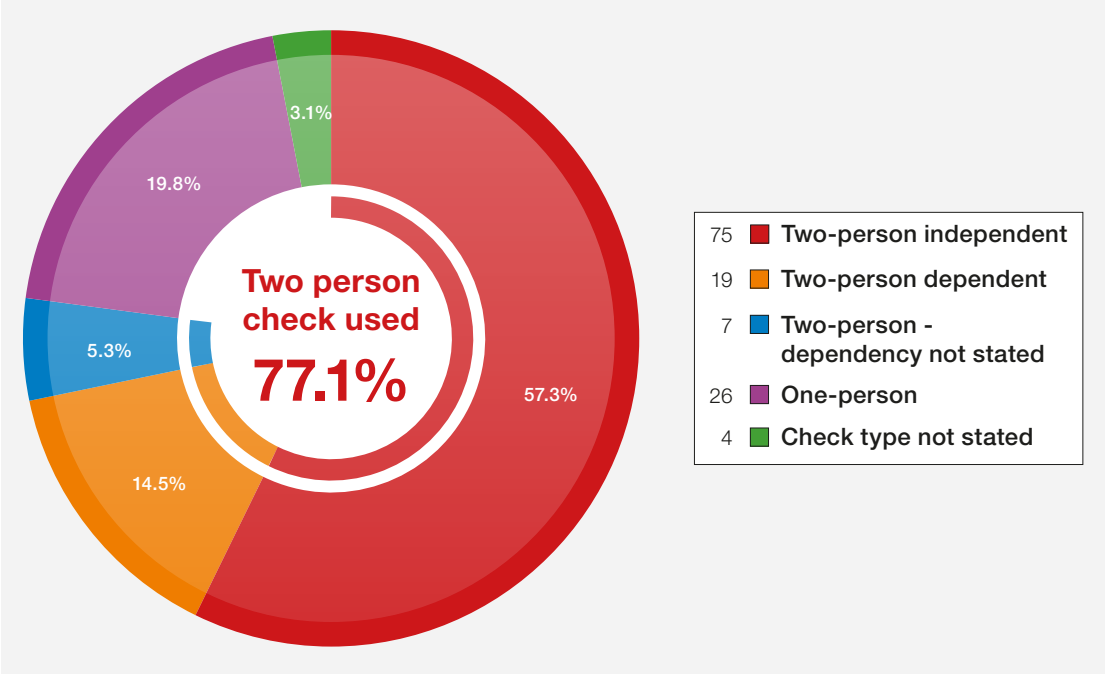


Figure 14.4: The presence of a pre-administration check in RBRP errors (n=207)

Pre-administration check - one or two person

In the 131 reports which stated a pre-administration checklist was used, most had a two-person check 101/131 (77.1%) and the majority of these 75/101 (74.3%) used a two-person independent check (Figure 14.5). Data regarding dependency of checks was not consistently reported.

Figure 14.5: Type of pre-administration check used in RBRP incidents (n=131)



SHOT recommends local blood transfusion policies reflect national guidelines and where this requires a two-person checking procedure, each person should complete all the checks independently (double independent checking) (BSH Robinson et al. 2018).

Learning points

- Use of a checklist at the collection of the blood component from the refrigerator/storage area can prevent most right blood right patient (RBRP) errors from reaching the patient
- A pre-administration checklist can pick up most remaining RBRP errors and near misses
- Get it right first time, every time – while checklists are important, they may not pick up all errors

Near miss cases n=93

There were 93 near miss RBRP incidents, 11/93 (11.8%) originating in the clinical area and 82/93 (88.2%) originating in the laboratory. There is a noticeable decrease year on year, and this is most evident in the clinical cases. The main laboratory errors were labelling errors, most of them transposed tags.

Most near misses 78/93 (83.9%) were detected by qualified nurses, healthcare assistants and operating department practitioners when collecting blood or at the patient side, and 65/93 (69.9%) using a formal electronic (n=4) or paper-based pre-administration checklist (n=61). The checklist is a vital tool in transfusion safety and must be implemented in all Trusts/Health Boards.

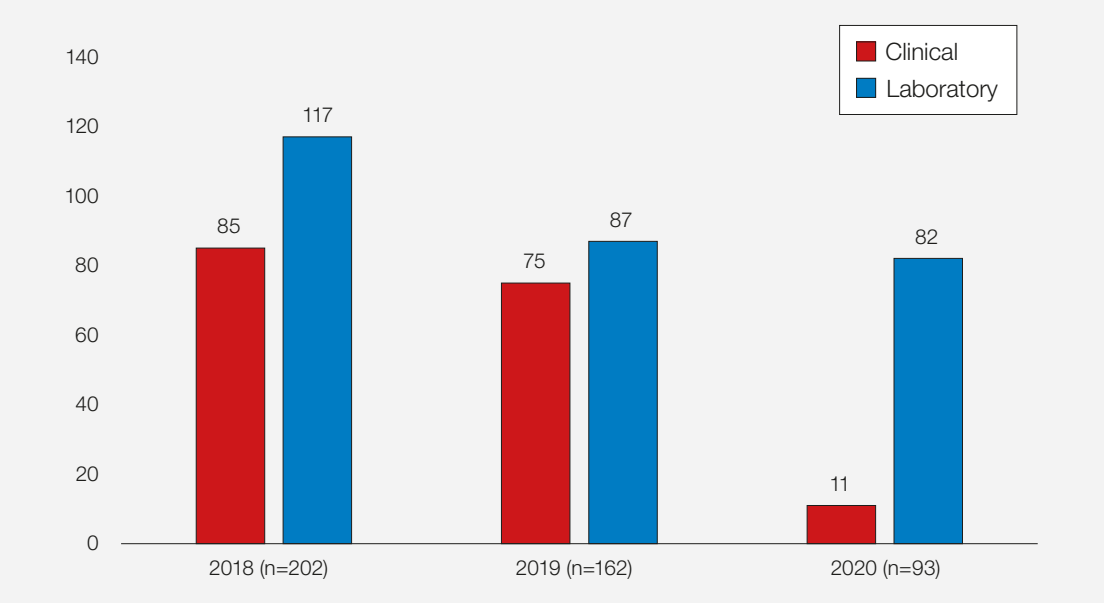


Figure 14.6: RBRP near misses 2018-2020

A collection check provides the opportunity to detect any errors prior to the blood being transported to the patient. The fact that most errors are detected at the bedside may indicate that the collection check is not as robust as it could be. The following aide memoire may help identify any errors at the time of component collection.

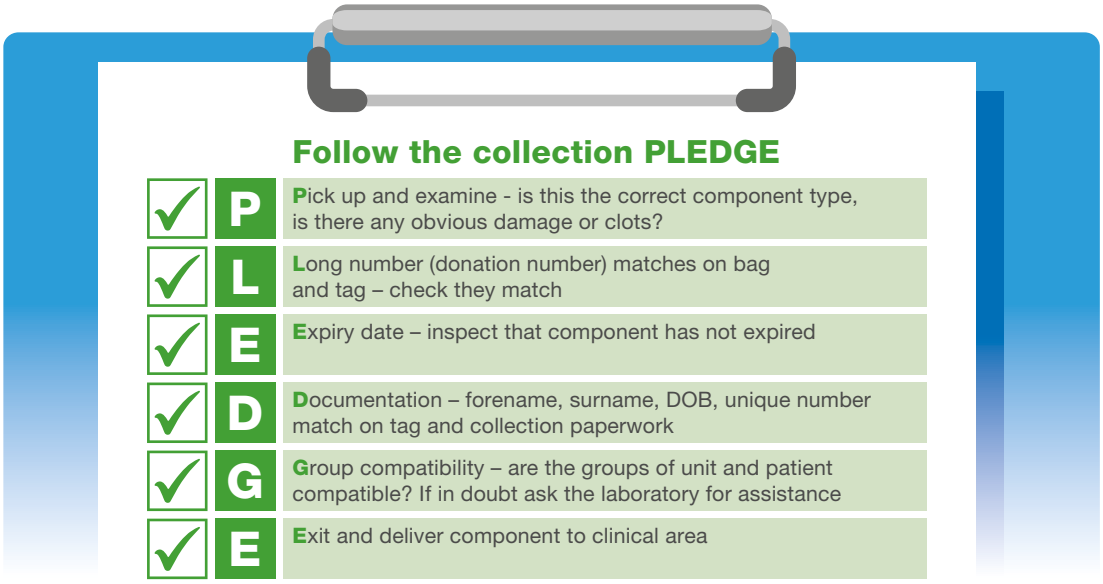


Figure 14.7: The PLEDGE aide memoire

Conclusion

Thorough investigation of RBRP and near miss-RBRP incidents is vital as findings from these investigations will provide 'free' learning opportunities. All staff must be trained, and competency assessed prior to performing tasks related to transfusion.

Although the collection process may vary between organisations, there are basic checks that should be made at this point which could greatly reduce the number of RBRP (and IBCT) incidents. BSH guidelines (BSH Robinson et al. 2018) state that the checks required when collecting blood components are correct component, expiry date and matching of four patient identifiers with collection paperwork. When performed in combination with a check of the donation number on the bag with the compatibility label, and a check of the ABO-compatibility of the component with that of the patient, the number of RBRP events could be reduced considerably.

A very small number of incident investigations reported that a change in policy or SOP was required. This would indicate that processes are in place to prevent RBRP errors, although a lack of incident investigation in some cases misses opportunities to identify the initial error. There is a misconception that IT solutions may be the only way to prevent RBRP errors - however some of the reports highlight that, unless there are integrated IT systems in use from patient registration to administration, errors are still possible. Overreliance on IT systems has the potential for error and staff should be aware of downtime procedures.

References

BSH Robinson S, Harris A, Atkinson S, et al. The administration of blood components: a British Society for Haematology Guideline. *Transfus Med* 2018;**28(1)**:3-21. http://onlinelibrary.wiley.com/doi/10.1111/tme.12481/full [accessed 25 March 2021].

Department of Health. Safe transfusion practice: use a bedside checklist (CAS) CEM/CMO/2017/005 (2017). https://www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAlert.aspx?AlertID=102663 [accessed 28 April 2021].

Narayan S (Ed), Poles D, et al. on behalf of the Serious Hazards of Transfusion (SHOT) Steering Group. The 2019 Annual SHOT Report (2020). https://www.shotuk.org/shot-reports/ [accessed 28 April 2021].

NHS Improvement (2018) Patient Safety alert NHS/PSA/RE/2018/008: Safer temporary identification criteria for unknown or unidentified patients. https://www.england.nhs.uk/wp-content/uploads/2019/12/Patient_Safety_Alert_-_unknown_or_unidentified_patients_FINAL.pdf [accessed 21 April 2021].

Laboratory Errors n=639 (439 errors and 200 near miss)

15

Authors: Victoria Tuckley, Heather Clarke and Peter Baker

Thank you

The SHOT laboratory working expert group would like to extend our huge appreciation to all staff working within laboratories for their commendable effort during this very difficult year. Many staff have faced numerous challenges supporting an already extremely stretched workforce and have supported each other through harrowing personal challenges. This laboratory chapter hopes to highlight areas where transfusion laboratory practice can be further improved and how we can support our patients and hospital community. We would also like to thank our reporters for continuing to report to SHOT during this challenging time and maintaining a strong collaborative reporting culture.

Key SHOT messages

- K-negative units should be provided to K-negative individuals of childbearing potential. Failure to do so puts future pregnancies at risk. Laboratory information management systems (LIMS) rules, which cannot be easily overridden, should be implemented to aid this process
- If in doubt, ask the right person for the right advice. SOP should include sufficient information and escalation procedures; however, it is in the interest of patient safety to check details of procedures with senior colleagues rather than assume

Abbreviations used in this chapter

ABID	Antibody identification
ABOi	ABO-incompatible
BMS	Biomedical scientist
CCP	COVID-19 convalescent plasma
DAT	Direct antiglobulin test
ED	Emergency department
EQA	External quality assessment
FFP	Fresh frozen plasma
HDFN	Haemolytic disease of the fetus and newborn
HSE	Handling and storage errors
HT	High-titre
IBCT	Incorrect blood component transfused
IBGRL	International Blood Group Reference Laboratory
IFU	Instructions for use
IQC	Internal quality control
IT	Information technology
LIMS	Laboratory information management system
MHRA	Medicines and Healthcare products Regulatory Agency
NM	Near miss
QC	Quality control
RCA	Root cause analysis
SOP	Standard operating procedure(s)
Sp-ICE	Specialist Services electronic reporting using Sunquest's Integrated Clinical Environment
SRNM	Specific requirements not met
SRR	Sample receipt and registration
UKNEQAS	UK National External Quality Assessment Scheme
UKTLC	UK Transfusion Laboratory Collaborative

Recommendations

- Trust/Health Board governance should review staffing levels in transfusion laboratories and ensure the skill mix is in compliance with UK Transfusion Laboratory Collaborative (UKTLC) standards and that there are sufficient numbers of staff in line with capacity plan (UKTLC 2014)

Action: Transfusion laboratory managers, clinical governance departments and chief executives

- Transfusion laboratories should have clear procedures for component selection to avoid ABO-incompatible transfusion. Complex situations should be discussed with a haematologist or UK Blood Transfusion Service (UKBTS) consultant for concessionary issue where time allows

Action: Transfusion laboratory managers, transfusion training leads and haematologists

- Handover is a safety critical point in the working day. Transfusion laboratories should implement a written handover log to support clear communication

Action: Transfusion laboratory managers, transfusion quality leads

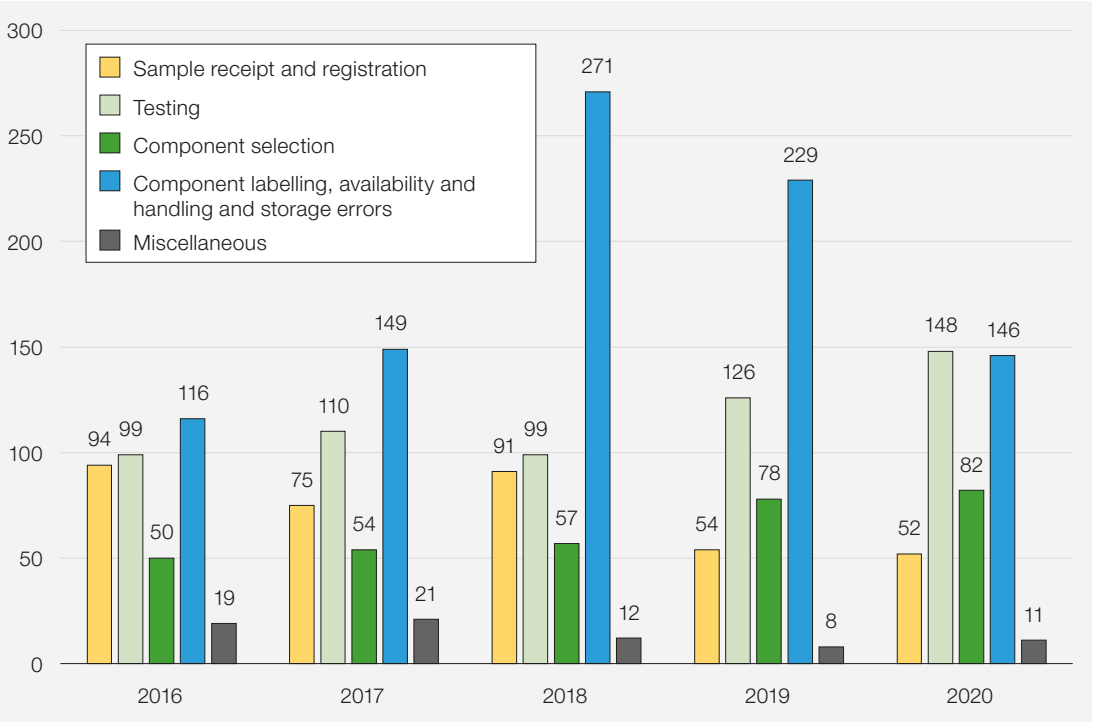
Introduction

The number of events reported in the laboratory has reduced by 19.7% to 639 from 796 in 2019. In 2019, 796/3397 (23.4%) SHOT reports were laboratory errors, in 2020 this is 639/3214 (19.9%). This is possibly due to improvements in practice, or due to the unprecedented pressures faced in the healthcare community this year due to the COVID-19 pandemic, leading to reduced reporting.

In challenging circumstances, it is vital to have robust emergency preparedness procedures. In 2021, SHOT issued a safety notice highlighting the key role of planning for such situations in the laboratory. This is discussed further in Chapters 6, Acknowledging Continuing Excellence in Transfusion (ACE) and Chapter 11, Handling and Storage Errors (HSE).

For the first time in several years, most laboratory errors resulted from omissions at the testing step 148/439 (33.7%), increasing from 126/495 (25.5%) in 2019. There has also been a dramatic drop in component labelling, availability and HSE errors to 146/439 (33.3%) in 2020 from 229/495 (46.3%) in 2019.

Figure 15.1: Laboratory errors 2016-2020 categorised by step where the error occurred



Deaths n=2

There were 20 deaths reported in total, 2 of which were possibly related to the transfusion (imputability 1). One case involved a patient with autoimmune haemolytic anaemia where there was a delay in provision of blood due to samples not being sent to the reference laboratory in a timely manner and multiple communication difficulties. The other case involved significant delays in provision of blood, which was compounded by IT failures, during a major haemorrhage. These cases are discussed further in Chapter 12a, Delayed Transfusions.

Major morbidity n=5

There were 5 cases of major morbidity relating to laboratory errors, all of which resulted in sensitisation to the K antigen in patients of childbearing potential. Anti-K has been implicated in many cases of HDFN which require antenatal intervention. Whilst antibody levels can be monitored by titration, this may not be a reliable indicator of disease severity (BSH White et al. 2016). Laboratories should take all steps possible (including the application of LIMS flags which are not easily overridden) to prevent sensitisation to the K antigen and so prevent increased risk for the fetus in future pregnancies.

Case 15.1: Historical transfusion of a unit of red cells resulted in antibody formation

An antenatal booking group and screen for a patient in her 30s at 16 weeks' gestation revealed a positive antibody screen. The sample was sent to the reference laboratory at the Blood Service for antibody identification and titration. Two antibodies were confirmed, anti-K and anti-Fy^a, both with high titration levels. On investigation by the hospital transfusion laboratory, it was found that this patient had been transfused one of two units of red cells issued in 2014 during a postpartum haemorrhage. The unit transfused was found to be K-positive and Fy^a status was not known.

Alloimmunisation is a risk with all transfusions, and every effort must be made to prevent this when possible. In this case the formation of anti-Fy^a was unpreventable, however the formation of anti-K was. All K-negative patients of childbearing potential (<50 years old) must be transfused with K-negative red cells (BSH Milkins et al. 2013). It is imperative that the LIMS alerts staff of this specific requirement, and that these alerts are heeded when issuing units for transfusion to prevent the unnecessary formation of this antibody which can cause HDFN.

Trends in error reports

The highest proportion of errors occurred within the IBCT-SRNM category 130/439 (29.6%), which is similar to previous years.

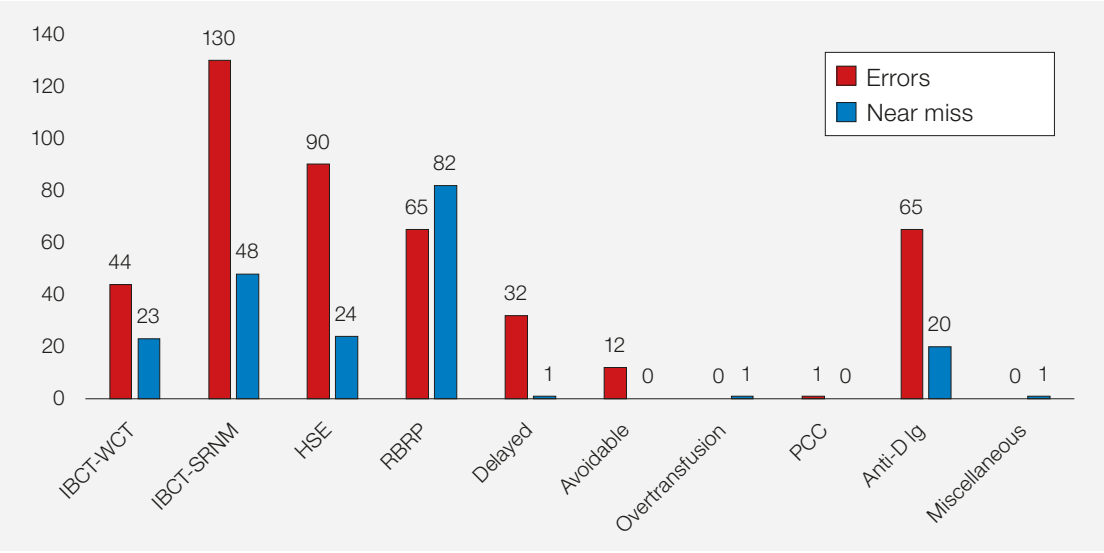
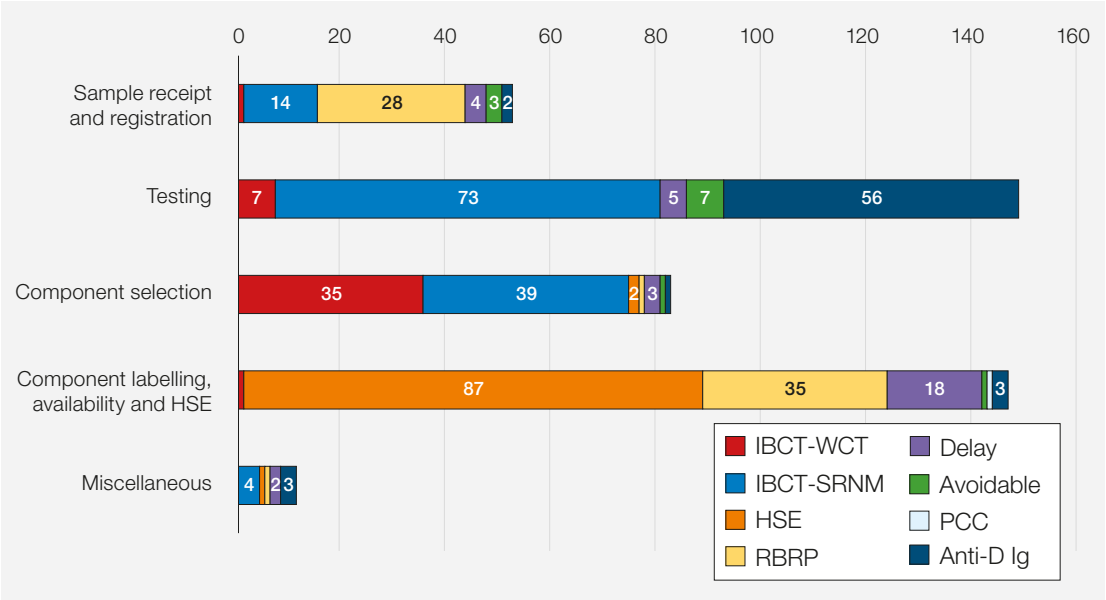


Figure 15.2: Laboratory incidents and near misses by category of outcome (n=639)

IBCT-WCT=incorrect blood component transfused-wrong component transfused; IBCT-SRNM=IBCT-specific requirements not met; HSE=handling and storage errors; RBRP=right blood right patient; PCC=prothrombin complex concentrate; Ig=immunoglobulin

Figure 15.3: SHOT laboratory data showing at which stage in the transfusion process the primary error occurred (n=439)

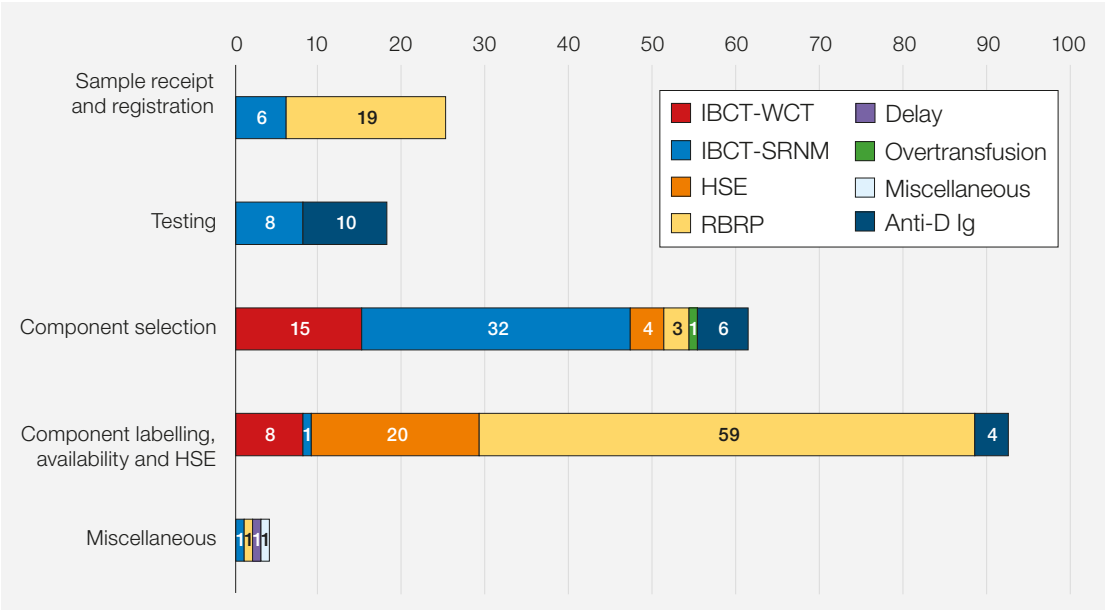


IBCT-WCT=incorrect blood component transfused-wrong component transfused; IBCT-SRNM=IBCT-specific requirements not met; HSE=handling and storage errors; RBRP=right blood right patient; PCC=prothrombin complex concentrate; Ig=immunoglobulin

Near miss cases n=200

There has been a reduction in NM laboratory errors, to 200 from 301 in 2019 (Narayan et al. 2020). In contrast to laboratory errors, the pattern of NM events is consistent, with the largest reporting category being component labelling, availability and HSE, 92/200 (46.0%). The highest proportion of laboratory NM cases remain RBRP events 82/200 (41.0%), of which 52/82 (63.4%) involved labelling errors. The use of electronic solutions to review component labelling may help detect these errors prior to components leaving the control of the laboratory and being available in the clinical area (BSH Jones et al. 2017). A total of 128/200 (64.0%) cases were due to failure to follow procedure and 129/200 (64.5%) laboratory errors were detected at pre-administration bedside checking. This demonstrates that robust transfusion policies and procedures, if followed correctly, can minimise errors in transfusion. Incident investigations should focus on why policies were not followed to reduce error recurrence.

Figure 15.4: SHOT near miss laboratory errors showing at which stage in the transfusion process the primary error occurred with outcome (n=200)



IBCT=incorrect blood component transfused; WCT=wrong component transfused; SRNM=specific requirements not met; HSE=handling and storage errors; RBRP=right blood right patient; Ig=immunoglobulin

Errors by step in the transfusion process in the laboratory

Sample receipt and registration (SRR) n=77 (52 transfused errors and 25 near misses)

The majority of SRR errors occur when available information on LIMS are not heeded. Distractions should be avoided at booking in, as this is the first opportunity to prevent mistakes potentially impacting on a patient's wellbeing.

Many cases reported this year have errors where data was available on a transfusion request form or on other IT platforms (such as Sp-ICE) but were not accessed or considered. Gaps in understanding the current clinical situation also lead to errors in testing and component selection.

Learning points

- All clinically relevant information should be taken into account at the sample receipt and registration stage of the laboratory process
- Patient records must be kept up to date
- All relevant transfusion history must be available to laboratory staff to aid with the decision-making process

Testing n=166 (148 transfused errors and 18 near misses)

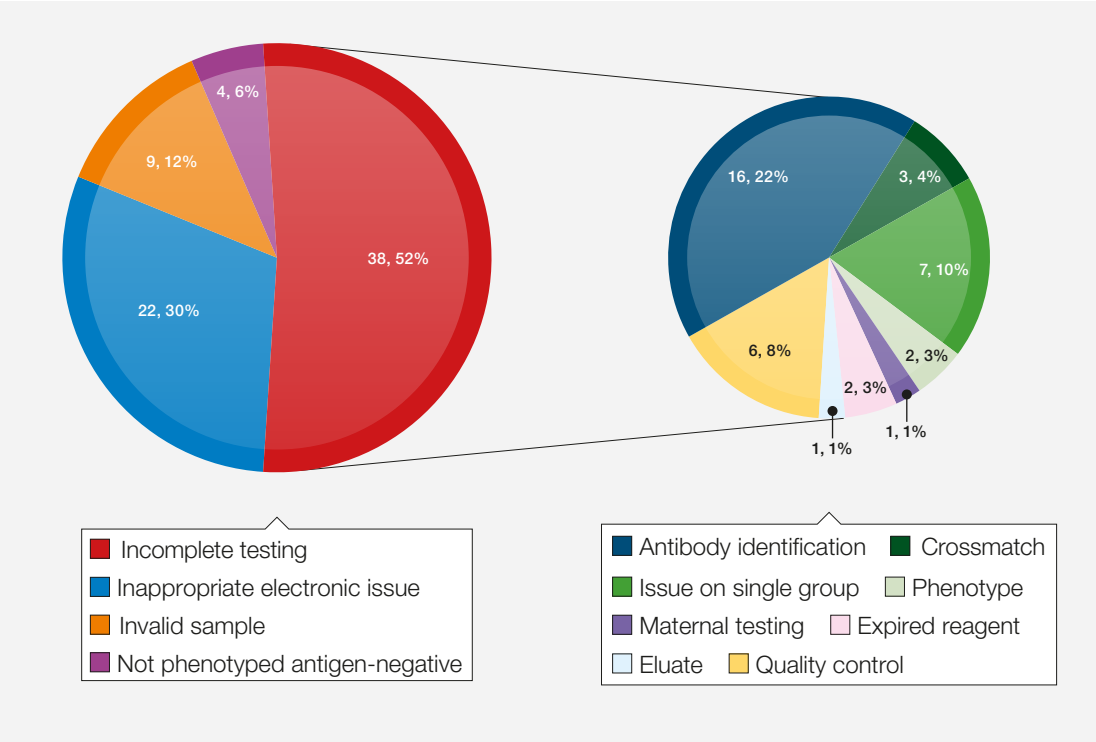
Laboratory testing errors have increased from 2019 and is the highest yearly total reported to SHOT. Most testing errors have been recorded as due to failure to follow procedure 84/148 (56.8%). Procedural errors are largely IBCT-SRNM errors 56/84 (66.7%), followed by anti-D Ig errors 22/84 (26.2%). The key SHOT message from 2019 remains pertinent, 'Laboratory staff should be comfortable working within routine procedures – these procedures should be safe and fit for use, especially in high-pressure situations'. If repeated errors with the same procedure are seen, it is important to review the SOP to ensure it reflects 'work as done', and whether adjustments are required to allow safer practice to occur.

IBCT-SRNM testing errors n=73

Most testing errors occurred in the IBCT-SRNM category 73/148 (49.3%) and were failures to complete relevant tests prior to blood issue 38/73 (52.1%). Most incomplete testing was due to failure to complete ABID in 16/38 (42.1%), followed by absence of up to date QC testing 6/38 (15.8%) (Figure 15.5).

Errors in ABID were mostly due to assumption of results and issue prior to completion of testing in 6/16 (37.5%) followed by incorrect interpretation 3/16 (18.8%), a lack of maternal testing for neonatal crossmatch 2/16 (12.5%) and positive screen not followed up, screen not performed and incorrect antigram used all occurring once each.

Figure 15.5: IBCT-SRNM laboratory testing errors separated by error subcategory (n=73)



Case 15.2: Red cell antibody identification error due to heterozygous cell selection

A male patient in his 50s was admitted with haematemesis and a Hb of 53g/L. The antibody screen was positive, and the initial antibody panel appeared to identify anti-c and anti-E. A full crossmatch was performed with c-negative and E-negative units and were found to be incompatible. The results were referred to the senior BMS who noted that anti-M and anti-S had not been excluded from the initial antibody panel and suggested it was probably anti-M and to select and crossmatch four M-negative units while more panel work was being done. One of these four units was found to be compatible, it was issued and subsequently transfused to the patient. A further four M-negative units were requested from the Blood Service and crossmatched but only one of these four was compatible. At this point the patient refused any more blood so the remaining compatible unit was kept on standby. The next day samples were sent to the Blood Service for antibody investigation as anti-S had still not been excluded. The Blood Service later rang the laboratory to say the patient had a historical anti-S from a sample sent from a different hospital and these results were available on the Sp-ICE system. On investigation the cells selected to exclude or confirm anti-M were homozygous but were heterozygous for the S antigen and gave a negative result (dosage effect). The Blood Service were contacted, and they confirmed the unit transfused was S-negative as was the unit on standby so there was no patient harm.

Laboratory procedures should include any limitations to be aware of during testing, such as dosage effect of panels cells that are heterozygous. There should be robust procedures in place for selection of blood in an emergency, and advice from senior colleagues, or reference centre staff sought if in doubt. It may not be possible to check Sp-ICE in emergency situations, but this should be checked when feasible to enable appropriate follow up to occur.

Misidentification of antibodies can have serious clinical consequences. In 2020, misidentification of an anti-Jk^{a} resulted in a delayed haemolytic transfuion reaction. This is discussed in more detail in Case 19.1, Chapter 19, Haemolytic Transfusion Reactions (HTR).

Anti-D testing errors n=56

Anti-D Ig errors account for 56/148 (37.8%) testing errors, which is an increase from 24/126 (19.0%) in 2019. Errors relating to cffDNA testing occurred in 23/56 (41.1%) of reports, with errors in prediction of fetal D-type conducted by testing laboratories accounting for 16/23 (69.6%) of these. An additional

cffDNA error was categorised as 'miscellaneous' and was not counted under 'testing' as it involved a member of laboratory staff providing incorrect advice.

Case 15.3: Anti-D Ig omitted due to misleading information in product instructions for use (IFU) document

A female patient in her 20s had antenatal booking blood samples received in the transfusion laboratory at hospital A. She was found to be D-positive (with a 3+ reaction strength) and had no antibodies detected, these results were also found at 28 weeks. Her care was later transferred to hospital B who used the same grouping analyser as hospital A. At hospital B she also had a 3+ strength reaction with anti-D, however her result was entered as D-negative, her sample was sent to the reference laboratory for confirmation and she was provided with anti-D Ig prophylaxis. The sample was further tested within IBGRL and the result found to be a D variant. For the analyser used by both sites, a 3+ reaction requests the BMS to review and acknowledge the results and the IFU documentation states 2+ or <2+ reactions are to be confirmed by an alternative method. No referral took place from hospital A as the results were 3+ for D grouping, however hospital B had experienced a previous incident regarding reaction strengths in 2017 and now referred all D-positive reactions of 3+ strength or below to the reference laboratory. Despite this previous incident, and this case being raised at user group meetings, the reporter had indicated they were yet to receive a field safety notice highlighting this issue, nor had the IFU been updated, though the manufacturer had indicated they would escalate this matter. The manufacturer had communicated to the reporter that they believed a review of 3+ reaction strength was a sufficient safety measure. Locally, the SOP at hospital A was updated and all staff informed of the change in procedure. This patient was scheduled to be followed up at 6 months post-delivery to determine if sensitisation to the D antigen had occurred.

The reagent manufacturer involved has confirmed the above case details as an accurate representation. The IFU is being reviewed to determine if additional information is required to provide further clarity in relation to D variants. There has been no communication circulated to customers so far regarding this issue.

It is vital that manufacturers provide accurate safety critical information within their documentation, and highlight these issues during training. Furthermore, there must be a robust feedback mechanism for when changes in practice are required to prevent patient safety incidents.

There are many cases reported this year that have the same underlying features around inadequate systems to stop the selection and issue of components, especially where incomplete/inadequate testing has occurred. Ideally automated group and screen analysers should prevent the processing of samples or transfer of results when outside of valid IQC or failed IQC. Regarding electronic issue, a key recommendation of BSH guidelines (BSH Milkins et al. 2013) states that 'The overall process for determining eligibility for electronic issue must be controlled by the LIMS and not rely on manual intervention or decision making.'

Learning points

- The laboratory information management system (LIMS) should be able to prevent component issue, especially electronic issue, until all relevant testing is complete without anomaly. If this is not possible then a robust procedure must be in place to ensure that all steps of testing, component selection and issue are completed and appropriate, for example having additional checks
- If a LIMS cannot determine eligibility for electronic issue, then this should not be used to issue red cells

Component selection n=143 (82 transfused errors and 61 near misses)

The principal failures in this section related to the selection of correct component specification. Many incidents occurred due to failure to follow information readily available within the LIMS (e.g. irradiated or K-negative red cells).

Learning point

- The competency-assessment of a biomedical scientist working in transfusion should include an understanding of requirements for irradiated components. Staff should also be aware of when to discuss with clinicians if the correct specification has not been requested

ABO-incompatible transfusion (ABOi) n=2

There were 2 cases of ABOi transfusions which were attributed to laboratory errors in 2020, and there were no adverse patient outcomes in either case. Both errors involved plasma components (1 FFP and 1 CCP) and occurred at component selection, and in both cases LIMS flags alerting to the incompatibility were overridden.

Case 15.4: Group O CCP transfused to a group A recipient

A female in her 30s who was blood group A, was enrolled on the convalescent plasma arm of the REMAP-CAP (A Randomised, Embedded, Multi-factorial, Adaptive Platform Trial for Community-Acquired Pneumonia) trial and was transfused with a unit of group O CCP. On investigation there was no ABO-compatible convalescent plasma in stock and instead of ordering this from the Blood Service the BMS selected group O after discussion with a less experienced member of staff and thought this would be acceptable because the unit was HT-negative. The LIMS had an alert flag for the ABO-incompatibility, but this was not heeded. A unit of group O CCP was also issued to the same patient the previous day, however this was wasted as it had been stored inappropriately in the ward refrigerator. The ABO-incompatibility was not detected upon return of this unit and was only raised when a different BMS was issuing the 2nd dose (3rd unit) and saw the ABOi units in the patient's history. The laboratory has now had the LIMS updated to prevent group O plasma components being issued to a non-group O recipient. No patient harm was reported.

This incident occurred in challenging circumstances with a new blood component. Appropriate advice for such situations should be provided in documentation and a central point of contact should be available 24/7 for escalation in critical situations. Incidents where the LIMS alerts and flags are being ignored and overridden occur year on year. LIMS providers need to address this particular outcome by making it impossible to issue group O plasma to a non-group O patient without specifying a reason for the exceptional issue of ABOi plasma (e.g. major incident). This process should also include communication and referral to a haematologist for concessionary release if required.

Case 15.5: Two units of group O FFP transfused to a group A recipient despite a LIMS flag being present

A female patient in her 50s was admitted as a code red trauma patient following a road traffic accident. She suffered a massive haemorrhage, arrived in the ED and received several units of emergency group O red cells before a group and screen sample could be taken. A sample was taken and processed by the laboratory, but the results showed dual populations because of the O red cells transfused and the group was inconclusive. There was a historical blood group from 1992, but this could not be linked to the current record in the LIMS. The patient's blood group was manually edited to group O with a flag added to the LIMS record to give universal components only as stated in the laboratory procedure for this situation. FFP was later requested and the BMS on duty selected, thawed, and issued two units of group O instead of AB or A as a universal plasma component. The alert flag to give universal components was shown but not acted upon. Both units were collected and transfused with no reported harm to the patient.

This case shows another example of LIMS warning flags and alerts being overridden. Critical LIMS flags should not be easily overridden and should require definitive action to overcome the influences of cognitive bias and alert fatigue. The laboratory has put in place a preventative action which now requires the BMS to enter a comment in the alert when it is displayed to acknowledge that the flag has been seen. This should be made a mandatory requirement of LIMS providers when building systems for laboratories. Distractions during critical transfusion processes are dangerous. Workspaces should

be designed in a manner that reduces distractions in safety critical steps.

These cases demonstrate the influence laboratory decision making can have on clinical care. All appropriate information should be contained in a clear SOP, however if staff are in doubt and cannot locate the appropriate information in a SOP, then appropriate escalation measures must be in place, in accordance with UKTLC standards (UKTLC Chaffe et al. 2014). Laboratories should foster a collaborative culture and encourage asking the appropriate person for advice when required as these decisions could impact a patient's safety.

Component labelling, availability and HSE n=238 (146 transfused errors and 92 near misses)

This is the last point where the component is under the control and care of the laboratory and should be treated as a critical safety step. Most errors at this step were HSE, such as cold chain errors.

Learning points

- Laboratory staff should stop and objectively review all component labelling prior to release to the clinical area. Never assume, and always check previous steps have been performed correctly
- Consideration should be made to ensure the labelling process is robust with appropriate checks as required to ensure the correct label is on the component pack
- Information technology (IT) solutions for label verification should be used wherever possible

Further laboratory learning

Rapidly changing workforce

The UKTLC survey (UKTLC 2019) showed that 28% of laboratories did not have the adequate staffing levels to fulfill capacity plans, approximtely 50% of responding laboratories carried vacancies and 79.4% of respondents were supporting trainees (in 16% of responses, >50% of staff required training). Whilst new staff are being recruited to these positions, many are trainees and cannot perform all tasks of registered and experienced staff. Continuity of service is required whilst training and supervising new recruits. Trainees require extra supervision and can increase the workload burden of experienced staff members. Once registered, these staff members are still relatively inexperienced, must be supported whilst gaining experience from practice and must have access to specialist support.

A total of 102/439 (23.2%) reports received involved a member of staff who was lone working. As the majority of work occurs during core hours, this figure is disproportionately high. Staff should feel empowered to raise concerns if they do not have sufficient training, knowledge, and skills to be working alone, and should never be allowed to work alone until they have passed a robust competency-assessment. The 2019 Annual SHOT Report suggested an UPTAKE model for competency-assessment, which remains a pertinent tool.

Please see additional case studies contained within supplementary information for this chapter (https://www.shotuk.org/shot-reports/report-summary-and-supplement-2020/), which reflect the effects of a rapidly changing workforce.

Handover in the laboratory

SHOT analysis of all laboratory incidents reported from 2015-2019 showed that 5.0% of incidents involved the handover process between members of staff and between shifts. Handover was found to be insufficient in 69.0%, no handover was documented in 26.9% of these. It is essential that accurate and timely information is communicated between members of staff to ensure continuity of care. This information should be written in a standardised format where possible to ensure clarity and limit any

interpretation errors. Structured, standardised communication methods overcome barriers and foster a safety culture. Communicating relevant information, focus on goals and actions and prioritising urgent needs is essential to reduce errors. Key questions to consider when developing handover procedures and quality improvement initiatives are:

- Who should be involved?
- When should it take place?
- Where should it occur?
- How should it happen?
- What needs to be handed over?
- Has this been appropriately actioned?

An example handover log is included in the supplementary material for this chapter, available on the SHOT website (https://www.shotuk.org/shot-reports/report-summary-and-supplement-2020/).

UK Transfusion Laboratory Collaborative (UKTLC): Culture Concerns

Author: Rashmi Rook, Chair UKTLC

SHOT have developed capacity plan guidance in conjunction with the UKTLC. This document should be used in conjunction with local process and can help provide a guide to developing a capacity plan which is line with UKTLC standards (see recommended resources section).

UK National External Quality Assessment Scheme (UK NEQAS)

Authors: Claire Whitham and Richard Haggis

The year 2020 certainly presented some unprecedented challenges on a global scale, and although the team at UK NEQAS Blood Transfusion Laboratory Practice felt the impacts of the pandemic, overall, the vast majority of the scheduled programme of EQA exercises were delivered, and our UK participants were able to test the samples and return results for analysis.

Participation in EQA offers the chance to learn from 'free lessons'; errors made during EQA exercises are those that can and do occur during clinical testing in the blood transfusion laboratory, and detection of these errors offers opportunities to improve. This is especially relevant during occasions when there are unusual pressures placed upon laboratories, such as the necessary additional precautions and re-prioritised workload that a pandemic naturally causes.

An examination of the errors that occurred during EQA testing during 2020 has shown that procedural errors, such as inadequate sample identification, sample transposition, result transcription and/or transposition, continue to cause the most problems for laboratories. Procedural errors occurred in all four of the 'R' exercises, and in five out of the six 'E' pre-transfusion testing exercises distributed during 2020. Learning points from these errors have centred on the need to confirm the identity of all samples before testing. For clinical samples, this requires a full check of the patient demographic details to ensure that results are assigned to the correct patient; EQA samples need to be subject to the same process, with a check of the patient number and exercise code on each sample. In crossmatching, a number of errors have been related to using the wrong samples for testing. The risks associated with using the wrong samples or assigning the wrong donors to a crossmatch are increased if more than one patient is crossmatched simultaneously. To reduce the potential for procedural errors it is advisable that crossmatching is only performed on one patient at a time. When entering data for EQA samples it is important to check that the data is recorded and transcribed against the correct patient or donor; this also applies to the data entry of results of manual testing into a LIMS.

The DAT programme became a full EQA scheme at the end of 2020. An examination of the errors has shown that there continues to be a failure of some laboratories to apply the manufacturers recommended interpretation when the internal inert control shows a positive reaction. For laboratories using automated technologies, any issues relating to the appearance of false positive reactions in an internal inert control should be referred to the supplier.

Conclusion related to laboratory reports

The overall themes seen in laboratory errors remain similar to previous years, however the impact of IT is even more pronounced. Implementation of flags and rules with the appropriate requirements for override could have prevented ABOi transfusions and would have vastly reduced the number of components provided to patients where testing was incomplete. These errors are compounded by staff performing workarounds and not following specified procedures when faced with staffing challenges and often working autonomously with very little experience. As a new generation of less experienced staff is welcomed into the laboratory, it is essential that the training provided to these individuals provides a safe and strong foundation which can then be built upon to create the expert scientists of the future. Long term fixes are needed for many of these highlighted problems, which may seem disheartening to those working within laboratories. It is essential that the contributing factors are recorded within incident investigation even if they cannot be immediately addressed, to provide evidence of deficiencies that can be trended and escalated frequently and consistently.

A detailed analysis and commentary on MHRA data can be found in Chapter 26, Medicines and Healthcare products Regulatory Agency Report.

Recommended resources

The UKTLC capacity plan guidance
https://www.shotuk.org/resources/current-resources/uktlc/

An example handover document
https://www.shotuk.org/shot-reports/report-summary-and-supplement-2020/

ABO-incompatible transfusions video
Laboratory errors video
https://www.shotuk.org/resources/current-resources/videos/

SHOT Bite No. 18: Transfusion errors in haemopoietic stem cell transplant patients
https://www.shotuk.org/resources/current-resources/shot-bites/

Blood Assist - a blood administration safety app developed by the Patient Blood Management team at NHS Blood and Transplant.
Apple (https://apps.apple.com/gb/app/blood-assist/id1550911130)
Google play (https://play.google.com/store/apps/details?id=uk.nhsbt.bloodassist)
Web based (www.bloodassist.co.uk)

References

BSH Jones J, Ashford P, Asher D, et al. Guidelines for the specification, implementation and management of information technology (IT) systems in hospital transfusion laboratories (2017). https://b-s-h.org.uk/guidelines/guidelines/specification-implementation-and-management-of-information-technology-it-systems-in-hospital-transfusion-laboratories/ [accessed 04 May 2021].

BSH Milkins C, Berryman J, Cantwell C, et al. Guidelines for pre-transfusion compatibility procedures in blood transfusion laboratories. *Transfus Med* 2013;**23(1)**:3-35. http://onlinelibrary.wiley.com/doi/10.1111/j.1365-3148.2012.01199.x/full [accessed 25 March 2021].

BSH White, J Qureshi H, Massey E, et al. Guideline for blood grouping and red cell antibody testing in pregnancy. *Transfus Med* 2016;**26**:246-263. https://onlinelibrary.wiley.com/doi/epdf/10.1111/tme.12299 [accessed 28 April 2021].

Chaffe B, Glencross H, Jones J, et al. UK Transfusion Laboratory Collaborative: minimum standards for staff qualifications, training, competency and the use of information technology in hospital transfusion laboratories. *Transfus Med* 2014;**24(6)**:335-340.

Narayan S (Ed), Poles D, et al. on behalf of the Serious Hazards of Transfusion (SHOT) Steering Group. The 2019 Annual SHOT Report (2020). https://www.shotuk.org/shot-reports/ [accessed 28 April 2021].

UKTLC. United Kingdom Transfusion Laboratory Collaborative (UKTLC) Survey (2019) https://www.shotuk.org/wp-content/uploads/myimages/UKTLC-2019-summary-final.pdf [accessed 28 April 2021].

Errors Related to Information Technology (IT) 16

Authors: Jennifer Davies, Alistair McGrann and Megan Rowley

Definition:

This category includes transfusion adverse events that relate to laboratory information management systems (LIMS) as well as other information technology (IT) systems and related equipment used in the delivery of hospital transfusion services.

Cases selected include events where IT systems may have caused or contributed to the errors reported, where IT systems have been used incorrectly and includes cases where IT systems could have prevented errors but were not used. Where the corrective and preventive action suggested in response to errors included IT solutions, these have been included.

Key SHOT message

- Electronic blood management systems should now be a standard integral part of safe transfusion practice

Abbreviations used in this chapter

BSH	British Society for Haematology
DHSC	Department of Health and Social Care
EBMS	Electronic blood management system
EPR	Electronic patient record
FHIR	Fast Healthcare Interoperability Resources
IBMS	Institute of Biomedical Science
IT	Information technology
LIMS	Laboratory information management system
NBTC	National Blood Transfusion Committee
NHS	National Health Service
SCRIPT	SHOT UK Collaborative Reviewing and Reforming IT Processes in Transfusion

Recommendations

With respect to clinical and laboratory transfusion information technology (IT) systems, organisations should:

- Ensure laboratory and/or clinical input alongside IT department expertise in any procurement and implementation to ensure that the system is fit for purpose
- Configure IT systems to ensure they are used to their full potential according to local requirements
- Validate IT systems for safe use as well as compliance with regulatory and best practice guidance
- Consider the interoperability of IT systems involved in patient care as part of both the procurement and upgrade processes
- Ensure downtime processes and procedures are robust, accessible, and easy to implement

Action: Chief information officers, IT departments, transfusion IT subject matter experts, and transfusion leads

Introduction

This chapter focusses on two key themes. Firstly, the importance of the interoperability between IT systems used in clinical transfusion practice and secondly the progress made with the SCRIPT initiative. In addition, a new SHOT Bite (no.13) was published in August 2020 on Information Technology in Transfusion – Highlights and Lessons.

A discussion of how IT contributes to errors in clinical and laboratory transfusion practice can be found in the individual chapters as detailed in Table 16.1.

Table 16.1: IT error by main reporting category n=474, and near miss cases n=250

IT errors by reporting category		Discussed in chapter	Number of cases	Near miss cases
Incorrect blood component transfused (IBCT)	Wrong component transfused (WCT)	Chapter 10	50	72
	Wrong blood in tube (WBIT)*	Chapter 13a	-	23
	Specific requirements not met (SRNM)	Chapter 10	111	36
Near miss WBIT		-	-	23
Handling and storage errors (HSE)		Chapter 11	137	37
Right blood right patient (RBRP)		Chapter 14	116	58
Avoidable, delayed or under/overtransfusion (ADU)		Chapter 12	39	6
Miscellaneous		N/A	-	1
Sub-total		-	**453**	**233**
Adverse events related to anti-D immunoglobulin (Anti-D Ig)		Chapter 9	21	17
Total		-	**474**	**250**

** WBIT that have resulted in transfusion are included under IBCT-WCT*

Interoperability in transfusion IT systems

The provision of safe and appropriate blood transfusion requires effective, comprehensive, and timely communication of complex information. IT provides us with powerful tools to interrogate data and communicate information and the benefits of this power have led to IT permeating all aspects of daily life.

We are all familiar with smartphone technology that is easy to use and saves time. Being aware of what IT *can do* makes our experience of what it *does do* in healthcare so jarring. It also makes the decision by reporters as to which SHOT-reportable errors are IT related fascinating; if every error in transfusion can be ascribed in part to IT systems, either through their commission or theoretical omission, then the selection of a particular case tells us a great deal about professional expectations of what IT systems *should do.*

We continue to learn that the lack of interoperability between the myriad IT systems involved in patient care is greatly limiting the potential of IT systems to deliver on their promise of enhancing the quality and safety of transfusion practice. Such interoperability must be meaningful. Terms relating to interoperability are explained below.

Technical interoperability – the ability to move data electronically from one system to another - reduces transcription error which, as with other manual steps, is identified as a major source of error (Benson 2016). It is, however, not enough to realise the full potential of IT.

Semantic interoperability - wherein the context and meaning of data is understood between IT systems – provides a great opportunity for error reduction (Arvanitis 2014). To give two theoretical examples which go beyond current functionality but would enhance patient safety; data on fludarabine prescription contained within an electronic chemotherapy prescribing system could be sent to the transfusion LIMS and be understood to require the insertion of an irradiated blood component flag; a Wi-Fi connected infusion pump could stop transfusion of a blood component if the cold chain data or sample validity indicated the unit to have expired.

IT-related error reports demonstrate that healthcare professionals have an expectation of this degree of interoperability but that it is rarely achieved. The problem is complex and difficult and will require the convergence of political, organisational, technical, and cultural solutions.

Interoperability is a clear goal for the UK. The DHSC England policy paper - The future of healthcare: our vision for digital, data and technology in health and care was published in 2018 (DHSC 2018). The Scottish Government have also produced a digital strategy (Scottish Government 2018), Wales have produced the Written Statement: Digital Health and Care Wales (2021) and Ireland have produced an eHealth strategy (Government of Ireland 2020). Innovation in transfusion IT should be aligned in this political direction.

The constraints and challenges posed by the COVID-19 pandemic have accelerated the need for widespread technology adoption over very short periods of time. The clear need and urgency of the situation have shown that healthcare staff can adapt quickly when the benefit is sufficiently clear. This past year has taught us that rapid cultural and organisational change has proved possible and the technical potential offered by the FHIR standard, if widely adopted, could give traction on the previously intractable challenge of achieving meaningful interoperability. Fast Healthcare Interoperability Resources (FHIR) is the global industry standard for passing healthcare data between systems. It is free, open, and designed to be quick to learn and implement (https://fhir.nhs.uk/).

SHOT UK Collaborative Reviewing and Reforming IT Processes in Transfusion (SCRIPT)

The SCRIPT group was formed initially comprising of the laboratory and IT SHOT working expert group members, to begin a constructive dialogue between transfusion departments and IT providers, as well as identifying the support required by transfusion experts to harness the opportunity of IT systems to improve patient safety. An early goal was to agree minimal standards for LIMS that support safe practice and to explore options for interoperability with other clinical systems that may provide safer practices.

To identify the requirements of clinical and laboratory transfusion professionals SHOT designed and distributed a survey to all registered reporters via email. The aim was to understand which IT systems relating to blood transfusion are in use throughout the UK. The survey has provided valuable information on the scope, as well as the successes and challenges of these systems and will be used to plan and prioritise the work of the SCRIPT group going forwards.

Responses received from NHS and private organisations represent a wide range of blood usage and, in addition to laboratory information management systems, information has been provided on clinical EBMS, electronic blood ordering and prescribing systems, electronic temperature monitoring systems for blood storage devices, and other systems used for medications, chemotherapy and vital observations.

The full results of the survey are available on the SHOT website and the key highlights and important messages are summarised below.

- There was a general lack of knowledge regarding electronic systems in use within the hospital and some respondents were unaware how blood components were authorised and/or prescribed. There appears to be a lack of an electronic systems forum, or group, within organisations where implementation of systems that may be interconnected can be discussed. Potential for interoperability and improvements to transfusion safety may be missed in the absence of such a group. For example, interaction between chemotherapy prescribing systems and LIMS as described earlier in this chapter. Fully integrated systems, such as EPR systems may provide safety checks at every point of the transfusion pathway
- There is a clear deficiency in the use of electronic systems for blood component prescribing compared to the use of systems for chemotherapy, medications, and clinical observations. Electronic ordering, clinical decision support and prescribing of blood components is accessible with fully integrated EPR systems, but these were only available for 26.7% of respondents. Alignment of transfusion systems with other electronic systems may bridge this digital gap for organisations that do not have EPR implemented

- Upgrades to LIMS are often not implemented by laboratories due to financial or time constraints. Opportunities for safety improvements are being missed if upgrades are not applied to the system. Upgrades provide resolution to deficiencies noted by other users and will increase safety and functionality of the system
- Many respondents indicated a desire for greater transparency and support from the IT providers. The relationship between users and suppliers is critical in ensuring that systems are functional, updated, supported and that deficiencies can be identified and resolved in a timely fashion
- Despite the clear evidence for patient safety provided by EBMS, 43% of respondents have not implemented a system. The majority of those that had implemented EBMS included blood refrigerator controls, but less than 30% had full vein-to-vein functionality. Blood refrigerator controls have a clear impact on the safety of collection of components, but bedside functionality is vital to reducing errors that occur at the administration stage
- A clear need for training and resources to support IT experts in transfusion was noted. The functionality of transfusion LIMS is complex compared to other pathology LIMS and needs subject matter experts with knowledge of IT and transfusion. Such experts are critical to bridge the gap between clinical and IT staff and to provide expert advice during the implementation of large projects such as the procurement and implementation of an EPR. The continuous change and improvements in national transfusion practice requires responsive IT development to stay current
- National standards for transfusion LIMS are required to ensure that all systems operate to the same level of safety and functionality to reduce the risk of error. SHOT intends to collaborate with IT suppliers, BSH and NBTC to establish minimum standards for safe delivery of care and to explore support from the NHS Business Services Authority and NHS Digital

The SCRIPT group would like to thank those who responded to the survey, the responses will be used to progress the project. The SCRIPT project will continue with a survey of suppliers and the systems provided by them to support transfusion activities. A joint workshop for suppliers and users will be organised later in 2021 to review the responses to the surveys. The SCRIPT group will continue to collaborate with all key stakeholders to address the digital gaps identified in this initial survey. Updates from this work can be found on the SCRIPT page of the SHOT website (https://www.shotuk.org/resources/shot-surveys/).

Recommended resources

SHOT Bite No. 13 Information Technology in Transfusion
https://www.shotuk.org/resources/current-resources/shot-bites/

SCRIPT User Survey
https://www.shotuk.org/resources/shot-surveys/

Laboratory and IT webinar 2020
https://www.shotuk.org/resources/current-resources/webinars/

References

Benson T and Grieve G. (2016). Principles of health interoperability: SNOMED CT, HL7 and FHIR. 10.1007/978-3-319-30370-3.

Arvanitis TN. Semantic interoperability in healthcare. Stud Health Technol Inform. 2014;202:5-8. PMID: 25000001.

DHSC. Policy paper. The future of healthcare: our vision for digital, data and technology in health and care (2018). https://www.gov.uk/government/publications/the-future-of-healthcare-our-vision-for-digital-data-and-technology-in-health-and-care/the-future-of-healthcare-our-vision-for-digital-data-and-technology-in-health-and-care [accessed 28 April 2021].

Scottish Government. Scotland's Digital Health and Care Strategy: enabling, connecting and empowering (2018). https://www.gov.scot/publications/scotlands-digital-health-care-strategy-enabling-connecting-empowering/ [accessed 28 April 2021].

Welsh Government. Written Statement: Digital Health and Care Wales (2021). https://gov.wales/written-statement-digital-health-and-care-wales-0 [accessed 28 April 2021].

Government of Ireland. eHealth Strategy for Ireland (2020). https://www.gov.ie/en/publication/6b7909-ehealth-strategy-for-ireland/ [accessed 28 April 2021].


LEARNING
LEARNING
TEAM
TEAM

REACTIONS IN PATIENTS

17 Febrile, Allergic and Hypotensive Reactions (FAHR) n=321

Authors: Janet Birchall, Jayne Peters and Catherine Booth

Definition:

The reactions assessed are isolated febrile-type (not associated with other specific reaction categories), allergic and hypotensive reactions occurring up to 24 hours following a transfusion of blood or components, for which no other obvious cause is evident.

Key SHOT messages

- When assessing a patient having a transfusion reaction, staff must use the symptoms and signs to classify the reaction type. This is fundamental to providing the correct treatment, both immediately and in future transfusion episodes. Training should emphasise that 'reaction to transfusion' is not a single diagnosis requiring a uniform standard treatment
- For febrile reactions alone, give paracetamol. If anaphylaxis is suspected, give adrenaline; for less severe allergic reactions, give antihistamine first line. The effect of steroids is delayed by several hours, will have no immediate effect, and should only be used to prevent a late recurrence. The use of steroids may further immunosuppress already immunocompromised patients and increase the risk of side effects such as infection
- Reporters are informed if SHOT experts change the reaction classification submitted. Such a process allows challenge, learning and a more skilled work force within hospitals to improve both the understanding and management of patients experiencing reactions

Abbreviations used in this chapter

AML	Acute myeloid leukaemia
BSH	British Society for Haematology
CCP	COVID-19 convalescent plasma
DHSC	Department of Health and Social Care
FAHR	Febrile, allergic and hypotensive reactions
FFP	Fresh frozen plasma
HLA	Human leucocyte antigen
HTR	Haemolytic transfusion reaction
HTT	Hospital transfusion teams
IHN	International Haemovigilance Network
ISBT	International Society for Blood Transfusion
IV	Intravenous
MB	Methylene blue treated
MDS	Myelodysplastic syndrome
PAS	Platelet additive solution
SABRE	Serious adverse blood reactions and events
SD	Solvent detergent treated
TACO	Transfusion-associated circulatory overload
TAD	Transfusion-associated dyspnoea
TRALI	Transfusion-related acute lung injury
TTI	Transfusion-transmitted infection
vCJD	variant Creutzfeldt–Jakob disease

Key recommendations

- Pooled platelets suspended in platelet additive solution (PAS) are associated with a reduction in allergic response (BSH Estcourt et al. 2017). Hospitals should consider preferential use of readily available pooled platelets suspended in PAS for patients with a history of allergic reactions. If reactions continue, despite antihistamine cover, then platelets re-suspended in 100% PAS can be supplied

Action: Hospital transfusion teams

- Give appropriate targeted treatment and if needed, preventative cover for future transfusion (BSH Tinegate et al. 2012), as indicated below:

Table 17.1: Targeted treatment for febrile and allergic transfusion reactions

Reaction	Treatment	Prevention of recurrent reactions
Febrile	Paracetamol	Paracetamol 60 minutes before anticipated time of reaction
Allergic	Antihistamine (steroid should not be used routinely) If anaphylaxis, adrenaline is essential	If previous reaction with apheresis platelets try pooled platelets in PAS; If reactions continue, give pre-transfusion antihistamine; If reactions continue, consider washed platelets/red cells; for FFP try a pooled component e.g. solvent-detergent treated plasma

Action: HTT and clinical staff managing patients receiving transfusions

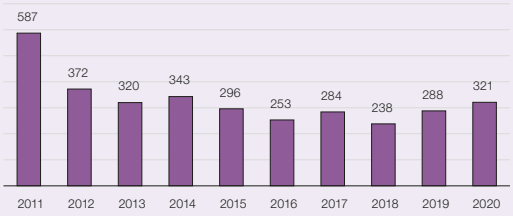
These recommendations have not changed in recent years and remain pertinent. They should be incorporated into hospital policies and routine practices.

For previous recommendations in full, see https://www.shotuk.org/shot-reports/previous-recommendations/

Headline data 2020

Number of reports n=321
Deaths n=0
Major morbidity n=80

FAHR reports by year



Demographic data

Male n=167
Female n=154
Adults n=267
Paediatric n=54

Blood component data

Red cells n=165
Platelets n=112
Plasma n=28
Multiple Components n=13
Granulocytes n=3

Introduction

Reactions are classified according to the ISBT/IHN definitions, which are summarised below in Table 17.2. These are also available online (ISBT/IHN 2011) and have been adopted by the BSH (BSH Tinegate et al. 2012).

Table 17.2: Classification of reactions

	1 = Mild	2 = Moderate	3 = Severe
Febrile-type reaction	A temperature ≥38°C and a rise between 1 and 2°C from pre-transfusion values, but no other symptoms/signs	A rise in temperature of 2°C or more, or fever 39°C or over and/or rigors, chills, other inflammatory symptoms/signs such as myalgia or nausea which precipitate stopping the transfusion	A rise in temperature of 2°C or more, and/or rigors, chills, or fever 39°C or over, or other inflammatory symptoms/signs such as myalgia or nausea which precipitate stopping the transfusion, prompt medical review AND/OR directly results in, or prolongs hospital stay
Allergic type reaction	Transient flushing, urticaria or rash	Wheeze or angioedema with or without flushing/urticaria/rash but without respiratory compromise or hypotension	Bronchospasm, stridor, angioedema or circulatory problems which require urgent medical intervention AND/OR, directly result in or prolong hospital stay, or **anaphylaxis** (severe, life-threatening, generalised or systemic hypersensitivity reaction with rapidly developing airway and/or breathing and/or circulation problems, usually associated with skin and mucosal changes)
Reaction with both allergic and febrile features	Features of mild febrile **and** mild allergic reactions	Features of both allergic and febrile reactions, at least one of which is in the moderate category	Features of both allergic and febrile reactions, at least one of which is in the severe category
Hypotensive reaction		Isolated fall in systolic blood pressure of 30 mmHg or more occurring during or within one hour of completing transfusion **and** a systolic blood pressure 80 mmHg or less in the absence of allergic or anaphylactic symptoms. No/minor intervention required	Hypotension, as previously defined, leading to shock (e.g. acidaemia, impairment of vital organ function) without allergic or inflammatory symptoms. Urgent medical intervention required

Total number of FAHR reactions n=321

The number of reactions reported represents an 11% increase over last year and the highest number reported for several years. This is remarkable given the decline in blood use in 2020 caused by the COVID-19 pandemic.

Deaths n=0

There were no deaths related to FAHR reactions reported in 2020.

Major morbidity n=80

The ISBT/IHN classification of a severe reaction has been used to define major morbidity.

Reactions are categorised in Table 17.3.

Table 17.3: Classification of FAHR in 2020

	Moderate	Severe	Total
Febrile	145	21	**166**
Allergic	65	54	**119**
Mixed allergic/febrile	23	4	**27**
Hypotensive	8	1	**9**
Total	**241**	**80**	**321**

NB: in 20 of the 80 reactions classified as severe this was primarily because the patient was admitted/kept in overnight

There were 469 cases initially reported as FAHR with 133 cases withdrawn and 15 transferred to other categories, leaving 321 for analysis. Of the withdrawn cases, 81/133 (60.9%) were withdrawn where 'mild' appears in the 'reason for withdrawal'. Mild reactions have not been reportable to SHOT since 2012. In 136/321 (42.4%) of FAHR cases, the type of reaction stated was reclassified according to the information provided (Table 17.4). This was communicated back to the reporter. The percentage of

severe reactions remains similar to previous years (80/321, 24.9%). Many, largely febrile-type, reactions continue to be difficult to classify because of insufficient information, the ISBT/IHN grade of reaction not being used and because of the difficulty in distinguishing true transfusion reactions from symptoms and signs associated with the patient's underlying condition.

Table 17.4: Reclassification of FAHR in 2020

		Confirmed FAHR category			
		Anaphylaxis/allergic	Febrile	Mixed febrile/allergic	Hypotensive
Reported category on SABRE	Anaphylaxis/allergic	74	16	9	1
	Febrile	2	96	3	-
	Mixed febrile/allergic	17	15	8	-
	Hypotensive	12	6	1	7
	Other / FAHR	6	15	1	-
	Other	4	9	4	1
	Other / TRALI	2	-	-	-
	Other / TACO	-	1	-	-
	Other / TAD	1	-	-	-
	Other / HTR	1	2	-	-
	TTI	-	6	1	-
	Total	**119**	**166**	**27**	**9**

Correct category	**185**	**(57.6%)**
Changed category	**136**	**(42.4%)**

Hyperacute reactions n=0

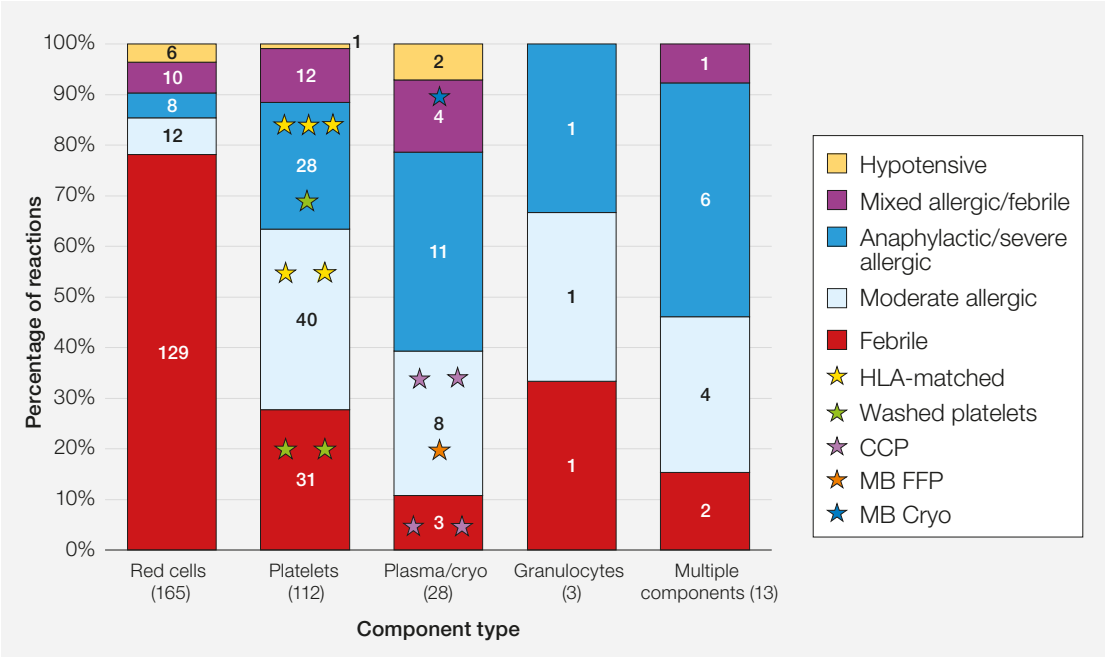
There were no allergic, febrile, or hypotensive cases clearly associated with IgA deficiency in 2020.

Type of reactions by component

This remains similar to previous Annual SHOT Reports; see Figure 17.1. Red cells are usually associated with febrile-type reactions (129/165, 78.2%) whereas plasma components and platelets more commonly cause allergic reactions (19/28 (67.9%) and 68/112 (60.7%) respectively). There were 4 reactions reported with the use of CCP, 1 with MB-FFP and 1 with MB-cryoprecipitate. None were associated with SD-FFP.

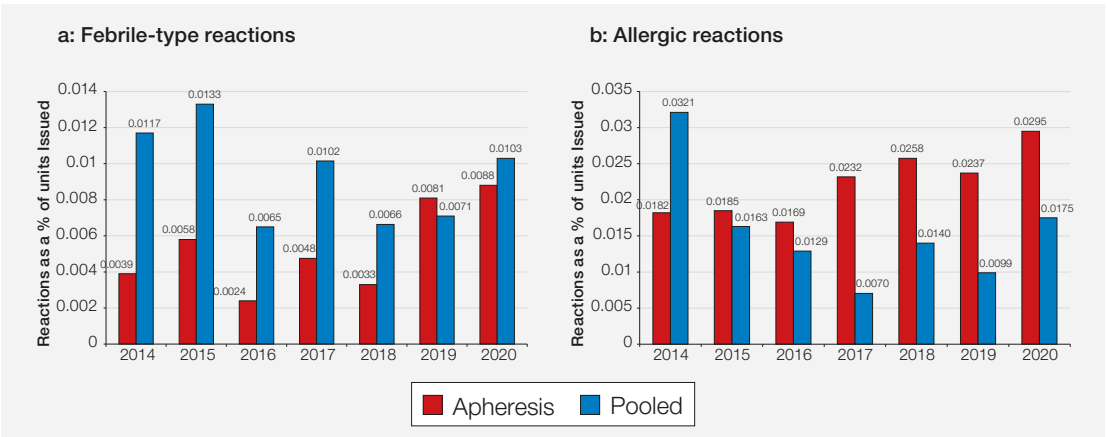
When FAHR reactions occur following transfusion of a single component unit, reporters are asked to provide the expiry date of the transfused unit. Analysis was limited to red cell and platelet units as plasma is usually stored frozen. Reactions were seen in 67/98 (68.4%) transfusions of red cells with less than 20 days' shelf life and in 52/75 (69.3%) transfusions of platelets with less than 3 days' shelf life. There was no obvious difference if allergic reactions and febrile reactions were considered separately. It is accepted that until data on the age of blood at the time of use is available for all transfusions, this may simply reflect that the majority of units are given towards the end of shelf life.

Figure 17.1: Reactions by component type



The incidence of allergic reactions linked to pooled platelets (suspended in PAS) continues to be lower than the incidence of allergic reactions linked to apheresis platelets and, as previously reported, this is likely to be associated with the reduction in plasma content. There remains little difference in the incidence of febrile reactions with pooled platelets compared to apheresis. Overall, there were fewer reactions (allergic and febrile reactions combined) reported with pooled platelets than apheresis platelets (0.03% [35/125715] and 0.04% [52/135776] respectively) and the incidence remains consistent. Reactions to platelets are partly caused by release of substances from the platelets themselves and therefore cannot be completely eliminated (Garraud et al. 2016, Maurer-Spurej et al. 2016). (Figures 17.2).

Figures 17.2: Percentage of reactions to apheresis and pooled platelets 2014 to 2020



Analysis of reactions remains comparable to previous years in the following characteristics (Table 17.5).

Table 17.5: Characteristics of FAHR

Recipient or transfusion characteristic	Percentage
Age distribution	83% of patients were aged 18 years or over
Gender	52% male and 48% female cases
Urgency of transfusion	*63% were given routinely
Timing of transfusion	^67% occurred within standard hours
Location	59% were on wards and 15% in outpatient/day case units

**Lower % of cases than in previous years likely associated with more cases reported as unknown*

^Higher % of cases than last year likely associated with fewer cases reported as unknown

Treatment of reactions

An antihistamine with or without steroid continues to be used inappropriately to treat reactions with only febrile/inflammatory type symptoms and/or signs; see Table 17.6. In addition to no evidence of benefit, the use of steroids may further immunosuppress already immunocompromised patients and increase the risk of side effects such as infection.

Year	Number	Medication stated	Antihistamine and/or steroid
2020	166	140/166 (84.3%)	58/140 (41.4%)
2019	146	130/146 (89.0%)	62/130 (47.7%)
2018	103	88/103 (85.4%)	39/88 (44.3%)
2017	140	121/140 (86.4%)	46/121 (38.0%)
2016	124	102/124 (82.3%)	51/102 (50.0%)
2015	142	101/142 (71.1%)	57/101 (56.4%)
2014	144	97/144 (67.4%)	42/97 (43.3%)

Table 17.6: Treatment of reported febrile reactions

Subsequent management

The prophylactic use of antihistamine with or without steroids to treat a subsequent purely febrile reaction appears to be reducing, although this data was not available in most cases (the single largest management category included treatment not stated or 'premedication'). Across both febrile and allergic reaction categories avoidance of transfusion was advised by some reporters and included: the cessation of routine platelet transfusions (n=2), 'only transfuse where necessary' (n=1), limit transfusion to 1 unit/day (n=1) and use of intravenous iron (n=2) (Table 17.7).

Year	Number where treatment stated	Antihistamine and/or steroid stated
2020	33	7/33 (21.2%)
2019	42	7/42 (16.7%)
2018	27	8/27 (29.6%)
2017	22	5/22 (22.7%)
2016	21	9/21 (42.9%)
2015	9	7/9 (77.8%)
2014	24	9/24 (37.5%)

Table 17.7: Planned treatment of subsequent febrile reactions

Illustrative cases

Cases managed generically as 'transfusion reactions' illustrate a failure to correctly classify the reaction and appropriately treat potentially serious causes.

Case 17.1: Inappropriate treatment of a febrile reaction

A patient in his 50s with AML attended the haematology day unit for a routine platelet transfusion. On completion he developed rigors, fever, and breathlessness. His temperature rose to 40.1°C from a baseline of 37.4°C and oxygen saturations fell to 94% on oxygen. He was given IV hydrocortisone and antihistamine with little effect. He was subsequently administered 1mg adrenaline, 4.5g piperacillin with tazobactam (tazocin) (antibiotic) IV, 1g paracetamol and IV fluids. His symptoms settled over the following hour, but he was admitted for observation. Blood cultures were negative and there was no rise in mast cell tryptase.

There were no clinical features in this case to suggest an allergic reaction. The range of treatments he received illustrates a failure to attempt to classify the reaction type, with possible delay in treating the most serious potential cause of this presentation – which in an immunocompromised patient would be infection (related or unrelated to transfusion). Adrenaline and hydrocortisone may be harmful in this scenario.

Case 17.2: Inappropriate treatment in the presence of a potential haemolytic transfusion reaction

A lady in her 70s with MDS and known alloantibodies attended for a scheduled two-unit blood transfusion. The units had been crossmatched at the reference laboratory due to slight reaction on crossmatch when performed in-house. Halfway through the second unit the patient developed rigors, a rise in temperature (38.4°C from baseline 37.7°C) and elevated blood pressure (130/60 to 167/88 mmHg). The nurse stopped the transfusion and asked for medical review. The registrar prescribed 10mg antihistamine and 100mg hydrocortisone and told the nurse to continue the transfusion in 30 minutes. However, the patient's symptoms worsened, and she complained of pain in her kidneys. She was given a further 100mg hydrocortisone and 1g paracetamol. Her symptoms resolved within a few hours. Samples sent for serological investigation revealed no evidence of a haemolytic transfusion reaction.

Here again hydrocortisone and antihistamine were used despite no symptoms of allergy. The use of empirical treatment suggests initial medical assessment failed to consider the possibility of a haemolytic transfusion reaction. This would have been the most serious differential to exclude, given the history of alloantibodies and concern about a reactive crossmatch. Even for an allergic reaction, there is never any rationale for giving a second dose of hydrocortisone in short succession, as this drug takes several hours to act.

Appropriate clinical assessment and management of a febrile reaction may allow a necessary transfusion to safely continue, without unnecessary interventions.

Case 17.3: Appropriate treatment

A man in his 20s who had suffered polytrauma received a postoperative blood transfusion. After 30 minutes, routine observations revealed a temperature rise from 37.6 to 39°C. He was treated with IV paracetamol and transfusion was continued. His temperature continued to reduce until returning to baseline around 12 hours post transfusion.

Conclusion

Over 40% of cases reported in this chapter were re-classified according to the information provided and similarly, when medication was stated over 40% of purely febrile reactions were given an antihistamine and/or a steroid. The key messages this year remain that; firstly, there is a need to differentiate the symptoms and signs of the separate reaction types, secondly a pure allergic reaction is not associated with fever, and thirdly treatment with an antihistamine and/or steroid should be limited to those with allergic features. It is recognised that in a sick patient with acute symptoms, it is not always easy to separate different reaction types at the time. It is encouraging to note that there is a downward trend in inappropriate antihistamine/steroid use, when future medication was stated for reactions classified as purely febrile (since 2014).

The incidence of allergic reactions due to apheresis platelets compared to pooled platelets (suspended in PAS) remains higher. Following publication of the Department of Health and Social Care document 'Risk assessment of the transmission of variant Creutzfeldt–Jakob disease (vCJD) by blood components' apheresis platelets are no longer preferentially recommended for patients born from 1996 (DHSC 2019).

Recommended resources

Resuscitation Council (2008) Emergency treatment of anaphylactic reactions
http://www.resus.org.uk/pages/reaction.pdf

NHSBT (2015/16) Histocompatibility and Immunogenetics diagnostic services user guide
http://hospital.blood.co.uk/diagnostic-services/diagnostic-user-guides/

Choosing Wisely UK (2018) Royal College of Pathologists (2018) Recommendation 3
https://www.choosingwisely.co.uk/i-am-a-clinician/recommendations/#1572879057348-632f8063-b7b4

References

BSH Estcourt LJ, Birchall J, Allard S, et al. Guidelines for the use of platelet transfusions. *Br J Haematol* 2017;**176(3)**:365-394.

BSH Tinegate H, Birchall J, Gray A, et al. Guideline on the investigation and management of acute transfusion reactions. Prepared by the BCSH Blood Transfusion Task Force. *Br J Haematol* 2012;**159(2)**:143-153.

DHSC. vCJD transmission by blood components: risk assessment (2019). https://www.gov.uk/government/publications/vcjd-transmission-by-blood-components-risk-assessment [accessed 28 April 2021].

Garraud O, Tariket S, Sut C, et al. Transfusion as an Inflammation Hit: Knowns and Unknowns. *Front Immunol* 2016;**7**:534.

ISBT/IHN. Haemovigilance Working Party of the ISBT: Proposed standard definitions for surveillance of non-infectious adverse transfusion reactions (2011). http://www.isbtweb.org/fileadmin/user_upload/Proposed_definitions_2011_surveillance_non_infectious_adverse_reactions_haemovigilance_incl_TRALI_correction_2013.pdf [accessed 28 April 2021].

Maurer-Spurej E, Larsen R, Labrie A, et al. (2016) Microparticle content of platelet concentrates is predicted by donor microparticles and is altered by production methods and stress. *Transfus Apher Sci* 2016;**55(1)**:35-43.

18 Pulmonary Complications n=188

Author: Shruthi Narayan with contributions from members of the pulmonary Working Expert Group (WEG)

Key SHOT messages

- Pulmonary complications of transfusion remain a leading cause of transfusion-related mortality and morbidity, contributing to 65.9% of transfusion-related deaths reported to SHOT from 2010 to 2020

Abbreviations used in this chapter

ADU	Avoidable, delayed and under/overtransfusion	**NM**	Near miss
ALICT	Acute lung injury caused by transfusion	**TACO**	Transfusion-associated circulatory overload
ARDS	Acute respiratory distress syndrome	**TAD**	Transfusion-associated dyspnoea
FAHR	Febrile, allergic and hypotensive reactions	**TRALI**	Transfusion-related acute lung injury
HTR	Haemolytic transfusion reactions	**UCT**	Uncommon complications of transfusion
NBTC	National Blood Transfusion Committee	**WEG**	Working Expert Group

Recommendations

- All cases with pulmonary complications occurring during or up to 24 hours post transfusion should be reported to SHOT with as much information as possible, to ensure adequate inference and effective learning. The clinical status (especially cardiac, respiratory status and other significant co-morbidities) of the patients prior to the transfusion episode helps in understanding the pulmonary reaction and contributing factors and should be included in the submitted reports

Action: All SHOT reporters, hospital transfusion teams

- A transfusion-associated circulatory overload (TACO) checklist should be utilised whenever possible prior to every transfusion, especially in vulnerable patients. This would also help provide further insight into cases reported as transfusion-associated dyspnoea (TAD) or transfusion-related acute lung injury (TRALI)

Action: All clinical staff involved in transfusion

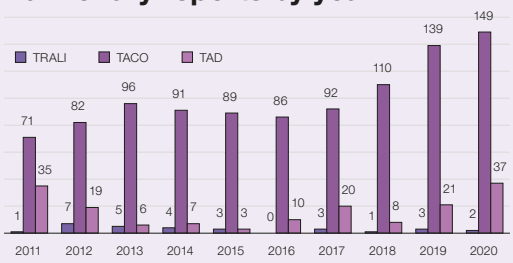
- A thorough post-event investigation should be carried out in all cases with severe complications following transfusion to identify improvements locally with respect to identification and mitigation of risks, patient monitoring and management

Action: All staff involved in investigation of transfusion incidents

Headline data 2020

Number of reports n=188
Deaths n=23
Major morbidity n=33

Pulmonary reports by year



Demographic data

Male n=91
Female n=97
Adults n=185
Paediatric n=3

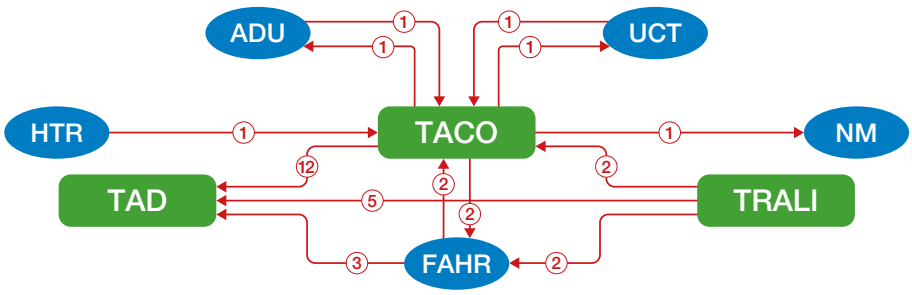
Blood component data

Red cells n=154
Platelets n=6
Plasma n=13
Multiple Components n=15
Other n=0

Introduction

Pulmonary complications continue to be the leading cause of transfusion-related mortality and morbidity, contributing to 114/173 (65.9%) of transfusion-related deaths reported to SHOT from 2010 to 2020. The total number of cases continue to increase year on year and in 2020, 188 reports were analysed under the 'pulmonary complications' categories. Three of the cases in 2020 were in children and pulmonary complications contributed to 23 deaths and 33 cases of major morbidity. These are discussed in detail in the respective chapters.

With sparse new evidence in relation to pulmonary complications post transfusion since the 2019 Annual SHOT Report, the categorisation of these reactions remains complex. There is ongoing international collaboration for harmonisation of definitions and data collection. The interpretation and categorisation of the cases remains challenging and is also limited by the available information included in the reports submitted to SHOT (clinical, radiological, and other investigations results). The respiratory and cardiovascular status of patients in the 12 hours prior to the transfusion episode helps in understanding the factors contributing to the patient's respiratory deterioration post transfusion but is often not available. Figure 18.1 shows the case transfers in 2020 when the SHOT WEG have reviewed all the cases submitted. This highlights the complexity and challenges in categorisation of pulmonary complications. Reporters are strongly encouraged to report all cases with respiratory deterioration up to 24 hours following transfusion. Focus must be placed on analysing the actual phenomena in these patients and what actions were performed to prevent reactions rather than trying to fit the clinical/radiological/laboratory picture into a single category. All relevant information must be included in the report to SHOT. The pulmonary WEG review the submitted cases, deliberate based on the information available and will assign the appropriate category.



TACO=transfusion-associated circulatory overload; TRALI=transfusion-related acute lung injury; TAD=transfusion-associated dyspnoea; HTR=haemolytic transfusion reactions; ADU=avoidable, delayed or under/overtransfusion; FAHR=febrile, allergic and hypotensive reactions; UCT=uncommon complications of transfusion; NM=near miss

Figure 18.1: Case transfers to and from the pulmonary categories in 2020 (n=34)

COVID-19 patients

A particular challenge faced by the pulmonary WEG members in 2020 was the interpretation of the clinical and radiological picture in patients with COVID-19 pneumonia who developed worsening respiratory status <24 hours after convalescent plasma administration under approved trials. Multiple factors could contribute to the deterioration in these patients, ranging from worsening of the COVID-19 pneumonitis (sudden respiratory deterioration with ARDS is well recognised in these patients), to other factors such as thromboembolism and cardiac effects of COVID-19. Secondary bacterial infections and other rare events such as pneumothorax and pneumomediastinum can also cause respiratory deterioration (Pooni et al. 2020). These cases are detailed further in the following chapters.

TRALI

The definition of TRALI continues to be under review. There were 2 confirmed cases of antibody-positive TRALI this year. The cases in this year's Annual SHOT Report are primarily classified using the SHOT nomenclature, which considers both the clinical history and the presence of leucocyte antibodies. In 2019, the consensus redefinition of TRALI (Vlaar et al. 2019) was proposed by an international working group which is more a clinical diagnosis not requiring the detection of cognate white cell antibodies making application of imputability from a haemovigilance perspective challenging.

It is imperative that the diagnosis of TRALI should not be applied loosely under different classification systems to refer to different entities. A new concept of 'acute lung injury caused by transfusion' (ALICT) has been proposed which could potentially be useful until the debate about terminology settles as it considers the aetiopathological and clinical elements of TRALI. ALICT as a concept refers to a reaction caused by something in the blood (which may include antibodies or other, perhaps undiscovered mediators). The relationships between the existing nomenclature/categories and the presence or absence of cognate antibodies has been explored further in the TRALI chapter. The authors hope that this helps define the questions for further research and validation.

TACO

The 2020 reporting year recorded 149 TACO cases which is the highest ever reported to SHOT. Cases were analysed using the same surveillance criteria as last year (Wiersum-Osselton et al. 2019). There continues to be suboptimal use of the pre-transfusion TACO risk assessment and weight-adjusted red cell dosing is not sufficiently implemented.

It is critically important that all TACO cases are used as a learning opportunity to prevent or mitigate TACO in other patients. A new recommendation for this year is the use of the TACO investigation and preventive action guidance tool, to ensure a structured and comprehensive review of cases to support effective preventive actions (see recommendations and recommended resources sections in Chapter 18b, Transfusion-Associated Circulatory Overload (TACO)).

TAD

TAD remains a diagnosis of exclusion and has no defining criteria. Some of the cases included as TAD had features suggestive of TACO or TRALI but due to insufficient information available to meet the SHOT criteria, have been included under TAD.

There is still much work that needs to be done to understand cases reported under TAD and this is limited by the clinical information available and co-morbidities. International collaborative work to help improve understanding of the epidemiology, pathophysiology in this group of complications is vital and will help identify risk factors and appropriate mitigating measures in the future.

Conclusion

TRALI, TACO and TAD are all potentially fatal complications of blood transfusion. The mechanisms for pulmonary deterioration in transfusion recipients are multifactorial and complex, involving both transfusion-specific and patient-specific factors. All staff dealing with transfusions must be vigilant for

these complications especially in vulnerable patients and must assess risk, initiate mitigating measures where possible and manage complications promptly. Thorough investigations of these complications will help identify any areas for improvement locally with respect to risk assessment of patients, clinical care provided and escalation policies.

Patients must be informed about these risks as part of their consent discussion. This is especially important in vulnerable patients with risk factors for pulmonary complications from transfusion. Patients having transfusions as day cases must receive information on when to seek urgent medical help, as these could be delayed and manifest when patients are back home after their transfusions. Blood components should be administered only after careful consideration of the risks of transfusion versus the potential physiologic benefit of the planned transfused blood component. Unnecessary blood transfusions must be avoided.

Work is ongoing to improve international harmonisation of the classification of pulmonary transfusion reactions, especially TRALI and TAD, to allow for uniform comparisons, improve understanding of these complications and enhance transfusion safety. An international collaborative including representatives from SHOT are working to develop a universal reporting form for respiratory transfusion reactions which will help to make comparisons of reaction rates between various haemovigilance systems.

Recommended resources

SHOT Bite No. 11: Respiratory symptoms during transfusion
https://www.shotuk.org/resources/current-resources/shot-bites/

SHOT educational video about pulmonary complications post transfusion
https://www.shotuk.org/resources/current-resources/videos/

References

Pooni R, Pandey G, Akbar S. Broadening the differential: pneumomediastinum and COVID-19 infection. *BMJ Case Reports CP* 2020;**13**:e237938.

Vlaar APJ, Toy P, Fung M, et al. A consensus redefinition of transfusion-related acute lung injury (TRALI). *Transfusion* 2019;**59**:2465-2476.

Wiersum-Osselton J, Whitaker BL, Grey S, et al. Revised international surveillance case definition of transfusion associated circulatory overload (TACO): a classification agreement validation study. *Lancet Haematol* 2019;**6(7)**:e350-e358. doi: 10.1016/S2352-3026(19)30080-8.

18a Transfusion-Related Acute Lung Injury (TRALI) n=2

Author: Tom Latham

Definition:

Transfusion-related acute lung injury (TRALI) is defined as acute dyspnoea with hypoxia and bilateral pulmonary infiltrates during or within 6 hours of transfusion, in the absence of circulatory overload or other likely causes, or in the presence of human leucocyte antigen (HLA) or human neutrophil antigen (HNA) antibodies cognate with the recipient.

Key SHOT message

- The definition of transfusion-related acute lung injury (TRALI) is currently under review. It is essential to be explicit about what is understood by the term 'TRALI' when comparing data and literature between different sources

Abbreviations used in this chapter

ALICT	Acute lung injury caused by transfusion	**HNA**	Human neutrophil antigen
ARDS	Acute respiratory distress syndrome	**IRC**	International revised consensus
CT	Computerised tomography	**LAH**	Left atrial hypertension
ECG	Electrocardiogram	**TACO**	Transfusion-associated circulatory overload
FAHR	Febrile, allergic and hypotensive reactions	**TAD**	Transfusion-associated dyspnoea
HLA	Human leucocyte antigen	**TRALI**	Transfusion-related acute lung injury

Recommendation

- Reporters should report all cases of suspected pulmonary complications. Cases should initially be reported using existing SHOT definitions and can be re-categorised by the SHOT experts if required

Action: All SHOT reporters

Introduction

There were 2 confirmed cases of antibody-positive TRALI. In total 16 cases were reported as suspected TRALI. Of these, 5 cases were transferred to TAD, 2 cases to TACO, 2 cases to FAHR and 5 were withdrawn.

The cases in this Annual SHOT Report are primarily classified using the SHOT nomenclature (Table 18a.1), which takes into account both the clinical history and the presence of leucocyte antibodies. In 2019, the consensus redefinition of TRALI (Vlaar et al. 2019) was proposed by an international working group, to which SHOT provided representation (Table 18a.2). This redefinition was intended to update the earlier Canadian Consensus criteria (Kleinman et al. 2004). An approximate mapping between the SHOT nomenclature and the redefinition is included in Table 18a.1.

Classification	Definition	Mapping to consensus redefinition
Highly likely	Cases with a convincing clinical picture and positive serology	TRALI type I + positive serology
Probable	Cases with positive serology but other coexisting morbidity which could independently cause acute lung injury or fluid overload	TRALI type II + positive serology
Equivocal	Cases with positive serology in the clear presence of lung injury due to other causes or fluid overload	ARDS or 'TRALI/TACO cannot be distinguished' + positive serology
Antibody-negative TRALI	Cases with a convincing clinical picture where serology is not available or negative	TRALI type I + absent or negative serology
Unlikely - reclassify as TAD	Cases where the history and serology were not supportive of the diagnosis. These cases are transferred to TAD	TRALI type II or 'TRALI/TACO cannot be distinguished' + negative or absent serology

Table 18a.1: SHOT criteria for assessment of TRALI cases

TRALI type I—Patients who have no risk factors for ARDS and meet the following criteria:

a. i. Acute onset
   ii. Hypoxemia (P/F ≤ 300* or SpO_2 < 90% on room air)
   iii. Clear evidence of bilateral pulmonary edema on imaging (e.g., chest radiograph, chest CT, or ultrasound)
   iv. No evidence of LAH† or, if LAH is present, it is judged to not be the main contributor to the hypoxemia
b. Onset during or within 6 hr of transfusion‡
c. No temporal relationship to an alternative risk factor for ARDS

TRALI type II—Patients who have risk factors for ARDS (but who have not been diagnosed with ARDS) or who have existing mild ARDS (P/F of 200-300), but whose respiratory status deteriorates§ and is judged to be due to transfusion based on:

a. Findings as described in categories a and b of TRALI Type I, and
b. Stable respiratory status in the 12 hr before transfusion

* If altitude is higher than 1000 m, the correction factor should be calculated as follows: [(P/F) × (barometric pressure/760)].
† Use objective evaluation when LAH is suspected (imaging, e.g., echocardiography, or invasive measurement using, e.g., pulmonary artery catheter).
‡ Onset of pulmonary symptoms (e.g., hypoxemia—lower P/F ratio or SpO_2) should be within 6 hours of end of transfusion. The additional findings needed to diagnose TRALI (pulmonary edema on a lung imaging study and determination of lack of substantial LAH) would ideally be available at the same time but could be documented up to 24 hours after TRALI onset.
§ Use P/F ratio deterioration along with other respiratory parameters and clinical judgment to determine progression from mild to moderate or severe ARDS. See conversion table in Appendix S2 to convert nasal O_2 supplementation to FiO_2.

Table 18a.2: Consensus redefinition criteria for TRALI

Table 2. New consensus TRALI definition from Vlaar et al. (2019)

Note: The P/F ratio equals the arterial pO2 ("P") from the ABG divided by the FIO2 ("F") – the fraction (percent) of inspired oxygen that the patient is receiving expressed as a decimal (40% oxygen = FIO2 of 0.40). SpO2 =oxygen saturation. O2 = oxygen. For information on appendix S2 see original paper by Vlaar et al. 2019.

Category	TRALI type I		TRALI type II	
	Antibody-positive	Antibody-negative	Antibody-positive	Antibody-negative
Highly likely	1	-	-	-
Probable	-	-	-	-
Equivocal	-	-	1	-
Antibody-negative	-	-	-	-

Table 18a.3: Summary of 2020 TRALI cases

Deaths n=1

Case 18a.1: Possible TRALI

A woman in her 80s was readmitted 4 hours after an outpatient two-unit red cell transfusion, with sudden onset of cough and breathlessness. Chest X-ray showed bilateral pulmonary oedema but also dense consolidation in the right upper lobe. A COVID-19 test was negative, and she had normal

C-reactive protein and ECG. She died on the night of admission. Investigation of donors showed a HNA 1b (auto)antibody in one donor which was cognate with the recipient however this was not detectable on the archive sample from the time of donation. The history appeared fairly classical, possibly with pneumonia acting as a 'first hit'. The case has been classified as 'TRALI type II' in the consensus redefinition due to the presence of another risk factor for lung injury (consolidation on chest X-ray). In the SHOT classification scheme the case has been classified as 'equivocal TRALI'. We are unable to exclude the pneumonia being the sole cause; the significance of the late detected antibody is unclear but should be considered as possibly causative given that it is not uncommon in other contexts, particularly neonatal alloimmune thrombocytopenia, for morbidity to occur with an antibody becoming subsequently detectable.

Major morbidity n=1

Case 18a.2: Highly likely TRALI

A dialysis-dependent man in his 70s received a two-unit transfusion while on dialysis, with fluid removal taking account of the transfusion volume. He developed acute pulmonary oedema around the time of the second unit. Fluid overload was suspected but he deteriorated following further ultrafiltration. Echocardiogram was normal. He improved after 24 hours of supportive care. Multiple HLA class I and class II antibodies cognate with the recipient were identified in the donor of the first unit. The features are consistent with a classical antibody-mediated TRALI, and thus has been classified as 'highly likely TRALI'. The case has been classified as 'TRALI type I' in the consensus redefinition schema because of the absence of other risk factors for acute lung injury.

Commentary

The pattern of cases reported as suspected TRALI this year is much the same as previous years. However, the understanding of what is meant by the term 'TRALI' is in a state of evolution in the light of the IRC definition of TRALI. International work is being performed to validate the IRC criteria; however, this has been slowed because of other priorities arising from the COVID-19 pandemic.

IRC (Table 18a.2) has not yet been universally implemented at an international level. It defines TRALI as an empirical syndrome of clinical features. This is a valid position to take, and a syndromic definition has the advantage of easy categorisation, cases either meet the criteria or do not. The IRC criteria do identify a recurrent pattern of pulmonary deterioration seen in association with transfusion, and thus a group of patients deserving analysis.

However, the informal usage of the term TRALI, for example the monitoring of TRALI cases as a performance indicator for Blood Services and the clinical requests for investigation 'to rule out TRALI', indicate that TRALI is commonly understood as implying a causative role for the transfused product. Causation is also implicit in the SHOT nomenclature which classifies cases as 'highly likely', 'probable', or 'equivocal' corresponding to the plausibility that the detected antibody caused the reaction. Additionally, the proposal by the IRC authors that 'in TRALI, the primary physiologic abnormality resulting in pulmonary oedema is an increase in capillary permeability.' This is certainly a valid viewpoint but perhaps extends the scope of TRALI, for example encompassing a recipient who is unable to tolerate the fluid load of the transfusion because of underlying sepsis. IRC thus represents a true redefinition rather than a simple refinement of criteria.

A concept of pulmonary complications based on causation remains useful to help identify appropriate risk-reduction strategies. Measures to prevent recurrent reactions due to leucocyte antibodies or other mediators in transfused components are distinct from identifying patients unable to tolerate fluid, as their underlying condition may affect endothelial permeability. It is currently impossible to provide objective criteria because of the multifactorial nature of pulmonary reactions with several possible contributing causes, and the absence of a gold standard diagnostic test. It is however possible to infer the plausibility that biologically active factors in the blood caused the reaction by taking in to account the clinical features and presence of leucocyte antibodies, in a similar manner to estimating imputability.

All classifications are artificial constructs, and thus their usefulness is context dependent. Haemovigilance systems need to classify adverse events into discrete categories which are internationally comparable,

so there is utility in strict empirical criteria. However, Blood Services need to be able to monitor the safety of products and have workable guidelines to identify which donors to investigate or defer, and for this purpose a classification based on the causative role of the product and the presence of antibodies is more useful. Treating clinicians need to understand what has caused adverse events in order to provide treatment and prevent adverse events in patients at risk, and also therefore have a need for a model based on causation, but with a wider scope than simply the transfused component.

What can be agreed is that it is unhelpful for different groups to use the same terminology to refer to different entities. Until universal definitions and criteria have been agreed, there may be value in specifying terminology to illustrate the concepts for these pulmonary reactions. One approach may be to use the nomenclature 'acute lung injury caused by transfusion' (ALICT) to refer to the concept of a reaction caused by something in the blood (which may include antibodies or other, perhaps undiscovered mediators).

The three related concepts suggested are as follows:

TRALI: *Hypoxaemia with clear evidence of bilateral pulmonary oedema on imaging and no evidence of left atrial hypertension, with onset within 6 hours of transfusion where the respiratory state has been stable in the 12 hours prior to transfusion.* This refers to the purely empirical clinical syndrome as defined by the IRC. Cases either meet or do not meet TRALI criteria, and therefore phrases such as 'probable TRALI' are no longer applicable.

Antibody-positive: *HLA or HNA antibodies are present in the donor of the transfused component which are cognate with the recipient*. This refers to objective presence or absence and carries no causative implication.

ALICT: *Acute lung injury caused by biologically-active agents in the transfused component.* This represents the 'causative/pathophysiological' concept understood by 'TRALI'. This cannot be objectively assigned but can be assigned a 'level of plausibility', similar to the current SHOT classification as 'highly likely, probable or equivocal,' taking into account all clinical and laboratory features of the case. The assignment of 'ALICT plausibility' is similar to the concept of imputability but is not identical because it excludes fluid in the transfusion as the causative principle.

Figure 18a.1 illustrates how these three concepts overlap. The intersection between all three categories 'classical antibody-mediated TRALI' is thus the common ground of understanding; the remainder of the diagram offers a model for defining the questions for further research and validation.

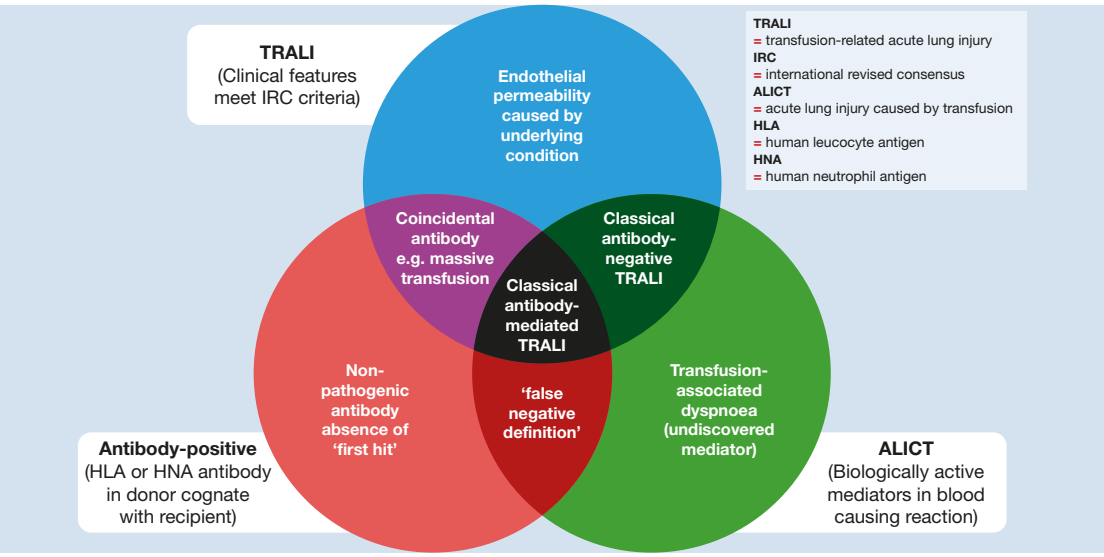


Figure 18a.1: Conceptual relationship between TRALI, ALICT and donor antibody

References

Vlaar APJ, Toy P, Fung M, et al. A consensus redefinition of transfusion-related acute lung injury (TRALI). *Transfusion* 2019;**59**:2465-2476.

Kleinman S, Caulfield T, Chan P, et al. Toward an understanding of transfusion-related acute lung injury: statement of a consensus panel. Transfusion. 2004;**44**:1774–1789.

18b Transfusion-Associated Circulatory Overload (TACO) n=149

Author: Sharran Grey

Definition:

TACO is defined as acute or worsening respiratory compromise and/or acute or worsening pulmonary oedema during or up to 12 hours† of transfusion, with additional features including cardiovascular system changes not explained by the patient's underlying medical condition; evidence of fluid overload and a relevant biomarker¥.

†SHOT accepts cases up to 24 hours
¥see Table 18b.2 for details of required and additional criteria for a surveillance diagnosis

Key SHOT message

- Patients who develop respiratory distress during or up to 24 hours following transfusion where transfusion is suspected to be the cause must be reported to SHOT. The transfusion-associated circulatory overload (TACO) definition criteria can be used as guidance, but this should not be restrictive. The SHOT Working Expert Group can transfer cases between categories

Abbreviations used in this chapter

Hb	Haemoglobin	**TACO**	Transfusion-associated circulatory overload
NT pro-BNP	N-terminal-pro B-type natriuretic peptide		

Recommendations

- A formal pre-transfusion risk assessment for transfusion-associated circulatory overload (TACO) should be undertaken whenever possible for all patients receiving blood transfusion (especially if older than 50 years or weighing less than 50kg) and mitigating actions taken, as TACO is the most commonly reported cause of transfusion-related mortality and major morbidity

Action: All staff authorising transfusions

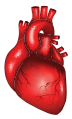
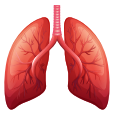
- A structured incident review should be undertaken for every case of TACO. This will ensure optimal organisational and individual patient safety measures are in place to protect patients from TACO as far as possible (see recommended resources)

Action: Trust/Health Board governance and clinical risk departments, all staff investigating transfusion incidents

- Weight-adjusted red cell dosing should be used to guide the appropriate volume required for all non-bleeding adult patients. Ideally tools which also highlight inappropriate transfusion should be used (Grey et al. 2018, NCA 2017)

Action: All staff authorising transfusions

The TACO pre-transfusion assessment infographic has been re-drafted as a checklist (Figure 18b.1) that can be incorporated as part of the transfusion care pathway in healthcare.

TACO Checklist	Patient Risk Assessment	YES	NO
	Does the patient have any of the following: diagnosis of 'heart failure', congestive cardiac failure (CCF), severe aortic stenosis, or moderate to severe left ventricular dysfunction?		
	Is the patient on a regular diuretic?		
	Does the patient have severe anaemia?		
	Is the patient known to have pulmonary oedema?		
	Does the patient have respiratory symptoms of undiagnosed cause?		
	Is the fluid balance clinically significantly positive?		
	Is the patient receiving intravenous fluids (or received them in the previous 24 hours)?		
	Is there any peripheral oedema?		
	Does the patient have hypoalbuminaemia?		
	Does the patient have significant renal impairment?		

If Risks Identified	YES	NO
Review the need for transfusion (do the benefits outweigh the risks)?		
Can the transfusion be safely deferred until the issue is investigated, treated or resolved?		

If Proceeding with Transfusion: Assign Actions	TICK
Body weight dosing for red cells	
Transfuse a single unit (red cells) and review symptoms	
Measure fluid balance	
Prophylactic diuretic prescribed	
Monitor vital signs closely, including oxygen saturation	

Name (PRINT):	
Role:	
Date:	**Time (24hr):**
Signature:	

Due to the differences in adult and neonatal physiology, babies may have a different risk for TACO. Calculate the dose by weight and observe the notes above.

TACO=transfusion-associated circulatory overload

Figure 18b.1: TACO pre-transfusion checklist

Introduction

The 2020 reporting year has recorded the highest number of TACO cases ever reported to SHOT. COVID-19 has complicated the assessment of some cases and the overall increase in number of reports received has been affected by patients on convalescent plasma trials. The increasing number of cases where preventive actions include the TACO pre-transfusion checklist being incorporated into documents and processes, including electronic systems and training programmes, is a welcome and positive change in practice. It is critically important that all TACO cases are used as a learning opportunity to prevent or mitigate TACO in other patients. A new recommendation for this year is the use of the TACO investigation and preventive action guidance tool, to ensure a structured and comprehensive review of cases to support effective preventive actions (see recommendations and recommended resources sections).

Deaths n=18

TACO resulted in the death of a patient in 18 reported cases. Although the imputability level was 1 (possibly related to transfusion) in most cases, this is a significant increase in the number of cases of TACO where patients died, and the transfusion was judged to be contributory. This may reflect the severity of underlying illness and in particular those with COVID-19 as such patients were unfortunately more likely to die.

Major morbidity n=25

There were fewer cases resulting in major morbidity than in the previous reporting year but again this may reflect the severity of underlying illness in some patients, in that they were possibly more likely to die than they were to survive following major morbidity. TACO remains the leading cause of transfusion-related combined mortality and major morbidity.

Table 18b.1: Demographic overview of cases

Demographic	Number of reports
Deaths (imputability 3)	0
Deaths (imputability 2)	2
Deaths (imputability 1)	16
Major morbidity outcome	25
Age†	Range: 9 days to 97 years Median: 73 years
Top 3 medical specialties†	Haematology, acute medicine, general medicine
Bleeding patients (indication code R1 or 'massive bleeding' indicated†	24
Non-bleeding patients (other indication codes or not stated)	125

† where data was provided

TACO is more commonly reported in the elderly, non-bleeding patients but is seen across all age groups and is consistent with the data from previous years. There were 2 cases in the under-18 age group both of which were neonates. Haematology and adult medical specialties are again the most common specialties where TACO is reported, and this should be considered when delivering TACO education and mitigation plans.

Analysis of cases

Analysis by definition criteria

Cases reported in 2020 were assessed using the surveillance criteria in Table 18b.2. It should be noted that the criteria are for the purposes of reporting and surveillance. They do not constitute a clinical diagnosis for the purpose of real-time interventions for the medical management of a patient presenting with respiratory compromise during or following transfusion. However, the surveillance criteria should promote recognition of TACO.

Figure 18b.2 shows the number of accepted TACO cases versus the number of TACO surveillance criteria met. One accepted case only met two TACO surveillance criteria but was otherwise a clinically compelling scenario. A patient with a positive fluid balance developed respiratory distress and increased oxygen requirement during transfusion, which improved following treatment with a diuretic. A chest X-ray was not performed and therefore the presence of pulmonary oedema could not be confirmed, and there were no cardiovascular changes reported. There was a slightly increased number of patients meeting all five criteria due to a slight increase in NT pro-BNP testing, which is a useful indicator of left atrial hypertension in patients with circulatory overload.

Table 18b.2: TACO surveillance definition (adapted from Wiersum-Osselton et al. 2019)

Patients classified with TACO (surveillance diagnosis) should exhibit at least one required criterion* with onset during or up to 12 hours after transfusion (SHOT continues to accept cases up to 24 hours), and a total of 3 or more criteria i.e. *A and/or B, and total of at least 3 (A to E)

*** Required criteria (A and/or B)**

A. Acute or worsening respiratory compromise and/or
B. Evidence of acute or worsening pulmonary oedema based on:
– clinical physical examination, and/or
– radiographic chest imaging and/or other non-invasive assessment of cardiac function

Additional criteria

C. Evidence for cardiovascular system changes not explained by the patient's underlying medical condition, including development of tachycardia, hypertension, jugular venous distension, enlarged cardiac silhouette and/or peripheral oedema
D. Evidence of fluid overload including any of the following: a positive fluid balance; clinical improvement following diuresis
E. Supportive result of a relevant biomarker, e.g. an increase of B-type natriuretic peptide levels (BNP) or N-terminal-pro brain natriuretic peptide (NT-pro BNP) to greater than 1.5 times the pre-transfusion value

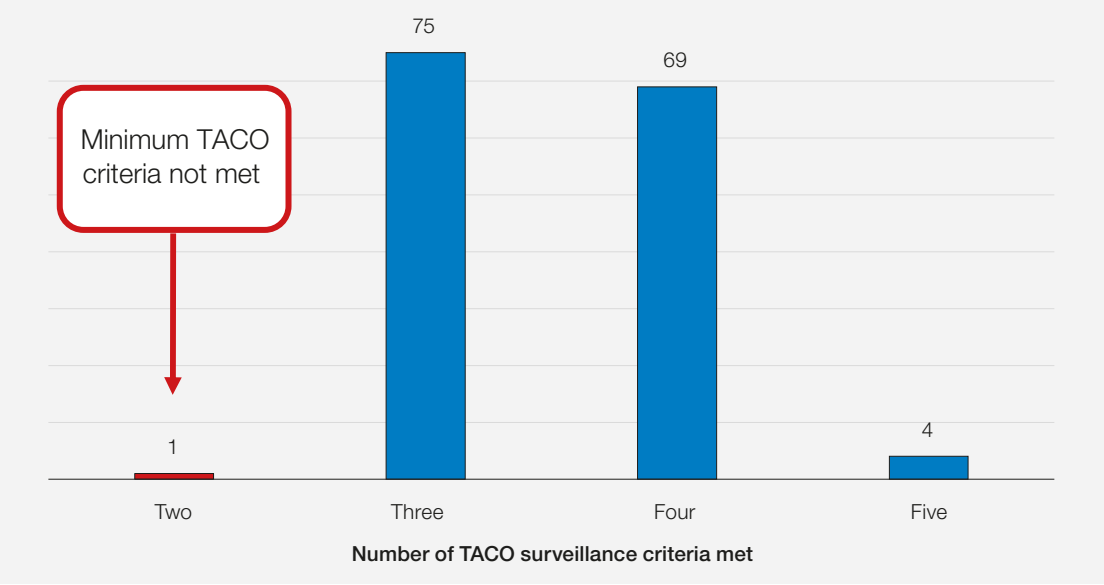


Figure 18b.2: Number of TACO surveillance criteria versus number of accepted TACO cases

Use of the TACO checklist

The TACO risk assessment recommendation was introduced in 2016 in the 2015 Annual SHOT Report (Bolton-Maggs et al. 2016). A question regarding the use of the TACO risk assessment and mitigating actions was added to the SHOT reporting questionnaire for the 2019 reporting year. An overview is shown in Figure 18b.3.

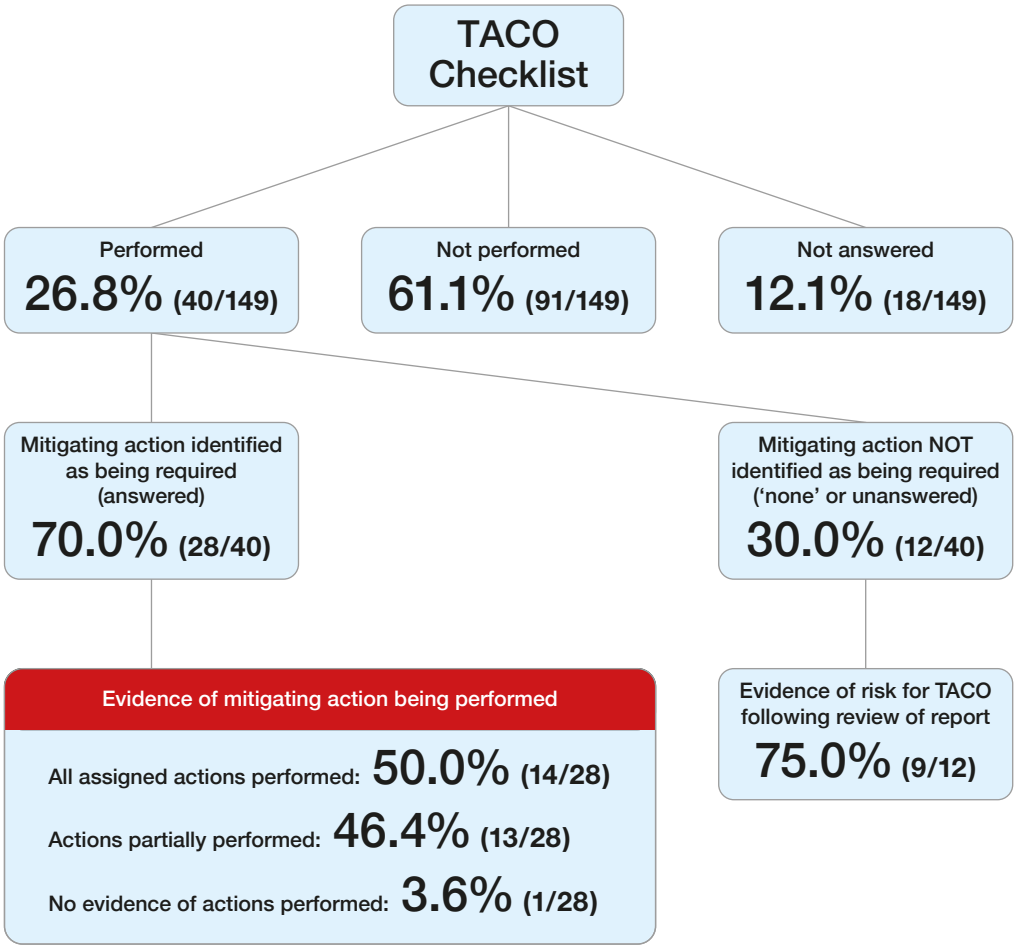


Figure 18b.3: Use of the checklist to identify patients at risk of TACO and implementation of mitigations

The TACO checklist had only been reported as performed in 40/149 (26.8%) of cases, resulting in missed opportunities to mitigate the risk of TACO. Where it had been performed, 28/40 (70.0%) of those cases were identified as requiring a TACO risk-reduction measure. This was performed in 14/28 (50.0%) of cases, with the majority of the remainder partially performed, or not fully assessable from the data available. A TACO risk-reduction measure was not identified as required in 12/40 (30.0%) of cases, but on review 9/12 (75.0%) of these cases had clear risk factors for TACO, suggesting the checklist had not been accurately performed.

TACO cases with evidence of excessive red cell volume to meet the target Hb

The recommendation for weight-adjusted red cell dosing for non-bleeding patients was introduced in 2018 in the 2017 Annual SHOT Report (Bolton-Maggs et al. 2018). Analysis of the 2019 data showed this was not implemented in practice and was contributing to a significant level of overtransfusion in reported cases of TACO.

In 2020 there were 73 cases where the patient was not bleeding, and body weight and pre-transfusion Hb level was reported. Thirty-four of these cases also had a post-transfusion Hb level reported. In 7/34 (20.6%) of cases their post-transfusion Hb target was exceeded. The number of red cell units transfused was reported in 28 cases. In 12/28 (42.9%) of cases the patient received more than the calculated weight-adjusted dose resulting in 5/12 (41.2%) exceeding their post-transfusion Hb target. This suggests that weight-adjusted red cell dosing is not sufficiently implemented, and this continues to result in excessive red cell transfusion.

Learning points

- Excessive volume of red cell transfusion to meet a target haemoglobin (Hb) level remains a significant factor in cases of transfusion-associated circulatory overload (TACO) in non-bleeding patients. This can be minimised by weight-adjusted red cell dosing, and medical management of anaemia where possible. The red cell calculation shown below helps estimate the volume of red cells required to meet the target haemoglobin (Norfolk 2013)

  [target Hb (g/L) - pre-transfusion Hb (g/L)] x weight (Kg) x 0.4mL red cells = volume of red cells (mL) required to meet target Hb

  (The volume of a unit of adult-specification red cells in the UK is 220 - 340mL)

  This volume calculation will help inform the number of units to be requested

- A significant number of reported TACO cases do not appear to have had a TACO checklist performed, and/or TACO risk-reduction measures not implemented where risk was identified. This should be embedded into the procedure for the request and authorisation of transfusion
- Every case of TACO is an opportunity to improve practice and reduce risk for other patients. Structured investigation and root-cause analysis allows implementation of effective preventive actions

Conclusion

TACO is in many cases a preventable complication of transfusion but remains the leading cause of transfusion-related mortality and major morbidity. More cases than ever were reported to SHOT in 2020, but cases of TACO continue to be under-recognised and under-reported. Most TACO cases have a recognised risk factor for circulatory overload. Although there are now well-established recommendations and tools to mitigate TACO in patients with risk factors, analysis of the data shows these are not being implemented in clinical practice, and opportunities are being missed to protect patients. It is critically important that every case of TACO is used as an opportunity to improve practice and reduce risks for other patients. Structured investigation and root cause analysis allows implementation of effective preventive actions for the future protection of patients.

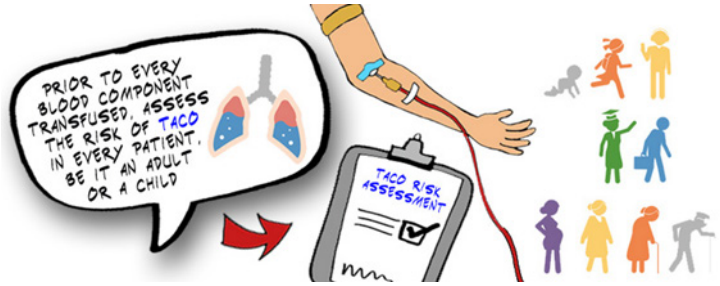
Recommended resources

Example of weight-adjusted red cell dosing implemented in clinical practice
www.rcdcalculator.co.uk

TACO investigation and preventive action guidance tool
https://www.shotuk.org/resources/current-resources/

TACO checklist: in risk assessment/checklist alternative format for incorporation into clinical documents
https://www.shotuk.org/resources/current-resources/

SHOT Bite number 11: respiratory symptoms during transfusion
https://www.shotuk.org/resources/current-resources/shot-bites/



SHOT
Serious Hazards of Transfusion

References

Bolton-Maggs PHB (Ed), Poles D, et al. on behalf of the Serious Hazards of Transfusion (SHOT) Steering Group. The 2015 Annual SHOT Report (2016). https://www.shotuk.org/shot-reports/ [accessed 28 April 2021].

Bolton-Maggs PHB (Ed), Poles D, et al. on behalf of the Serious Hazards of Transfusion (SHOT) Steering Group. The 2017 Annual SHOT Report (2018). https://www.shotuk.org/shot-reports/ [accessed 28 April 2021].

Grey S, Farrar K, Kinsella P, et al. A web-App for weight-adjusted red cell dosing: post-development implementation and clinical effectiveness. *B J Haem* 2018;**181(1)**:146.

NCA. National Comparative Audit of Blood Transfusion: Transfusion associated circulatory overload audit 2017 https://nhsbtdbe.blob.core.windows.net/umbraco-assets-corp/14909/2017-taco-national.pdf [accessed 28 April 2021].

Norfolk D (ed). Handbook of Transfusion Medicine (5th edn) (2013). The Stationery Office, London URL https://www.transfusionguidelines.org/transfusion-handbook [accessed 28 April 2021].

Wiersum-Osselton J, Whitaker BL, Grey S, et al. Revised international surveillance case definition of transfusion associated circulatory overload (TACO): a classification agreement validation study. *Lancet Haematol* 2019;**6(7)**:e350-e358. doi: 10.1016/S2352-3026(19)30080-8.

18c Transfusion-Associated Dyspnoea (TAD) n=37

Author: Shruthi Narayan

Acknowledgements: All members of the Pulmonary WEG

Definition:

TAD is characterised by respiratory distress within 24 hours of transfusion that does not meet the criteria for transfusion-related acute lung injury (TRALI) or transfusion-associated circulatory overload (TACO) or allergic reaction. Respiratory distress in such cases should not be adequately explained by the patient's underlying condition (International Society of Blood Transfusion (ISBT) definition).

Key SHOT message

- Pathophysiology of transfusion-associated dyspnoea (TAD) is still not known and with no definite diagnostic criteria, our understanding is evolving. Cases submitted are reviewed by SHOT experts including pulmonologists to verify imputability, causality and categorisation. International collaborative work in this area will help identify causal and contributory factors and identify appropriate risk-reduction measures

Abbreviations used in this chapter

ARDS	Acute respiratory distress syndrome
CCU	Critical care unit
CP	Costophrenic
CT	Computed tomography
CXR	Chest X-ray
ECMO	Extracorporeal membrane oxygenation
FAHR	Febrile, allergic and hypotensive reactions
FFP	Fresh frozen plasma
Hb	Haemoglobin
HDU	High dependency unit
HLA	Human leucocyte antigen
ICU	Intensive care unit
PPH	Postpartum haemorrhage
PRES	Posterior reversible encephalopathy syndrome
WEG	Working Expert Group
TACO	Transfusion-associated circulatory overload
TAD	Transfusion-associated dyspnoea
TAD-C	TAD with adequate clinical information
TAD-IC	TAD with inadequate clinical information
TRALI	Transfusion-related acute lung injury

Recommendation

- Patients who develop respiratory distress during or up to 24 hours following transfusion where transfusion is suspected to be the cause must be reported to SHOT with as much detail (clinical and laboratory aspects) as possible

Action: All staff involved in transfusion

Introduction

TAD is a pulmonary complication post transfusion that cannot be classified as TACO or TRALI, nor can it be ascribed to a patient's pre-existing disease. This entity is useful for the surveillance function of haemovigilance systems, but little is known that ties all the cases included in this category other than the temporal correlation between respiratory deterioration and transfusion. The pathophysiology of this group of complications remains unclear (Badami et al. 2015). Appropriate risk-reduction strategies are only possible once we have a better understanding of these reactions. There is some evidence that patients with sepsis are more at risk of respiratory complications following transfusion (Roubinian 2018), a reminder that every transfusion should be reviewed to ensure it is indicated, particularly platelets, which are a rich source of biological response modifiers (Garraud et al. 2013; Garraud et al. 2016).

Categorisation of pulmonary complications following transfusion remains a complex area with ongoing international collaboration for harmonisation of definitions and data collection. Often, the interpretation of the cases submitted is limited by the available clinical information including results of relevant investigations. The SHOT pulmonary WEG continue to attempt to apply the new proposed TRALI consensus definitions (Vlaar et al. 2019) to those cases reported under TAD to assess whether it helped re-categorise these reactions. There were 2 cases categorised as TRALI type II with risk factors for ARDS, and these are detailed below.

Cases included under TAD have been subdivided based on adequacy of the clinical information available. TAD-C (those with complete or adequate clinical information) and TAD-IC (those with inadequate information). Transfers of cases submitted between categories (FAHR, TACO, TRALI, etc.) reflect the challenges involved in interpreting these real-life cases. TAD represents cases with atypical or overlapping entities with varying severity of reaction and impact on patients, and with currently unexplained pathophysiology.

The following figure summarises these cases.

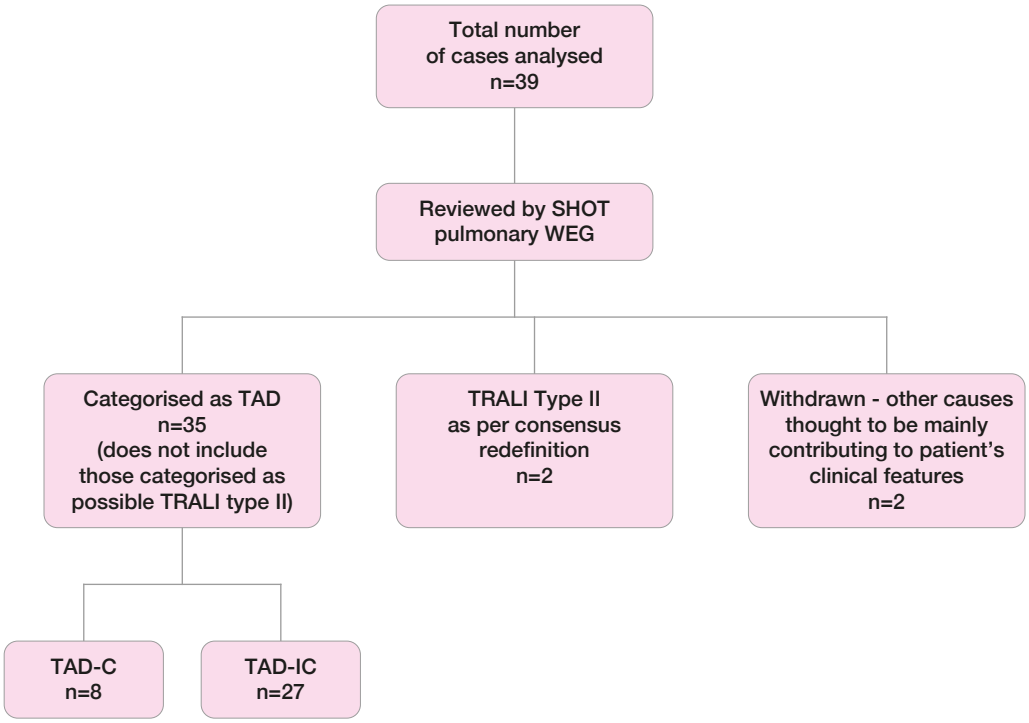


Figure 18c.1: Summary of cases included under TAD

TAD=transfusion-associated dyspnoea; TAD-C=TAD with adequate clinical information; TAD-IC=TAD with inadequate clinical information; TRALI=transfusion-related acute lung injury; WEG=working expert group

Deaths n=4

All 4 deaths were possibly related to the transfusion (imputability 1).

Case 18c.1: Severe shortness of breath and agitation

A patient in her 70s admitted with suspected acute coronary syndrome had multiple co-morbidities: lung cancer, chronic kidney disease, paroxysmal atrial fibrillation, and hypertension. The patient had a deterioration in her respiratory status in the 12 hours prior to transfusion. During a red cell transfusion, the patient developed severe shortness of breath and agitation. Hydrocortisone, chlorphenamine and diuretics were given with no effect and the patient went into cardiac arrest.

Case 18c.2: Cardiac arrest following transfusion

A man in his 70s was admitted with shortness of breath and suspected community acquired pneumonia. He had acute kidney impairment, congenital isolated hyperinsulinism, right bundle branch block, hypertension and had clinical evidence of fluid overload prior to transfusion. Whilst being transfused a unit of red cells, the patient's condition deteriorated quickly leading to cardiac arrest. The patient was resuscitated, admitted to ICU following arrest, but died 4 days later.

Case 18c.3: Respiratory distress and tachycardia following a platelet transfusion

A man in his mid-70s with metastatic prostate cancer and bone marrow failure was admitted following collapse for further evaluation and treatment. During transfusion of irradiated apheresis platelets, the patient developed acute respiratory distress and tachycardia. There was no clinical evidence of circulatory overload. No information regarding input/output was available. He had received two red cell units in the 24 hours prior to this. He was given steroids, diuretics and O_2. The diuresis response was not recorded. The patient worsened, was reviewed by the critical care team, and a decision was made for no escalation in care and to remain on the ward for palliative care. The CXR post transfusion showed patchy consolidation in the right lower zone.

Case 18c.4: TRALI type II

A patient in his 70s, with metastatic lung adenocarcinoma, was admitted with community acquired pneumonia and suspected sepsis. He was transfused two units of red cells for Hb 54g/L, 5 hours and 40 minutes later the patient went into respiratory failure requiring non-invasive ventilation and admission to ICU. He later deteriorated and died. The case was discussed with the Blood Service consultant and investigated for TRALI. A CXR done post transfusion showed bilateral ground-glass opacities with relative sparing of lung apices. Blunting of the CP angles was seen, more on the left suggestive of pleural effusion. Findings were consistent with pulmonary oedema. TRALI investigations revealed HLA class I antibodies in the donor of this unit, but not cognate to the patient. No HLA class II antibodies or granulocyte-specific antibodies were found. These results do not support a diagnosis of antibody-mediated TRALI. This case has been included in TAD and would qualify for TRALI type II under the consensus redefinition.

Major morbidity n=7

All cases included here are those where patients needed admission to HDU/ICU/CCU following respiratory deterioration post transfusion. In 1 case, a patient needed to be admitted briefly following respiratory distress after transfusion as a day case. All patients subsequently recovered.

TRALI type II as per redefinition consensus criteria n=2

Cases included here were originally submitted under TRALI, but investigations did not reveal cognate antibodies and the patients had risk factors for ARDS, had stable respiratory parameters prior to the transfusion episode but deteriorated significantly following transfusions. These would qualify as TRALI type II under the consensus redefinition but considered under TAD due to a lack of positive serology with cognate antibodies. These cases are described separately here in trying to map to the new consensus redefinition criteria, one resulted in death and one in major morbidity. Both are included in the numbers above.

Case 18c.5: Imputability 1 (possible)

A woman in her mid-20s was admitted to the maternity unit having suffered an eclamptic seizure at home at 27+5 weeks gestation. Intrauterine fetal demise was diagnosed due to a large abruption. She then underwent an emergency caesarean section, was coagulopathic and developed severe PPH. She received several blood components: four units of FFP, four pools of cryoprecipitate, four units of packed red cells and one unit of platelets. After leaving theatre, she was transferred to ICU. At this point a positive bacterial culture (BactAlert) from the platelets had been reported to the Blood Service consultant who then contacted the clinical area to inform them of potential contamination. There were no infective issues reported at the time. The organism was later identified as Propionibacterium acnes. The patient did not recover as would be expected postoperatively. Her CXR showed non-specific diffuse ground glass shadowing consistent with ARDS. There were no positive blood cultures from the patient. A head CT 4 days after surgery showed changes consistent with PRES. The chest CT showed ARDS. She deteriorated and was increasingly difficult to ventilate so was transferred for ECMO and improved slowly. A possible diagnosis of TRALI was considered 4 days after the transfusions. HLA A2 Antibody detected not cognate to the patient.

This was originally reported as possible 'equivocal TRALI' to SHOT due to the finding of antibodies, onset within 6 hours and a plausible clinical history but with many other possibilities. But as only immune TRALI cases are included in the SHOT TRALI category, this has been moved to TAD. This fits in the TRALI type II category according to the consensus redefinition as risk factors for ARDS, not clinically overloaded prior to transfusion; developed hypovolaemic shock after PPH; CXR changes consistent with ARDS; no respiratory infection symptoms prior to transfusion.

The second case was Case 18c.4 described above under the section 'Deaths'. The case was submitted to SHOT in the TRALI category. Investigations revealed HLA class I antibodies in the donor of this unit, but not cognate to the patient. No HLA class II antibodies or granulocyte-specific antibodies were found. These results did not support a diagnosis of antibody-mediated TRALI. They are included in TAD and would qualify for TRALI type II under the consensus redefinition.

COVID-19 convalescent plasma related cases n=4

Four cases were reported in 2020 where patients with COVID-19 pneumonia enrolled onto the RECOVERY trial and developed worsening in their respiratory status <24 hours after convalescent plasma administration. The imputability is difficult to assess in these patients as deterioration could be related to worsening of the COVID-19 pneumonitis. Sudden respiratory deterioration with ARDS is well recognised in these patients and other factors such as thromboembolism and cardiac effects of COVID-19 could also be contributory. Secondary infections, sepsis and rarely pneumothorax and pneumomediastinum could complicate the clinical picture as well (Pooni et al. 2020). All cases have been included for analysis with an imputability of 1 (possible).

Learning point

- Clinicians should report all cases of post-transfusion pulmonary complications to the Blood Service so that further investigation can allow for further classification of such cases. There are cases where such distinction may not always be possible. This is in addition to SHOT reporting

Conclusion

Pulmonary complications following transfusions account for the majority of morbidity and mortality associated with transfused blood components in hospitalised patients. The 'terrible T's': TRALI, TACO, and TAD primarily damage the lung, leading to respiratory failure. The differential diagnosis for patients who develop respiratory distress during or within a few hours after transfusion include TRALI, TACO, an anaphylactic transfusion reaction, and transfusion of contaminated (bacteria) blood components. Often these are in patients with multiple ongoing clinical issues, many of which may also be contributing to the deterioration. TAD with no definitive criteria remains a diagnosis of exclusion. Information about

pre-transfusion clinical state of the patient especially the respiratory status in the preceding 12 hours prior to the transfusions help in categorisation along with results of investigations. Reporters are encouraged to provide as detailed a report as possible to increase understanding of these complications from a haemovigilance perspective. This would also help identify how healthcare providers can risk-stratify individual patients or patient populations to determine whether a given transfusion is more likely to benefit or harm the patient based on the transfusion indication, risk, and expected outcome.

References

Badami KG, Joliffe E and Stephens M. Transfusion-associated dyspnea: shadow or substance? *Vox Sang* 2015;**109(2)**:197-200.

Garraud O, Cognasse F, Hamzeh-Cognasse H, et al. [Blood transfusion and inflammation]. *Transfus Clin Biol* 2013;**20(2)**:231-238.

Garraud O, Cognasse F, Tissot JD, et al. Improving platelet transfusion safety: biomedical and technical considerations. *Blood Transfus* 2016;**14(2)**:109-122.

Pooni R, Pandey G, Akbar S. Broadening the differential: pneumomediastinum and COVID-19 infection. *BMJ Case Reports CP* 2020;**13**:e237938.

Roubinian N. TACO and TRALI: biology, risk factors, and prevention strategies. *Hematology Am Soc Hematol Educ Program* 2018;**2018(1):**585-594. doi:10.1182/asheducation-2018.1.585.

Vlaar APJ, Toy P, Fung M, et al. A consensus redefinition of transfusion-related acute lung injury (TRALI). *Transfusion* 2019;**59**:2465-2476.

Haemolytic Transfusion Reactions (HTR) n=46

19

Authors: Tracey Tomlinson and Anicee Danaee

Definitions:

Acute haemolytic transfusion reactions (AHTR) are characterised by fever, a fall in haemoglobin (Hb), rise in bilirubin and lactate dehydrogenase (LDH) and a positive direct antiglobulin test (DAT). They generally present within 24 hours of transfusion.

Delayed haemolytic transfusion reactions (DHTR), occur more than 24 hours following a transfusion and are associated with a fall in Hb or failure to increment, rise in bilirubin and LDH and an incompatible crossmatch not detectable pre transfusion.

Hyperhaemolysis is characterised by more severe haemolysis than DHTR, with haemolysis affecting the transfused red cells and the patient's own red cells; there is a decrease in Hb to below pre-transfusion levels, which is often associated with a reticulocytopenia. It may be triggered by a new red cell alloantibody, but frequently no new red cell antibody is identified. Hyperhaemolysis can be divided into acute and delayed hyperhaemolysis.

Key SHOT messages

- Monitoring the key markers of haemolysis pre and post transfusion is important to allow the identification and classification of haemolytic transfusion reactions
- Reporters should include all relevant clinical and laboratory details when reporting cases with hyperhaemolysis. This will help improve understanding of the management of this complex syndrome
- Monitoring the patient's reticulocyte and ferritin levels can help to distinguish hyperhaemolysis from other haemolytic transfusion reactions

Abbreviations used in this chapter

AHTR	Acute haemolytic transfusion reactions	**HTR**	Haemolytic transfusion reactions
BSH	British Society for Haematology	**IV**	Intravenous
DAT	Direct antiglobulin test	**IVIg**	Intravenous immunoglobulin
DHTR	Delayed haemolytic transfusion reactions	**LDH**	Lactate dehydrogenase
EPO	Erythropoietin	**Sp-ICE**	Specialist Services electronic reporting using Sunquest's Integrated Clinical Environment
Hb	Haemoglobin	**TACO**	Transfusion-associated circulatory overload

Recommendations

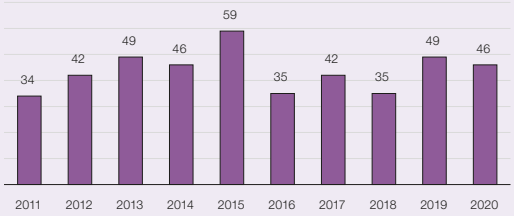
- Controls should be in place to ensure compliance with British Society for Haematology (BSH) guidelines relating to management of transfusions in patients with sickle cell disease and thalassaemia including pre-transfusion compatibility procedures in blood transfusion (BSH Milkins et al. 2013). Local hospital transfusion policies and procedures should reflect these guidelines
- Procedures for investigation of transfusion reactions should be compliant with the BSH guidelines covering investigation and management of acute transfusion reactions (BSH Tinegate et al. 2012)

Action: Hospital transfusion teams, hospital transfusion committees, laboratory management

Headline data 2020

Number of reports n=46
Deaths n=0
Major morbidity n=12

HTR reports by year



Demographic data

Male n=21
Female n=25
Adults n=43
Paediatric n=3

Blood component data

Red cells n=46
Platelets n=0
Plasma n=0
Multiple Components n=0
Other n=0

Number of cases n=46

A total of 46 cases have been included, 12 acute, 25 delayed reactions and 9 cases of hyperhaemolysis. The total number of cases is comparable to the 49 cases reported in 2019, however it must be noted that the total numbers of transfusions occurring in 2020 was reduced due to a decrease in elective procedures during the COVID-19 pandemic.

One HTR case resulted from emergency transfusion of antigen-positive blood due to clinical need for immediate transfusion.

In 1 case of acute HTR, the patient also experienced TACO and this is included and discussed in more detail in Chapter 18b, Transfusion-Associated Circulatory Overload (TACO).

Age range and median

The age range was 8 to 95, with a median age of 57. This is shown in Figure 19.1, broken down further by patient gender. HTR were reported in 3 paediatric patients.

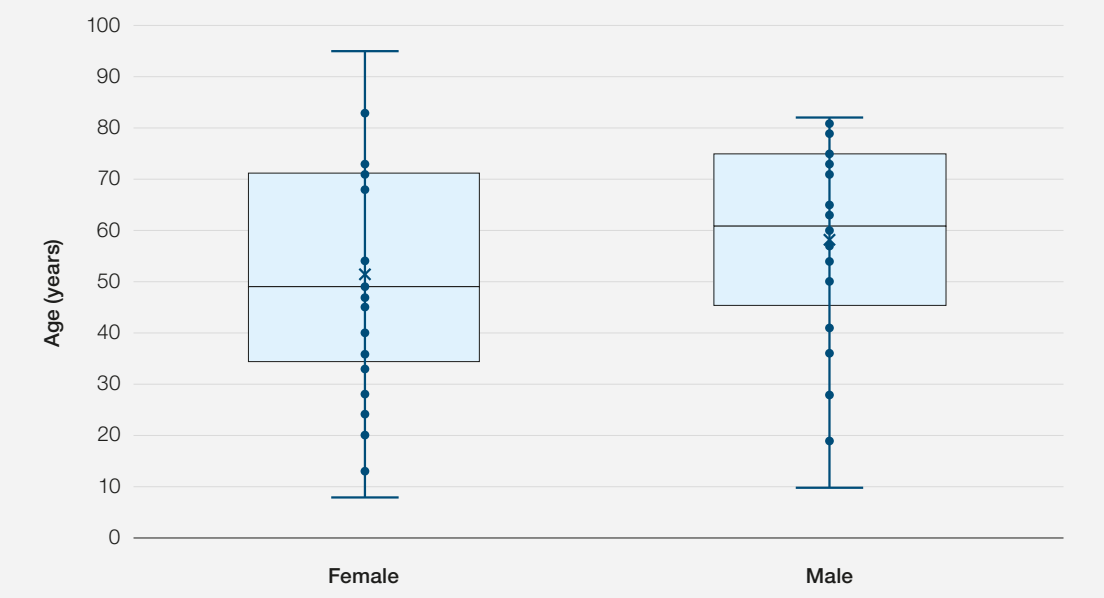


Figure 19.1: Age range in males and females experiencing a HTR

Figure 19.1 is a box and whisker diagram showing the median age and the age range of patients experiencing a HTR reported to SHOT separated by gender. The middle bar in the shaded box indicates the median age, the outer bars of the box represent the upper and lower quartiles. The lines extending from the boxes (whiskers) indicate the lowest and highest values.

Deaths n=0

There were no patient deaths reported resulting from haemolytic transfusion reactions.

Major morbidity n=12

There were 12 cases reported in which the patient suffered major morbidity. SHOT considers that all reported cases of probable hyperhaemolysis where there is a significant fall in Hb should be considered as major morbidity. Following application of this criterion all cases of hyperhaemolysis reported with 'minor morbidity' were reclassified.

Hyperhaemolysis n=9

Nine cases of hyperhaemolysis syndrome were reported which is a significant increase from previous years (4 were reported in 2019). All these cases were reported in patients with sickle cell anaemia, and each patient made a full recovery. It is likely that this increase in reports is related to an increase in awareness of hyperhaemolysis syndrome amongst clinical teams leading to better diagnosis, treatment and haemovigilance reporting. However, it is likely that hyperhaemolysis is still under-reported. Ongoing education is required to ensure that all cases are submitted to SHOT.

Historically it has been difficult to distinguish hyperhaemolysis from other HTR. In contrast to other HTR, hyperhaemolysis has been reported to be accompanied by a decrease in the patient's absolute reticulocyte count and an increase in the ferritin level (Win et al. 2019). In 2020 SHOT started collecting data on these results. The patient's pre-transfusion and post-transfusion reticulocyte level was provided in 5/9 reports and in all 5 cases the reticulocyte count did drop. Unfortunately, the pre- and post-transfusion ferritin results were only provided in 1/9 reports however this did show a dramatic increase from 46 to 540ng/mL. If a pre-transfusion ferritin level is not available serial monitoring with steep increases in ferritin combined with falling Hb and a drop in reticulocyte count will help support the diagnosis of hyperhaemolysis syndrome.

Hyperhaemolysis can be divided into acute and delayed hyperhaemolysis. Acute hyperhaemolysis occurs within 7 days of transfusion and the DAT is usually negative. Delayed hyperhaemolysis occurs more than 7 days post transfusion and the DAT is often positive. In contrast to a classical DHTR, in delayed hyperhaemolysis both patient and transfused red cells are haemolysed (Danaee et al. 2015). Of the 9 cases reported 7 of the reactions occurred within the first 7 days post transfusion.

Treatment of hyperhaemolysis

Various treatment protocols for management of hyperhaemolysis have been suggested including the use of IVIg, steroids and EPO. There have been no published randomised trials in the effectiveness of these however eculizumab has been licensed to treat ongoing brisk haemolysis (NHS England 2020). The treatment methods used in the 9 hyperhaemolysis cases reported in 2020 is summarised in Table 19.1.

Table 19.1: Summary of treatment protocols used

Treatment type given	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9
IVIG	Yes	Yes	Yes	No	Yes	Yes	Yes	No	No
IV Steroids	Yes	Yes	Yes	Yes	No	Yes	No	No	Yes
EPO	Yes	No	No	No	No	No	Yes	No	No

Learning points

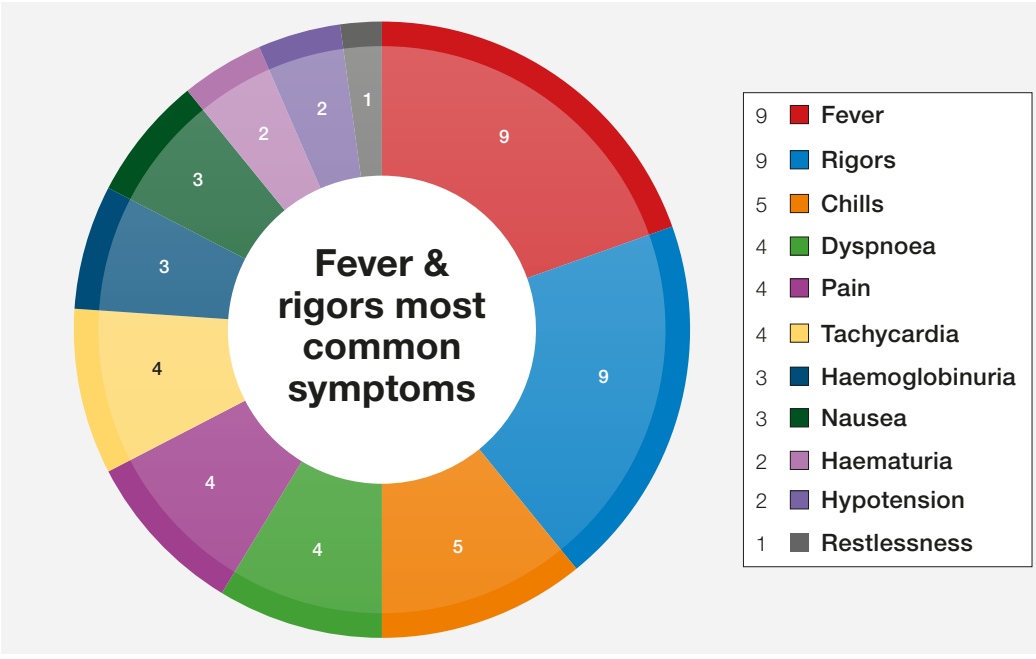
- Hyperhaemolysis can be accompanied by a drop in the patient's absolute reticulocyte levels
- Monitoring of the patient's reticulocyte and ferritin levels can be helpful in distinguishing hyperhaemolysis from other haemolytic transfusion reactions
- All cases of hyperhaemolysis should be considered as major morbidity

Clinical and laboratory signs and symptoms

Acute haemolytic transfusion reactions n=12

The clinical symptoms reported in AHTR are shown in Figure 19.2.

Figure 19.2: Clinical symptoms reported in AHTR



Delayed haemolytic transfusion reactions n=25 (excluding potential cases of hyperhaemolysis)

No clinical symptoms of a transfusion reaction were reported in 11/25 (44.0%) delayed haemolytic transfusion reaction cases submitted to SHOT. This remains comparable to previous years.

Most delayed haemolytic transfusion reactions were initially identified due to a lack of Hb increment following transfusion (13/25, 52.0%) or the development of a positive DAT (12/25, 48.0%).

Laboratory investigation of HTR

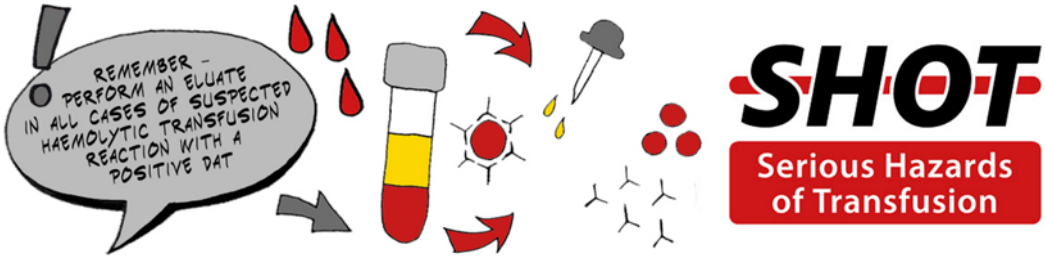
This year the diagnosis of HTR was complicated by a lack of availability of pre- and post-transfusion testing results. Reporters had noted that this was in response to the COVID-19 pandemic and it most often related to the pre-transfusion chemistry results. Additionally, 2/46 (4.3%) reports stated that no post-transfusion DAT had been performed and a further 11/46 (23.9%) provided no post-transfusion serology results.

Case 19.1: HTR investigation prompted by a failure in Hb increment post transfusion

A patient with B cell lymphoma was transfused to treat chronic anaemia. A non-specific antibody was reported in the pre-transfusion antibody investigation and two units of crossmatch-compatible red cells were issued. The patient did not show any clinical symptoms of HTR except that they failed to show the expected increment in Hb post transfusion. Repeat samples were sent to the transfusion laboratory. The post-transfusion DAT was positive and anti-Jk^a was identified in the plasma. The pre-transfusion serology was reviewed, and it was concluded that the pre-transfusion sample also showed evidence of anti-Jk^a.

Learning point

- A lack of the expected increment in haemoglobin or the development of a positive direct antiglobulin test (DAT) post transfusion can be the first indication of a haemolytic transfusion reaction



Antibodies implicated in HTR

Anti-Jk^a continues to be the most frequent antibody specificity implicated in HTR. The antibody specificities reported are shown in Figure 19.3.

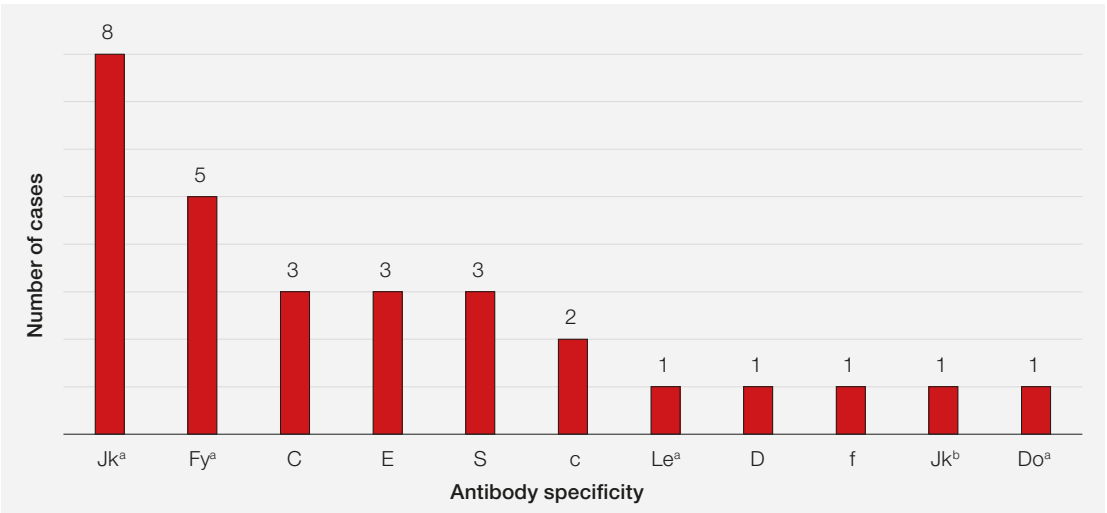


Figure 19.3: Antibody specificities implicated in HTR

In 21/25 (84.0%) cases of DHTR antibodies were detected in the post-transfusion sample which were not detectable in the pre-transfusion sample.

Two cases were reported in which information on the presence of the antibody was available on Sp-ICE at the time of pre-transfusion testing. In another case, a patient with sickle cell anaemia experienced a reaction caused by anti-C and anti-E which could have been avoided if extended Rh matched red cells had been selected in compliance with BSH (BSH Milkins et al. 2013) and local hospital guidelines.

Case 19.2: Failure to issue extended Rh matched units

A young patient with sickle cell anaemia received an exchange transfusion in 2014 without being tested for an extended phenotype. In 2020 the patient was given another exchange transfusion. The patient had the Ro (D+C-c+E-e+) phenotype however the units transfused were only matched for ABO and K type. Following transfusion, the patient showed signs of haemoglobinuria, jaundice and a falling Hb and anti-C and anti-E were detected in the post-transfusion sample.

Learning points

- All individuals involved in the transfusion process must be aware of the need to share information pertinent to the patient's transfusion requirements including details of their underlying diagnosis and antibody history
- Patients should be informed when clinically significant antibodies are detected. This is especially important in multi-transfused patients, and in shared care
- Where possible, patients should be asked whether they have antibodies as part of the pre-transfusion process and any information obtained relayed to the transfusion laboratory and acted on
- Transfusion databases (such as Specialist Services electronic reporting using Sunquest's Integrated Clinical Environment (Sp-ICE)) can provide vital information in cases where antibody levels have dropped below the detectable titre. Hospitals should have local policies to decide which patients to check on transfusion databases

Recommended resource

SHOT Bite No. 15: Hyperhaemolysis
https://www.shotuk.org/resources/current-resources/shot-bites/

HTR Webinar 2021
https://www.shotuk.org/resources/current-resources/webinars/

References

BSH Milkins C, Berryman J, Cantwell C, et al. Guidelines for pre-transfusion compatibility procedures in blood transfusion laboratories. Transfus Med 2013;**23(1)**:3-35. http://onlinelibrary.wiley.com/doi/10.1111/j.1365-3148.2012.01199.x/full [accessed 25 March 2021].

BSH Tinegate H, Birchall J, Gray A, et al. (2012) Guideline on the investigation and management of acute transfusion reactions. Prepared by the BCSH Blood Transfusion Task Force. *Br J Haematol* 2012;**159(2)**:143-153.

Danaee A, Inusa B, Howard J, et al. Hyperhaemolysis in patients with hemoglobinopathies: a single-center experience and review of the literature. *Transfus Med Rev* 2015;**29(4)**:220-230.

NHS England. Clinical Commissioning Policy; Rituximab and eculizumab for the prevention and management of delayed haemolytic transfusion reactions and hyperhaemolysis in patients with haemoglobinopathies [URN 1821] [200602P] (2020). https://www.england.nhs.uk/wp-content/uploads/2020/09/1821_Rituximab_Eculizumab_Clinical_Commissioning_Policy.pdf [accessed 28 April 2021].

Win N, Lucas S, Hebballi S, et al. Histopathological evidence for macrophage activation driving post-transfusion hyperhaemolysis syndrome. *Br J Haematol* 2019;**186(3)**:499-502.

20 Uncommon Complications of Transfusion (UCT) n=12

Author: Shruthi Narayan

Definition:

Occurrence of an adverse effect or reaction temporally related to transfusion, which cannot be classified according to an already defined transfusion event and with no other risk factor other than the transfusion, and no other explanation.

Serious reactions in this category are reportable to the European Union (EU) as 'uncategorised unintended responses'.

Key SHOT message

- It is important that atypical complications seen in patients post transfusion continue to be reported to SHOT. This category includes those that are temporally correlated to transfusion but with non-specific clinical features that cannot be classified into any of the other known categories. This will help gain a better understanding of these complications, identify risk factors, and develop risk-reduction strategies

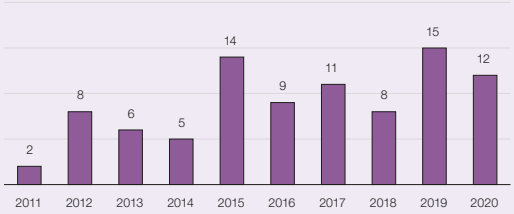
Abbreviations used in this chapter

AML	Acute myeloid leukaemia	**TANEC**	Transfusion-associated NEC
NEC	Necrotising enterocolitis		

Headline data 2020

Number of reports n=12
Deaths n=3
Major morbidity n=0

UCT reports by year



Demographic data

Male n=5
Female n=7
Adults n=11
Paediatric n=1

Blood component data

Red cells n=6
Platelets n=4
Plasma n=0
Multiple Components n=1
Other n=1

Recommendation

- Reporters are encouraged to continue to report cases with unusual reactions to transfusion

Action: All staff involved in transfusion, hospital transfusion teams

Introduction

Reactions are occasionally reported with temporal relation to transfusions which cannot be classified into other SHOT categories. These cases are included in this chapter. Often several other contributory factors can be identified that may have resulted in the patient's reactions. Reporting and reviewing these cases will help in our ever-evolving understanding of transfusion complications, helping improve patient safety by implementing appropriate risk-reduction measures. Occasionally, error reports that do not fit under other categories are included here to ensure learning is captured and shared.

Deaths n=3

There were 3 deaths reported in this category, all with imputability recorded as 'possible'.

Of these, 1 was a suspected case of TANEC, in an extremely premature baby who developed NEC ~ 6.5 hours following red cell transfusion. Another patient death where transfusion possibly contributed was a young patient with AML, neutropenic post-chemotherapy, who received one unit of apheresis platelets on the haematology day unit. On returning home they became severally unwell and were admitted to critical care and intubated. The patient died, the medical team related this to toxic shock and sepsis. The last death in this category involved a man in his mid-50s with oesophageal cancer and liver metastases. He had been admitted with fatigue, nausea and vomiting, chemotherapy reaction and bleeding. He received one unit of red cells and was on tranexamic acid. The patient was stable and alert prior to transfusion. The transfusion started and 15-minute vital signs completed, 10 minutes later the patient was found collapsed and unresponsive across the bed and pronounced dead. There were no signs of anaphylaxis or angioedema. The treating team concluded that death was related to underlying metastatic malignant disease.

TANEC

NEC is a serious neonatal gastrointestinal condition associated with significant morbidity and mortality. It affects 5-7% of preterm low birth weight (500g-1500g) infants. It is postulated that trigger events and environmental factors initiate intestinal injury in a vulnerable infant, prompting a hyper-inflammatory response. TANEC is NEC occurring within 48 hours of a red cell transfusion. From numerous observational/ case-control studies it is estimated to occur after approximately 25-35% of transfusions, generally in older infants born more preterm than others with NEC; multiple pathogenic mechanisms have been proposed. It has been difficult to establish causation or true association (Amin et al. 2012, Faraday et al. 2020, Hackam et al. 2019, MohanKumar et al. 2019).

Between 2011-2019, 19 cases of TANEC have been reported to SHOT. All babies had received a red cell transfusion. Of those who had gestational age recorded (13/19, 68.4%) were preterm, with a median gestation of 26^{+6} weeks (range 23^{+3} to 33). Age at presentation with TANEC was less than 28 days for 5 cases (youngest 10 days), 1 month for 13 cases, and 2 months for a single case. For all cases where a time of onset of symptoms following transfusion was stated (16/19, 84.2%) these occurred within 24 hours of transfusion with a mean of 3 hours. This was a very sick cohort of infants and 7 babies died. Nine babies were assessed to have had major morbidity in relation to TANEC. The imputability in 6 deaths was concluded as possibly related to transfusion and 1 was unrelated.

TANEC is associated with significant morbidity and mortality. The cases reported to SHOT had gestational and postnatal age characteristics in line with those previously described for TANEC. Based on available observational studies, there appears to be under-reporting of these cases to SHOT. Staff should be aware of this potential association between transfusion and NEC in sick infants. TANEC cases are SHOT reportable, reporting helps share the learning and can identify common themes with increasing cohort numbers.

Major morbidity n=0

Other cases n=9

The remaining cases reported under this category are described in the supplementary information on the SHOT website (https://www.shotuk.org/shot-reports/report-summary-and-supplement-2020/).

Learning point

- Patients experiencing symptoms or signs consistent with an acute reaction during or after a transfusion must be evaluated promptly, with input from the Blood Service. These should be treated as expeditiously as possible to minimise the impact of the reaction and reported to SHOT as appropriate

Conclusion

Transfusion reactions range from bothersome yet clinically benign to life-threatening and can be acute or delayed. The nature of the reaction may not be immediately apparent, as many reactions begin with nonspecific symptoms such as fever or chills. In addition, patients receiving transfusions often have complex underlying clinical conditions, the symptoms of which may mimic a transfusion reaction. As evident from the cases included in this chapter, it is often challenging to attribute imputability of the patient's reaction/complication to transfusion when there are multiple ongoing medical and surgical issues in the patient. All cases need to be reviewed to ensure learning from these events helps inform and improve practices.

References

Amin SC, Remon JI, Subbarao GC, et al. Association between red cell transfusions and necrotizing enterocolitis. *J Matern Fetal Neonatal Med* 2012;**25(5)**:85-89. doi:10.3109/14767058.2012.715465.

Faraday C, Hamad S, Jones KD, et al. Characteristics and incidence of transfusion-associated necrotizing enterocolitis in the UK. *J Matern Fetal Neonatal Med* 2020;**33(3)**:398-403. doi: 10.1080/14767058.2018.1494147.

Hackam DJ, Sodhi CP, Good M. New insights into necrotizing enterocolitis: From laboratory observation to personalized prevention and treatment. *J Pediatr Surg* 2019;**54(3)**:398-404. doi:10.1016/j.jpedsurg.2018.06.012.

MohanKumar K, Namachivayam K, Song T, et al. A murine neonatal model of necrotizing enterocolitis caused by anemia and red blood cell transfusions. *Nat Commun* 2019;**10(1)**:3494. doi:10.1038/s41467-019-11199-5.

Transfusion-Transmitted Infections (TTI) n=0 (1 probable)

21

Authors: Tali Yawitch, Heli Harvala and Su Brailsford

Definition:

A report was classified as a TTI if, following investigation:

- The recipient(s) had evidence of infection post transfusion with blood components, and there was no evidence of infection prior to transfusion, and no evidence of an alternative source of infection

and, either:

- At least one component received by the infected recipient(s) was donated by a donor who had evidence of the same transmissible infection

or:

- At least one component received by the infected recipient was shown to contain the agent of infection

These may be identified as a result of infection in the patient where transfusion is the suspected source or alternatively via lookback investigations. A lookback investigation is carried out if a donation is found to be positive for infection and retrospective testing finds a previous donation to also be positive at low levels below the detection level of screening.

Note that for the purposes of the EU legislation, serious adverse reactions (SAR) are defined as any reactions in patients that are 'life-threatening, disabling or incapacitating, or which result in, or prolongs, hospitalisation or morbidity.'

These must be reported to the Medicines and Healthcare products Regulatory Agency (MHRA) (a legal requirement). This includes all confirmed transfusion-transmitted infections.

Abbreviations used in this chapter

ALT	Alanine transaminase	**NAT**	Nucleic acid testing
BSH	British Society for Haematology	**NBL**	National Bacteriology Laboratory
DNA	Deoxyribonucleic acid	**NHSBT**	National Health Service Blood and Transplant
EIR	Emerging Infection Report	**NIBTS**	Northern Ireland Blood Transfusion Service
EU	European Union	**OBI**	Occult hepatitis B virus infection
FAIR	For the assessment of individualised risk	**PHE**	Public Health England
FFP	Fresh frozen plasma	**PTR**	Post-transfusion reactions
HAV	Hepatitis A virus	**RNA**	Ribonucleic acid
HBc	Hepatitis B core antigen	**SaBTO**	Advisory Committee on the Safety of Blood, Tissues and Organs
HBsAg	Hepatitis B surface antigen	**SACTTI**	Standing Advisory Committee on Transfusion Transmitted Infection
HBV	Hepatitis B virus	**SAR**	Serious adverse reactions

HCV	Hepatitis C virus	**SARS-CoV-2**	Severe acute respiratory syndrome coronavirus 2
HEV	Hepatitis E virus	**SNBTS**	Scottish National Blood Transfusion Service
HIV	Human immunodeficiency virus	**STI**	Sexually transmitted infection
HTLV	Human T cell lymphotropic virus	**TTI**	Transfusion-transmitted infections
JPAC	Joint UKBTS Professional Advisory Committee	**UK**	United Kingdom
LGBTQ+	Lesbian, gay, bisexual, transgender and queer	**vCJD**	Variant Creutzfeldt Jakob Disease
MHRA	Medicines and Healthcare products Regulatory Agency	**WBS**	Welsh Blood Service

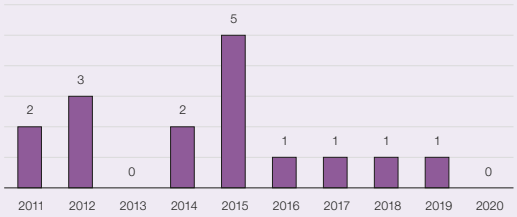
Key SHOT messages

- Any suspicion of a transfusion-transmitted infection (TTI) should be reported to the appropriate United Kingdom (UK) Blood Service as soon as possible for it to be fully investigated
- The UK Blood Services store a sample from every blood donation for at least three years. Testing can be performed on these samples if a TTI is suspected during this time
- All lookback investigations should be reported by the UK Blood Services to the infectious diseases expert on the SHOT Working Expert Group
- It is important that all healthcare professionals consenting patients for blood transfusion have up-to-date knowledge of blood donation screening and the small potential for TTI, or be aware of how to access this information

Headline data 2020

Number of reports n=0
Deaths n=0
Major morbidity n=0

Confirmed TTI reports by year



Demographic data

Male n=0 | Female n=0 | Adults n=0 | Paediatric n=0

Blood component data

Red cells n=0
Platelets n=0
Plasma n=0
Multiple Components n=0
Other n=0

Introduction

This chapter describes TTI incidents investigated by the UK Blood Services and reported to the NHSBT/PHE Epidemiology Unit's surveillance scheme in 2020.

The risk of a TTI in the UK remains extremely low. During 2020, 1 TTI investigation was concluded as probable, and there was 1 near miss investigation into a bacterial contamination. An additional probable TTI first reported in 2019 was finalised in 2020.

Annual reports from the Epidemiology Unit surveillance schemes are available here: https://hospital.blood.co.uk/epidemiology-reports/

Summary of reports made to the NHSBT/PHE Epidemiology Unit in 2020

During 2020, UK Blood Services investigated 135 suspected bacterial incidents and 5 suspected viral incidents (Figure 21.1). From these, there has been:

- One probable transfusion-transmitted HBV incident reported by NHSBT
- One near miss investigation into bacterial contamination (*Staphylococcus aureus*) reported by NHSBT
- One probable transfusion-transmitted HEV incident that was not reported in 2019, but has now been finalised by NHSBT

Figure 21.1 includes all investigations reported in 2020 in England, Northern Ireland, Scotland, or Wales. In previous Annual SHOT Reports investigations in Northern Ireland, Scotland, or Wales, concluded as PTR or not, were not included here.

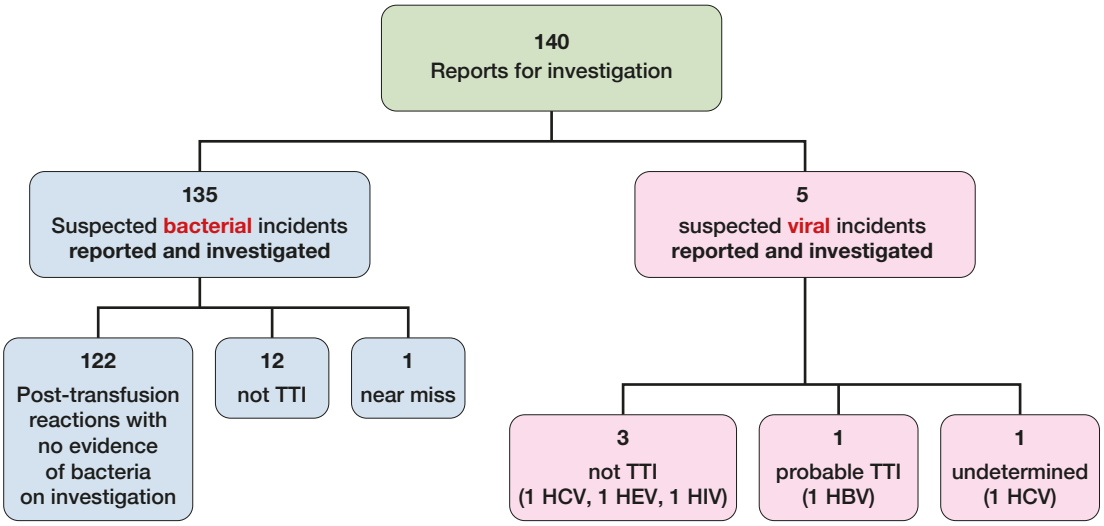


Figure 21.1: Outcome of reports of suspected TTI made to the NHSBT/PHE Epidemiology Unit in 2020 update

TTI = transfusion-transmitted infection; HCV = hepatitis C virus; HEV = hepatitis E virus; HIV = human immunodeficiency virus; HBV = hepatitis B virus

***Note**:*

- *The undetermined HCV case was related to donations from 1990, which was before HCV screening was introduced*
- *A **PTR** occurs when a blood transfusion recipient develops a reaction following a transfusion and bacteria were suspected. However, no bacteria were cultured in the recipient, units or donor(s), i.e. no evidence of any bacterial contamination*
- *A **confirmed TTI** is classified as in the above TTI definition with evidence that the virus/bacterium is indistinguishable on molecular typing between patient and donor/pack*
- *A **probable TTI** is classified as a TTI as in the above definition, but where molecular typing cannot be carried out to confirm this*
- ***Not a TTI** is defined as an investigation that concluded the infection in the recipient was NOT caused by transfusion, either as no infected donors identified (after all donors traced) or bacteria/virus identified in the recipient, but all units cleared (no bacteria/virus) in the unit and/or implicated donors*
- *A **near miss** is defined as either an infection was identified in the unit due to be transfused however the unit was NOT used in transfusion (e.g. bacterial growth seen in unit and returned to bacteriology laboratory prior to transfusion for investigation) or an infected donor calls post donation, and the unit is recalled and infection found in unit before it is transfused*

Deaths n=0

No patient deaths occurred due to confirmed transfusion-transmitted infections in 2020.

Major morbidity n=0

The probable HBV was an asymptomatic infection. The patient had significant underlying health issues with potential for severe consequences, and their HBV infection was identified via routine dialysis screening.

The investigation of probable HEV concluded in 2020 found the recipient did not develop hepatitis.

Bacterial TTI reports 2020

No reported suspected bacterial TTI investigations were concluded to be confirmed, probable or possible. All bacterial TTI investigations were concluded to be either:

- post-transfusion reaction with no evidence of bacteria in the implicated or associated products or in the recipient
- not a TTI, with evidence of bacteria in either the products or the recipient(s) but not both

The four UK Blood Services all use the BacT/ALERT system for bacterial screening which has been successful in reducing the risk of bacterial TTI (McDonald et al. 2017). Sampling methods have recently become more consistent across the four Blood Services, but some slight variation still exist, details of which are described in Table 21.1.

Near miss bacterial TTI (*Staphylococcus aureus*)

An apheresis platelet pack was returned to NBL after a 'visual abnormality' of numerous white clots ('scrambled egg' appearance) was noted by the hospital, before it was transfused. Both BacT/ALERT bottles set up from this pack had flagged positive and Gram-positive cultures were obtained from the index pack and from both bottles. *Staphylococcus aureus* was identified in the index pack. Repeat cultures confirmed the presence of *S. aureus* in the index pack. An associated pack had not been issued to a hospital and was recalled to NBL. There were no abnormalities noted in this pack. Both BacT/ALERT bottles set up from this pack were negative at day 7 and no organisms were seen in the Gram stain from the pack. Bacterial screening of this donation was reported as negative and the bottles had been discarded 2 days after unloading and therefore were not available for further analysis. *S. aureus* was subsequently isolated from a swab from the implicated donor. Molecular typing from the reference laboratory confirmed that the donor isolate and pack isolate were indistinguishable and therefore represented a single strain. The donor was informed and advised to check for any eczema, and subsequently removed from the donor panel.

Bacterial TTIs 1996 – 2020

Screening of platelet components cannot guarantee the absence of bacterial contamination. Packs are released for issue as 'negative-to-date', which may be before bacteria have multiplied sufficiently to trigger detection on screening. There have been ten bacterial near misses, all but one in platelet components, reported between 2011 and 2020. Overall, out of a total of 44 bacterial transfusion-transmissions to individual recipients, 37 (34 donations) have been caused by the transfusion of platelets, and 7 by red cells (Table 21.3) since reporting began in 1996.

Haemovigilance systems for bacterial TTI are passive, relying on clinical colleagues to suspect and report TTI. Current BSH guidance recommends that patients are advised to report any symptoms that occur within 24 hours of transfusion (BSH Tinegate et al. 2012) although our experience suggests that patients with confirmed bacterial TTI become unwell very rapidly, often during transfusion.

Table 21.1: Bacterial screening methods used by the UK Blood Services

UK Blood Service	Time of sampling (hour)	Volume sampled (mL)	Apheresis sample	Time at release (hour)	Length of screening
NHSBT	≥36	2 x 8	Post-split	6	Day 7
NIBTS	≥36	2 x 8	Pre-split	6	Day 9
SNBTS	≥36	2 x 8	Pre-split	6	Day 7
WBS	≥36	2 x 8	Post-split	12	Day 7

**Screening methods in Wales changed mid-2018 from testing on day 1 and day 4 to testing on day 2 only*

Viral TTI reports 2020

In 2020, there was one probable HBV TTI reported by NHSBT.

Case 21.1: Probable HBV TTI case: (Morbidity: – 0; imputability: 2 – probable)

A male in his 50s was diagnosed with an acute HBV infection following a routine dialysis screening, which included testing for HBsAg. The case was initially reported to PHE by the renal team following the first HBsAg positive result.

Retrospective testing of patient samples found HBV DNA in a December 2019 sample; samples tested prior to that were negative for HBV including anti-HBc. No other source or risk factors for HBV infection were identified, but it should be noted that the patient was born in a part of the world where HBV is endemic, and hence reactivation cannot be completely excluded. Staff and patient screening were performed, and no obvious source was found. The patient had not been vaccinated against HBV and did not present with any symptoms.

Blood transfusions from the previous 6 months were identified; these included 11 donor exposures. A total of 10 returning donors tested negative for anti-HBc, the remaining blood donor tested positive for anti-HBc. They had given three previous donations, and these were found positive for anti-HBc in retrospective testing. HBV DNA was detected in the implicated red cell donation at 8.6IU/mL; lookback into FFP and two HBV DNA-negative donations are still on-going. All three donations were HBsAg negative on screening, and no HBV DNA was detected at the time of donation. This is in keeping with an OBI in the donor, who was born in an HBV endemic country. The donor has been informed that they have OBI and has been referred for specialist care. They can no longer donate blood.

A large volume follow-up sample was obtained from this donor to allow further sequence comparison between their sample and recipient sample. Unfortunately, HBV DNA was not detectable on the donor sample despite concentration (note low levels of fluctuating HBV DNA is typical in OBI). The recipient sample was identified as HBV genotype E; the common type identified in Sub-Saharan Africa and keeping with transmission.

Based on our investigations, it is probable that this patient acquired HBV infection via blood transfusion.

Case 21.2: 2019 - Probable HEV TTI case from 2019

This was a multi-transfused female in her 20s with aplastic anaemia and Turners syndrome. She was diagnosed with HEV infection in August 2019, and although the virus has now cleared from her blood, anti-viral treatment has not been stopped yet (due to her immunosuppression). Fortunately, her ALT levels have remained normal and she has not developed a hepatitis.

It was identified retrospectively that a red cell donation she received in June 2019 contained a small amount of HEV RNA (31IU/mL). This unit was tested correctly at the time of donation testing, but HEV RNA was not detectable with the screening assay at this level (a detection limit around 500IU/mL). Due to the small viral load, we could not do sequencing to confirm the transmission and hence the case is reported as probable. It is recognised that the current HEV screening in place in England will not be able to identify donations with a very small amount of HEV RNA.

Viral TTI 1996 – 2020

Transfusion may occur many years prior to the year in which the incident is investigated and reported to SHOT because of the chronic nature, and therefore late recognition, of some viral infections. Since 1996, 42 confirmed transfusion-transmitted viral infections have been documented in the UK, involving 35 donors. Among these, HBV (n=12) and HEV (n=12) were the most commonly reported and proven viral TTI. This is partly because the 'window period' where an infectious donation from a recently infected donor cannot be detected by the screening tests is longer for HBV than for HCV or HIV, despite NAT screening of blood donations.

Evidence relating to transmission of OBI in the UK is emerging. Donors with this chronic form of HBV

infection were thought to typically have a level of HBV DNA that was very unlikely to transmit, however 5 reports have been made of an HBV infection in recipients who had received components from donors with OBI in England; transmission could not be confirmed because of a lack of sequencing information.

All except 2 HEV transmissions were reported before the HEV RNA screening was introduced in April 2017 in the UK. The UK Blood Services were amongst the first to introduce HEV screening; since then 1,770 HEV RNA containing donations have been successfully identified by screening and removed from the blood supply. The rate of HEV RNA detected among donors is greater than other viral infections because it is generally acquired through food, and there is no specific donor selection to minimise donations from those infected. This gives rise to an increased chance of a donation being collected from an infected donor/individual. Furthermore, as screening is performed in pools, it is recognised that donations containing a small amount of HEV RNA can be missed and potentially transmitted via blood transfusion.

Residual risk of HBV, HCV, or HIV

The risks of a potentially infectious HBV, HCV or HIV donation not being detected (due to the window period) in the UK are very low at less than 1 per million donations tested (Table 21.2) (JPAC, 2020). The calculations are made annually, but for HBV only consider the risk of non-detection of acute infections and not the risk of non-detection of an OBI.

Table 21.2: The estimated residual risk (and 95% confidence interval) that a donation made in the HBV, HCV and HIV window period is not detected on screening UK: 2017-2019

	HBV	HCV	HIV
Number per million donations	0.87	<0.01	0.04
95% confidence interval	*(0.35-1.70)*	*(0.00-0.05)*	*(0.01-0.09)*
At 1.9 million donations per year, testing will miss a potentially infectious window period donation every:	6 months	90 years	15 years

**The window period is the time very early in the course of infection when tests in use do not detect the virus but the viral load may be sufficient to transmit infection*

Far fewer TTI are observed in practice than the estimated risks in Table 21.2 indicate, partly because the estimates have wide uncertainty and the model used to calculate risk is based on the risk in all donations tested. The model does not adjust for other factors, such as packs which are not transfused, recipient susceptibility to infection, or under-ascertainment/under-reporting, for example due to recipients dying from an underlying medical condition before a chronic asymptomatic viral condition is identified, or, in the case of HBV, an asymptomatic acute infection.

Blood donation screening process

Every blood donation in the UK is screened for HBV, HCV, HEV, HIV and syphilis. HTLV is screened for in donations from new blood donors and other infections such as malaria are screened for depending on travel history of the donor. A separate bacterial screening process is also in place for platelets as the storage of platelets at 22 ±2°C encourages bacterial growth.

At the time of blood donation, blood samples are collected for screening purposes. For the screening of viral nucleic acids (RNA or DNA) blood samples from different donors are pooled together in a batch of six, 16 or 24 prior to screening. If RNA/DNA is detected in that pool, then individual samples known to be in that pool are re-tested individually in order to identify positive samples. All antibody and/or antigen testing is done using individual blood samples. If RNA/DNA is detected, or antibody result is repeatedly positive suggesting an infection then the donation is discarded, and the sample is sent to a reference laboratory for further testing to confirm the result. If a positive result is confirmed the donor will be notified, offered an opportunity to discuss these results in detail and referred to the appropriate medical care as necessary.

Testing and selection of donors - update 2020

No major changes to testing procedures or donor selection in regard to known TTI occurred in 2020. The HBV and HEV screening processes are currently under review by SaBTO.

The FAIR (For the Assessment of Individualised Risk) steering group concluded their work and reported on their findings that a recommendation for a more individualised approach to donor selection was feasible in the UK. The group included representatives from the UK Blood Services, PHE, University of Nottingham and a range of stakeholders including donors, recipients and LGBTQ+ groups. This approach was accepted by health ministers and is expected to be implemented in the summer of 2021. Under this new donor selection policy, donors who have had the same sexual partner (and no others) in the last three months and who do not have an STI should be eligible to donate. This will allow more gay and bisexual men to donate blood.

More information is available here: https://www.blood.co.uk/news-and-campaigns/news-and-statements/fair-steering-group/

Parasitic TTI

There were no reported parasitic infections for investigation in 2020.

Emerging infections

The EIR produced by the NHSBT/PHE Epidemiology Unit is distributed monthly. A range of sources are reviewed for relevant infection issues relating to patient safety and/or blood and tissue availability in the UK and collated into a monthly listing. Sources include outbreak alerts, various regular outbreak surveillance reports, journals, websites, and online news resources, listed in more detail below.

The EIR is sent to the chair of the SACTTI. The chair of SACTTI also receives early warning communications or other reports deemed urgent as they arise.

These monthly listings, alongside other sources of information are reviewed by SACTTI and may lead to further risk assessment and changes to the donor selection guidelines, or other blood safety measures, where necessary.

Currently West Nile Virus and Usutu virus are spreading in Europe, with the latter presenting in birds in the UK. The current situation is being monitored carefully and all blood donors from infected regions are screened for both viruses.

Variant Creutzfeldt Jakob Disease (vCJD) 2020

There were no vCJD investigations in 2020.

vCJD 1996-2020

Three vCJD incidents (Table 21.3) took place prior to the introduction of leucodepletion and other measures taken by the UK Blood Services to reduce the risk of vCJD transmission by blood, plasma and tissue products. All these measures have been reviewed and endorsed by SaBTO (SaBTO 2013).

One of these measures, the provision of imported plasma for individuals born on or after 1st January 1996, was withdrawn in September 2019. This followed a recommendation by SaBTO based on evaluation of the risk of transmission of vCJD. Other risk-reduction measures, such as leucodepletion, remain in place (SaBTO 2019).

SARS-CoV-2

As part of the convalescent plasma trials, NHSBT screened over 1000 donors for SARS-CoV-2 RNA, even though the risk of viremia is considered to be very low. All of the screened donations were negative. In addition to this, any units obtained from donors subsequently diagnosed with SARS-CoV-2 (within 5 days from infection) were re-called and discarded. There were no known cases of transfusion-transmitted SARS-CoV-2 infections reported to NHSBT in 2020 and there is currently no evidence that SARS-CoV-2 is a TTI. SNBTS reported two investigations for recipients who developed COVID-19; the archive samples were tested and found to be negative.

Table 21.3: Number of confirmed TTI incidents, by year of transfusion with total infected recipients and outcomes (death, major morbidity, minor morbidity) in the UK between October 1996 and December 2020 (Scotland included from October 1998)

Year of transfusion*	Number of incidents (recipients) by infection											Implicated component				
	Bacteria	HAV	HBV	HCV	HEV	HIV	HTLV I	Parvovirus (B19)	Malaria	vCJD/prion	Total	RBC	Pooled platelet	Apheresis platelet	FFP	Cryo
Pre 1996	-	-	1 (1)	-	-	-	2 (2)	-	-	-	**3 (3)**	3	-	-	-	-
1996	-	1 (1)	1 (1)	1 (1)	-	1 (3)	-	-	-	1 (1)	**5 (7)**	5	1	-	1	-
1997	3 (3)	-	1 (1)	1 (1)	-	-	-	-	1 (1)	2 (2)	**8 (8)**	6	1	1	-	-
1998	4 (4)	-	1 (1)	-	-	-	-	-	-	-	**5 (5)**	2	1	2	-	-
1999	4 (4)	-	2 (3)	-	-	-	-	-	-	‡ (1)	**6 (8)**	5	3	-	-	-
2000	7 (7)	1 (1)	1 (1)	-	-	-	-	-	-	-	**9 (9)**	1	5	3	-	-
2001	5 (5)	-	-	-	-	-	-	-	-	-	**5 (5)**	-	4	1	-	-
2002	1 (1)	-	1 (1)	-	-	1 (1)†	-	-	-	-	**3 (3)**	2	1	-	-	-
2003	3 (3)	-	1 (1)	-	-	-	-	-	1 (1)	-	**5 (5)**	1	1	3	-	-
2004	††	-	-	-	1 (1)	-	-	-	-	-	**1 (1)**	1	-	-	-	-
2005	2 (2)	1 (1)	1 (1)	-	-	-	-	-	-	-	**4 (4)**	1	3	-	-	-
2006	2 (2)	-	-	-	-	-	-	-	-	-	**2 (2)**	-	1	1	-	-
2007	3 (3)	-	-	-	-	-	-	-	-	-	**3 (3)**	2	1	-	-	-
2008	4 (6)	-	-	-	-	-	-	-	-	-	**4 (6)**	-	2	4	-	-
2009	2 (3)	-	-	-	-	-	-	-	-	-	**2 (3)**	1	-	2	-	-
2010	-	-	-	-	-	-	-	-	-	-	**-**	-	-	-	-	-
2011	-	-	1 (2)	-	1 (2)	-	-	-	-	-	**2 (4)**	2	-	-	2	-
2012	-	-	1 (1)	-	1 (1)	-	-	1(1)	-	-	**3 (3)**	2	-	-	1	-
2013	-	-	-	-	-	-	-	-	-	-	**-**	-	-	-	-	-
2014	-	-	-	-	2 (3)	-	-	-	-	-	**2 (3)**	1	-	-	2	-
2015	1 (1)	-	-	-	4 (5)	-	-	-	-	-	**5 (6)**	-	3	1	1	1
2016	-	-	-	-	1 (1)	-	-	-	-	-	**1 (1)**	1	-	-	-	-
2017	-	1 (1)	-	-	-	-	-	-	-	-	**1 (1)**	-	-	1	-	-
2018	-	-	-	-	1 (1)	-	-	-	-	-	**1 (1)**	-	-	1	-	-
2019	-	-	-	-	1 (1)	-	-	-	-	-	**1 (1)**	-	-	1	-	-
2020	-	-	-	-	-	-	-	-	-	-	**-**	-	-	-	-	-
Number of incidents	**41**	**4**	**12**	**2**	**12**	**2**	**2**	**1**	**2**	**3**	**81**	-	-	-	-	-
Number of infected recipients	44	4	14	2	15	4	2	1	2	4	**92**	**36**	**27**	**21**	**7**	**1**
Death due to, or contributed to, by TTI	11	0	0	0	2	0	0	0	1	3	**17**					
Major morbidity	29	3	14	2	9	4	2	1	1	1§	**66**					
Minor morbidity	4	1	0	0	4	0	0	0	0	0	**9**					
Implicated component																
RBC	7	1	11	2	4	2	2	1	2	4	**36**					
Pooled platelet	21	2	1	-	2	1	-	-	-	-	**27**					
Apheresis platelet	16	1	1	-	3	-	-	-	-	-	**21**					
FFP	-	-	1	-	5	1	-	-	-	-	**7**					
Cryoprecipitate	-	-	-	-	1	-	-	-	-	-	**1**					

Notes:

Numbers in brackets refer to recipients, and probable incidents are excluded.

No screening has been ever in place for vCJD, hepatitis A virus (HAV) or parvovirus B19. Human T cell lymphotropic virus (HTLV) screening began in 2002 and HEV was not in place at the time of the documented transmissions. In both malaria transmissions, malaria antibody testing was not applicable at the time according to information supplied at donation.

HCV investigations where the transfusion was prior to screening are not included in the above figure.

** Year of transfusion may be prior to year of report to SHOT due to delay in recognition of chronic infection.*

† The 2 HIV incidents were associated with window period donations (anti-HIV negative/HIV RNA positive) before HIV NAT screening was in place. A third window period donation in 2002 was transfused to an elderly patient, who died soon after surgery. The recipient's HIV status was therefore not determined and not included.

†† In 2004 there was an incident involving contamination of a pooled platelet pack with Staphylococcus epidermidis, which did not meet the TTI definition because transmission to the recipient was not confirmed, but it would seem likely. This case was classified as 'not transfusion-transmitted'.

‡ Same blood donor as one of the 1997 transmissions so counted as the same incident; note: counted as two separate incidents in previous reports.

§ In a further prion case the patient died but transfusion was not implicated as the cause of death. The outcome was assigned to major morbidity instead because although there was post-mortem evidence of abnormal prion proteins in the spleen the patient had died of a condition unrelated to vCJD and had shown no symptoms of vCJD prior to death.

For further information or alternative breakdown of data please contact the National Coordinator for Transfusion Transmitted Infections via the NHSBT/PHE Epidemiology Unit at epidemiology@nhsbt.nhs.uk

References

BSH Tinegate H, Birchall J, Gray A, et al. Guideline on the investigation and management of acute transfusion reactions. Prepared by the BSH Blood Transfusion Task Force. *Br J Haematol* 2012;**159(2)**:143-153.

JPAC. Position Statement: The estimated residual risk that a donation made in the infectious window period is not detected on testing: risks specific for HBV, HCV and HIV in the UK (2020). https://www.transfusionguidelines.org/document-library/position-statements [accessed 28 April 2021].

McDonald C, Allen J, Brailsford S, et al. Bacterial screening of platelet components by National Health Service Blood and Transplant, an effective risk reduction measure. *Transfusion* 2017;**57(5)**:1122-1131. doi:10.1111/trf.14085.

SaBTO. Measures currently in place in the UK to reduce the potential risk of transmitting variant Creutzfeldt-Jakob disease via blood (2013). https://www.gov.uk/government/publications/current-measures-to-reduce-the-risk-of-vcjd-transmission-by-blood [accessed 28 April 2021].

SaBTO. Importation of plasma and use of apheresis platelets as risk reduction measures for variant Creutzfeldt-Jakob Disease (2019). https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/829906/SaBTO_PC_report.pdf [accessed 28 April 2021].


LEARNING
TEAM
LEARNING
TEAM

SPECIAL CLINICAL GROUPS

22 Cell Salvage (CS) n=23

Author: Sarah Haynes

Definition:

Any adverse events or reactions associated with cell salvage (autologous) transfusion methods, including intraoperative and postoperative cell salvage (washed or unwashed).

Key SHOT messages

- All cell salvage related incidents should be reported to SHOT
- All staff members involved in the cell salvage process should have a level of knowledge and understanding consistent with their role

Abbreviations used in this chapter

CS	Cell salvage
EPR	Electronic patient record
ICS	Intraoperative cell salvage
ICU	Intensive care unit
LIMS	Laboratory information management system
MHRA	Medicines and Healthcare products Regulatory Agency
IV	Intravenous

Recommendations

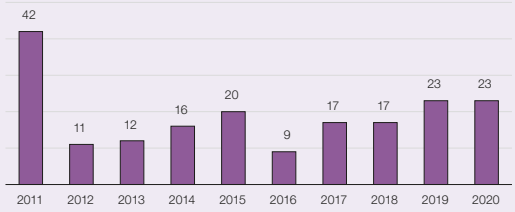
- Organisations should ensure that the provision of cell salvage is recorded within the patient record in an auditable format that includes the volume of red cells transfused. Consideration should be given as to how this data might be shared electronically (e.g. within the electronic patient record (EPR) or laboratory information management system (LIMS))
- All organisations should develop a robust system for reporting all adverse incidents/reactions related to cell salvage, preferably reporting to the hospital transfusion committee and onward to SHOT
- Healthcare organisations should ensure that adequate and appropriate training is delivered to all staff groups involved in the cell salvage process
- Devices should be checked after servicing to verify that everything is as expected before the device is put back into use. Operators should go through a basic system check before starting a procedure which includes programming parameters

Action: Cell salvage leads, theatre leads, hospital transfusion teams, hospital transfusion committees

Headline data 2020

Number of reports n=23
Deaths n=0
Major morbidity n=0

CS reports by year



Demographic data

Male n=9
Female n=14
Adults n=23
Paediatric n=0

Blood component data

Red cells n=23
Platelets n=0
Plasma n=0
Multiple Components n=0
Other n=0

Introduction

Twenty-three cases were reported from eight reporting Trusts/Health Boards; on review none were withdrawn or transferred from other reporting categories. All 23 cases related to the use of ICS. There were no reported adverse reactions, deaths or morbidities attributed to cell salvage.

All reported incidents were categorised as adverse events. Of these, 12 were attributed to failures of machine or disposables, the majority of these being related to a field safety notice published by the MHRA in October 2019 (MHRA 2019).

As with previous years, incidents were probably under-reported. Without robust denominator data however, it is difficult to know how this reporting rate compares to previous years. It is highly likely that the use of cell salvage in elective surgery was reduced as surgical activity itself was impacted by COVID-19.

Deaths n=0

Major morbidity n=0

Cell salvage adverse events n=23

All 23 incidents were in adult patients, with an age range of 18 to 85 years old. Fourteen patients were women, 9 were men.

Speciality	Elective	Emergency	Total
Gynaecology	1	-	**1**
Obstetrics	2	7	**9**
Orthopaedic	2	1	**3**
Spinal	3	-	**3**
Trauma	-	2	**2**
Urology	2	-	**2**
Vascular	3	-	**3**
Total	**13**	**10**	**23**

Table 22.1: Specialty for cell salvage reports

Equipment failure n=12

In October 2019, a field safety notice (MHRA 2019) identified a potential issue with one manufacturer's bowl sets (single use disposables) used to process red cells. The issue related to radial cracks developing in the inner core of some bowl sets, leading to fluid leaking into the core. The user is alerted to this issue by the device displaying a 'Long Empty' error message as the expected volume on emptying is exceeded as the fluid draining from the core is added to the processed red cells. The risks of this are that the fluid retained in the core is not washed and may contain haemolysed red cells and free haemoglobin which could be reinfused to the patient. Suggested corrective actions included changing the bowl set and rewashing any processed blood.

In this year's incidents, 9 equipment failures related to 'Long Empty' error messages. On all occasions the problem was identified mid procedure after a number of processing cycles had been completed. This resulted in interruption (whilst disposables were replaced) or curtailment of the cell salvage process. All of these incidents were reported to the MHRA under the yellow card scheme.

The remaining 3 equipment failures related to manufacturing flaws in the collection reservoir in 2 cases and a bowl set in 1 case. Only 1 of these incidents was notified to the MHRA.

Over the same reporting period the MHRA yellow card scheme had 24 incident reports relating to cell salvage devices and disposables, suggesting a further 14 cases not reported to SHOT.

Technical errors n=6

There were 4 incidents involving incorrect selection of the appropriate administration set for infusion. In 3 incidents a standard fluid giving set as opposed to a blood administration set was set up or used. All 3 cases occurred in the obstetric setting following emergency caesarean section and involved handover to another member of staff. In 1 of these cases, the administration set was changed, but infusion was subsequently abandoned as a pressure cuff was inappropriately and unsuccessfully employed. In the 4th case a standard blood giving set was used where a leucocyte depletion filter was indicated for a malignant urology case.

In another incident non-IV saline was used for the swab wash which resulted in the cell salvage collection being abandoned. The patient in his 80s was undergoing an open reduction internal fixation of a left distal femur periprosthetic fracture. He subsequently received a unit of allogeneic blood 4 days postoperatively which may have been avoided if the cell salvage process had not been contaminated. Contraindicated substances were aspirated into the blood collection in another incident resulting in abandonment of the cell salvage process.

Learning points

- Cell salvage involves the collection, processing, and reinfusion of blood. Several staff may be involved in that chain of events and they should have sufficient knowledge and training to understand their responsibilities to ensure the safety of the procedure
- Reinfusion of salvaged red cells should be undertaken using an administration set designed to filter particles that are potentially harmful to the patient. The use of a more specialised filter, such as a leucocyte depletion filter, should be considered in relation to clinical need and policy

Other adverse events n=5

As seen in previous years, there were 3 further cases of unidentified black particles seen in the salvaged red cell reinfusion bag. Two of these incidents were in obstetric cases and 1 in orthopaedic surgery. All were from the same reporting centre and the reporter states that there have now been 11 such cases since January 2019. Further investigations are underway in collaboration with the manufacturer to assess practice, environment, and any other contributory factors.

Case 22.1: Massive obstetric haemorrhage patient unable to receive reinfusion of red cells due to suspected machine failure

In an emergency caesarean section, 3L of blood was collected and was being processed. The cell salvage operator became concerned that the quality of the reinfusion product was suboptimal as the device was not showing the washing efficiency as it normally would. The machine was swapped for a second device and the same issue occurred. After discussion with the anaesthetist, the cell salvage process was abandoned and a decision to use allogeneic blood made. Subsequent investigation revealed that the cell salvage devices had been serviced by a third-party engineer. The programming was changed to factory default settings with the wash quality settings routinely used in the hospital turned off. This had not been communicated to the cell salvage lead and the devices were assumed to be working as normal after servicing.

This case demonstrates the importance of a process for device acceptance testing post service or repair. Any issues should be identified at this point and rectified to prevent adverse patient impact.

Case 22.2: Cell salvage used outside of guidelines in massive obstetric haemorrhage with successful outcome

A parturient in her 20s, with an abnormally invasive placenta, underwent an emergency caesarean section. Massive blood loss ensued, estimated in the region of 10L, and a hysterectomy was required. Cell salvage was utilised and within the urgency of the situation the surgeons made an on the spot decision to salvage blood lost from the vagina as well as the abdomen. This was not communicated to the cell salvage operator or anaesthetist at the time. Blood salvage from vaginal loss was outside of institutional guidelines. All blood collected was processed and 2496mL of salvaged red cells reinfused without the use of a leucocyte reduction filter, along with over 30 units of allogeneic blood components. The patient recovered well without the need for ICU admission. There were no signs of transfusion reaction or bacterial contamination.

Commentary: Salvaging red cells from lower genitourinary tract bleeding has been proposed previously but remains controversial. Teare et al. (2015) published a small study in 50 women where vaginal blood loss was collected and processed, but not reinfused. The quality of the salvaged product was tested and found to be satisfactory. Bacterial contamination was present, but not in significantly high enough concentration to be deemed clinically significant. In 2018, a small series of cases was published (Lim et al. 2018) in which 10 out of 28 women had sufficient salvaged red cells to be reinfused after vaginal delivery. Although there were no instances of postpartum sepsis, wound infection or thromboembolism, there was one suspected amniotic fluid embolism, but symptoms started before the reinfusion of the salvaged red cells. More research is needed in larger clinical trials before the safety and effectiveness of this intervention can be proven if it is to be adopted into routine practice. However, in the case reported above, in extremis, the additional red cells salvaged may have made a difference. The issue here was that not everyone was engaged in making the decision and given the opportunity to consider the relative risks and benefits to the patient.

Learning point

- A fast-moving emergent scenario may result in decisions that are centred on an individual patient's circumstances and fall outside of current guidance. Care should be taken to ensure that any decisions align within the standard of care provided by a medical practitioner (Hurwitz 2004). These decisions must be clearly documented in the patient's clinical notes including the rationale for the decision

Conclusion

The safe execution of cell salvage relies on everyone involved in the process understanding their role and responsibilities. There are three distinct phases to cell salvage that cannot be undertaken by a single person. The quality of the collected blood, the correct processing of that blood and the safe reinfusion

of the washed red cells can be influenced by all those involved. It is imperative to provide adequate and appropriate training, including updates, to support all staff involved in the cell salvage process.

Recommended resources

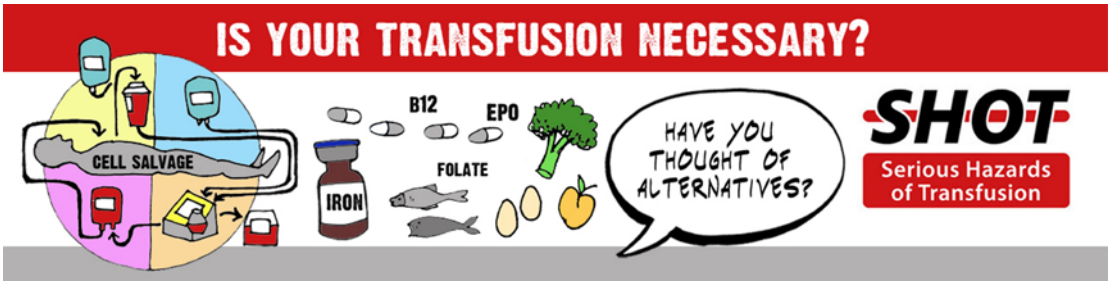
UKCSAG technical factsheets

Staff responsibilities: https://www.transfusionguidelines.org/document-library/documents/factsheet-10-staff-responsibilities-version-1/download-file/Factsheet%2010%20-%20Staff%20Responsibilities%20%28version%201%29.pdf

Use of filters: https://www.transfusionguidelines.org/document-library/documents/factsheet-7-use-of-filters-version-2/download-file/Factsheet%207%20-%20Use%20of%20filters%20%28version%202%29.pdf

Intraoperative cell salvage education

https://www.transfusionguidelines.org/transfusion-practice/uk-cell-salvage-action-group/intraoperative-cell-salvage-education



References

Hurwitz B. How does evidence based guidance influence determinations of medical negligence? *BMJ* 2004;**329**:1024-1028.

Lim G, Kotsis E, Zorn JM, et al. Cell salvage for postpartum haemorrhage during vaginal delivery: a case series. *Blood Transfus* 2018;**16(6)**:498-501.

MHRA. Field Safety Notice 2019/011/001/701/025 (2019). https://mhra-gov.filecamp.com/s/AYMLuOqjtldEbwql/d. [accessed 28 April 2021].

Teare KM, Sullivan IJ and Ralph CJ. Is cell salvaged vaginal blood loss suitable for re-infusion? *Int J Obstet Anesth* 2015;**24(2)**:103-10.

Paediatric Cases n=159

23

Authors: Anne Kelly and Helen New

Definition:

Paediatric cases comprise all reports for patients under 18 years of age, including all paediatric cases from the other chapters in this report. Paediatric reports have been subdivided by recipient age group: neonates ≤28 days; infants >28 days and <1 year; children ≥1 year to <16 years and young people aged 16 to <18 years.

Key SHOT messages

- Massive blood loss in children is less common than in adults and hospitals should have protocols in place for appropriate and timely management
- Communication and education regarding specific requirements and their indications remains vital
- Management of D-incompatible platelet transfusions in neonates and children should be discussed with a haematologist
- Education and training resources should be provided for those administering neonatal transfusions to reduce errors

Abbreviations used in this chapter

ADU	Avoidable, delayed and under/overtransfusion
ATG	Anti-thymocyte globulin
BMS	Biomedical scientist
BSH	British Society for Haematology
CMV	Cytomegalovirus
DHTR	Delayed haemolytic transfusion reaction
ECMO	Extracorporeal membrane oxygenation
ED	Emergency department
FAHR	Febrile, allergic and hypotensive reactions
FFP	Fresh frozen plasma
Hb	Haemoglobin
HSE	Handling and storage errors
HTR	Haemolytic transfusion reactions
IBCT	Incorrect blood component transfused
Ig	Immunoglobulin
IT	Information technology
IV	Intravenous
LIMS	Laboratory information management system
MB	Methylene blue-treated
NHSBT	National Health Service Blood & Transplant
NM	Near miss
PAS	Platelet additive solution
PICU	Paediatric intensive care unit
RBRP	Right blood right patient
SCID	Severe combined immunodeficiency
SRNM	Specific requirements not met
TACO	Transfusion-associated circulatory overload
TAD	Transfusion-associated dyspnoea
TANEC	Transfusion-associated necrotising enterocolitis
TRALI	Transfusion-related acute lung injury
TTI	Transfusion-transmitted infection
UCT	Uncommon complications of transfusion
VSD	Ventricular septal defect
WCT	Wrong component transfused

Recommendations

- Departments should ensure major haemorrhage protocols for children are available and are used (see also Recommendations in Chapter 12a, Delayed Transfusions)
- Irradiation guidelines have been revised and published recently. Local education programs should be updated to include indications for special requirements in line with national guidelines

Action: Hospital transfusion laboratory, transfusion practitioners, clinical transfusion staff

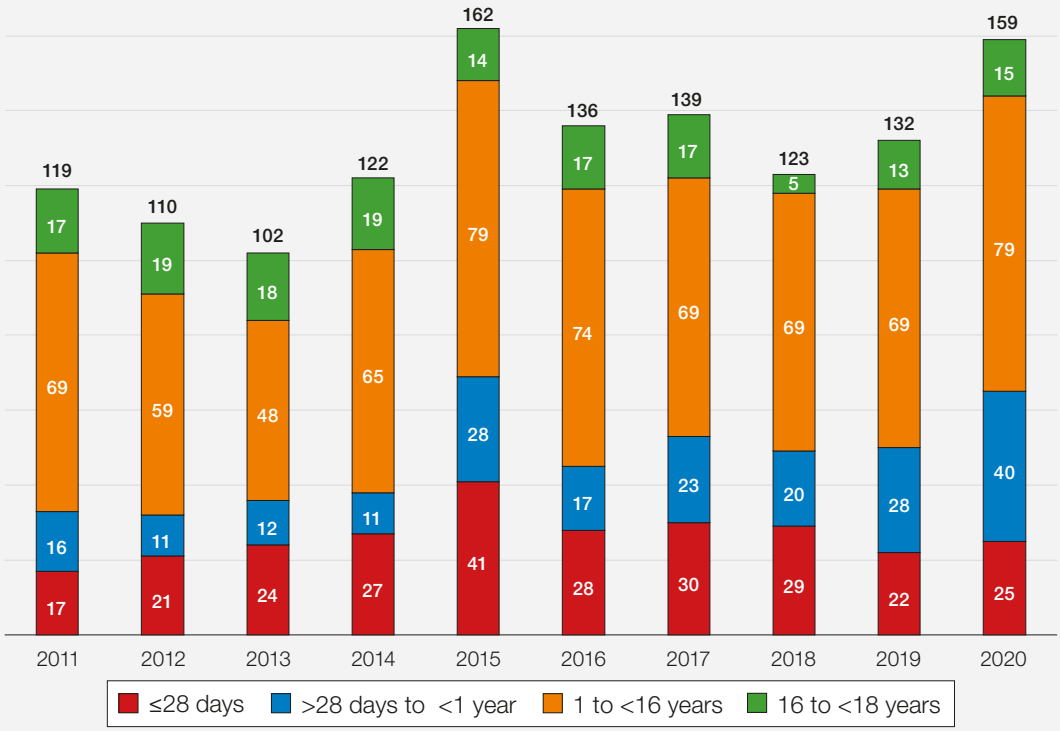
Introduction

There were more reports in 2020 compared to the previous year (159 vs 132, Figure 23.1). Paediatric cases accounted for 8.5% (159/1877) of total cases analysed excluding NM and RBRP, and 8.4% (271/3214) if NM and RBRP are included.

Approximately a third of reports are in children under the age of 1 year, highlighting the issues around transfusion in this patient group, particularly for error-related reports (Figure 23.2). The overall pattern of case reports is consistent with previous years (Figure 23.3). Children continue to be over-represented in reports in the FAHR and IBCT-WCT categories, and there was a striking increase in the number of paediatric FAHR reports following platelet transfusion. This year there were no FAHR cases reported in infants under the age of 1 year.

The proportion of error reports considered to originate primarily in the laboratory was 51.6% (48/93). This proportion increased significantly from 39.5% (34/86) in 2019, but 9 cases were from a single centre following a look back exercise. The laboratory error reports were in the following categories: ADU, 12/35 reports (34.3%); IBCT-WCT 19/23 (82.6%); IBCT-SRNM, 15/21 (71.4%) and HSE, 2/15 (13.3%).

Figure 23.1: Trends in paediatric reports from 2010-2020



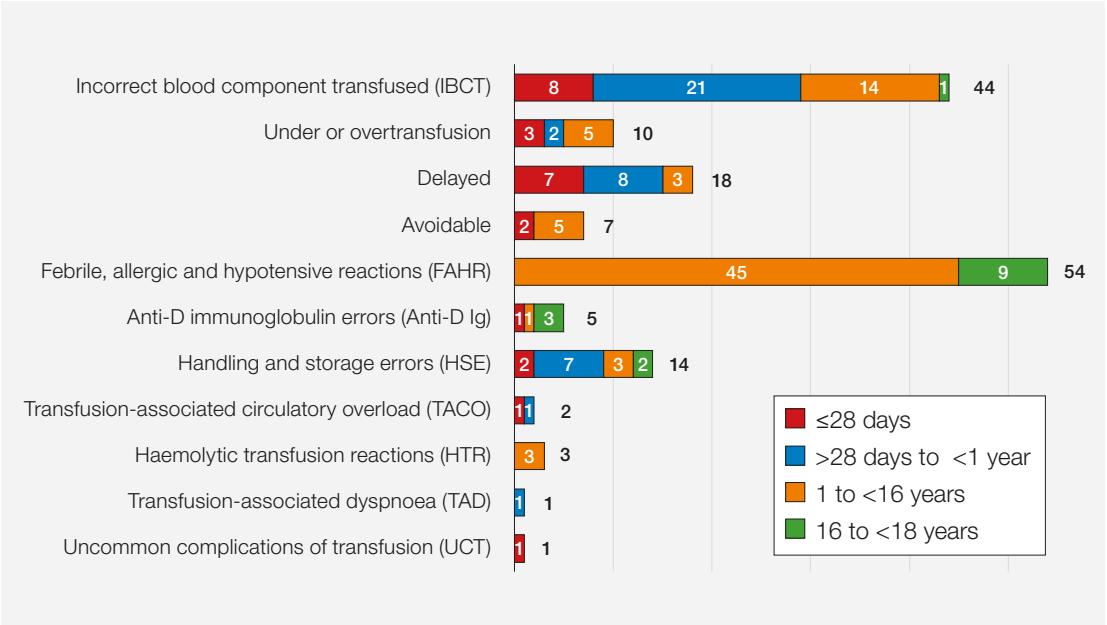


Figure 23.2: Summary of paediatric cases by category and age 2020 (n=159)

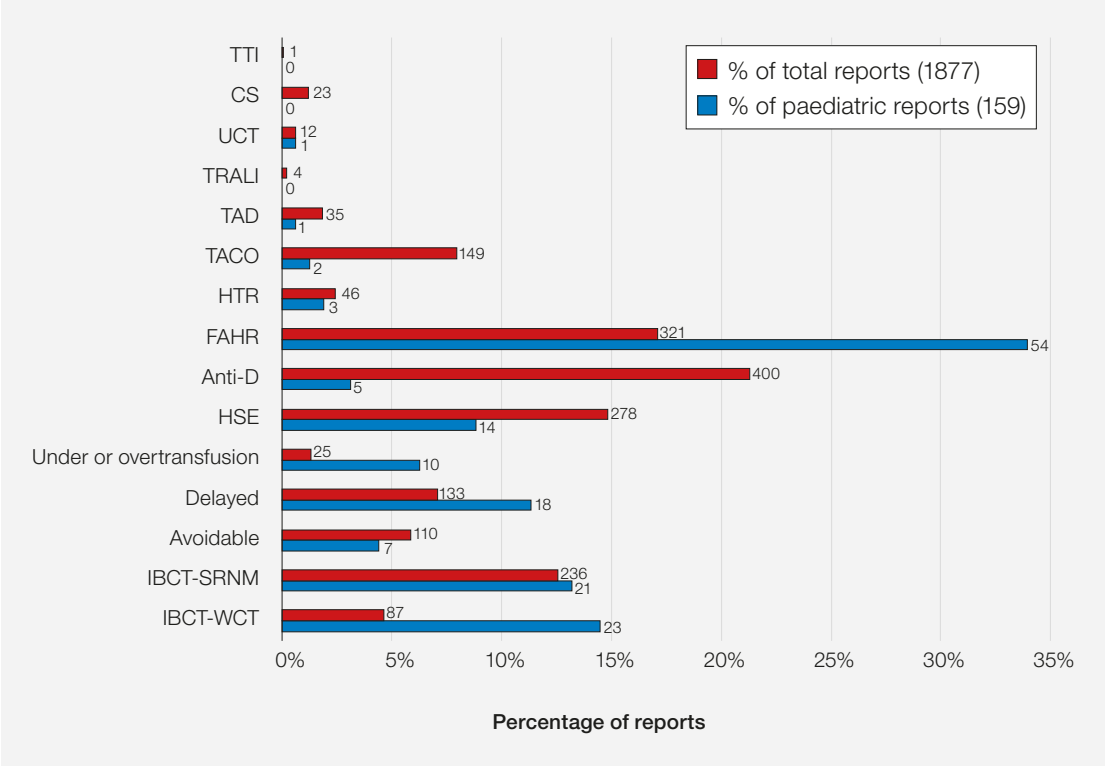


Figure 23.3: Percentages of paediatric and total reports in each category

TTI=transfusion-transmitted infection; UCT=uncommon complications of transfusion; TRALI=transfusion-related acute lung injury; TAD=transfusion-associated dyspnoea; TACO=transfusion-associated circulatory overload; HTR=haemolytic transfusion reactions; FAHR=febrile, allergic and hypotensive reactions; HSE=handling and storage errors; IBCT-SRNM=incorrect blood component transfused-specific requirements not met; IBCT-WCT=IBCT-wrong component transfused

Deaths due to transfusion n=3

There were 9 deaths, with 3 assessed as being possibly or probably related to transfusion. One of these was a case of TANEC where the imputability was only 1 (possible).

The other 2 cases involved the timely management and provision of blood components to bleeding patients following biopsies. Both were in the ADU category, with significant delays in recognition of the severity of haemorrhage and in activating major haemorrhage protocols.

Case 23.1: Transfusion delay and death due to multiple factors

A young infant had a liver biopsy performed. Post procedure they developed internal bleeding, and this was not noticed. There was then a delay activating the major haemorrhage protocol and a delay in recognising the need for the neonatal O D-negative blood, which was available. This resulted in a delay of over 3 hours before the infant received any red cells. This was partly due to communication issues. The patient did not survive.

Case 23.2: Delay in recognising major haemorrhage

A 2kg infant was admitted to the ED overnight with rectal bleeding following a suction rectal biopsy which had been performed the day before. There was history of two blood filled nappies at home and a further nappy in the ED which was filled with blood and clots. There was a nearly 2-hour delay in obtaining IV access, including a delay in escalation to intra-osseous access. The major haemorrhage protocol was not activated. The baby became significantly acidotic. During resuscitation the baby suddenly developed bleeding from the mouth and nose and had a cardiopulmonary arrest. A chest X-ray performed shortly afterwards showed a 'white out'. Overall significant volumes of red cells and Octaplas® were given. The child was transferred to PICU but did not survive.

Delays in recognising the severity of the bleeding and activation of the major haemorrhage protocol contributed to patient death.

Imputability was recorded as probable in cases 23.1 and 23.2. Both cases illustrate the need for specific paediatric major haemorrhage protocols to be available and activated in massive haemorrhage situations (see also Chapter 12a, Delayed Transfusions).

Learning points

- Protocols should be in place for the management of massive haemorrhage in infants and children. These should include guidance on the appropriate component volumes to be used in resuscitation
- If in doubt the major haemorrhage protocol should be activated

Major morbidity n=19

FAHR was the most common cause of major morbidity in the paediatric reports (16/19, 84.2%), 2 following red cells and 14 platelets.

The other major morbidity cases included:

- One in the ADU category involving a delay in transfusion with a missed opportunity to use available emergency neonatal O D-negative red cells
- A case of HTR involving a young teenager with sickle cell anaemia who developed a delayed haemolytic transfusion reaction secondary to anti-E
- A case of hyperhaemolysis in a child with sickle cell anaemia who had several alloantibodies

Error reports n=98

Incorrect blood component transfused (IBCT) n=44

IBCT-wrong component transfused (WCT) n=23

There was a significant increase in IBCT-WCT compared to last year's report (2019 n=10) due to an increase in laboratory errors, with 9 coming from the same reporting organisation.

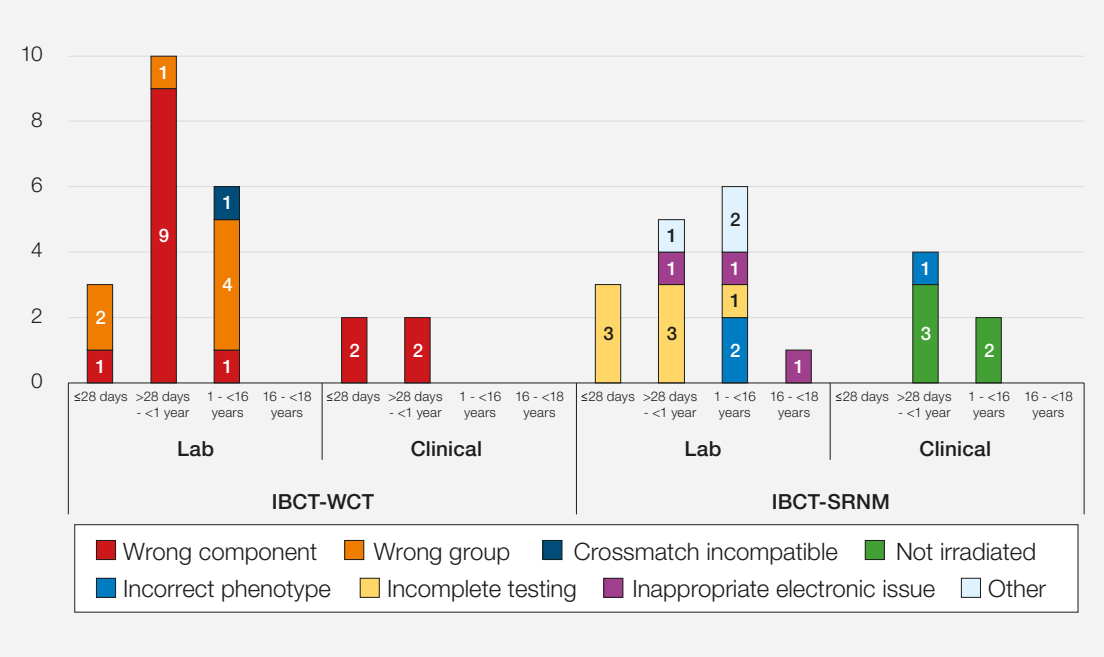


Figure 23.4: Breakdown of incorrect blood component transfused reports (n=44)

IBCT-WCT=incorrect blood component transfused-wrong component transfused; IBCT-SRNM=IBCT-specific requirements not met; MB=methylene blue-treated; SD=solvent-detergent treated

Note: Category 'other' includes invalid sample (n=1), K positive red cells to individual with childbearing potential (n=1), failure to provide washed platelets (n=1)

IBCT-WCT clinical errors n=4

Adult emergency blood given to neonates n=4

All 4 cases where the error was judged to be clinical involved transfusion of adult specification O D-negative red cells to a child under the age of 1 year. Two were newborn babies and 2 were 1 month of age. In all 4 cases the correct neonatal/infant specification red cells were available in the same blood refrigerator, but the adult component was selected in error. This is an ongoing issue, discussed in previous Annual SHOT Reports.

IBCT-WCT laboratory errors n=19

Of these, 9 reports were from the same hospital (part of a 'look-back' exercise), involving adult components issued to infants ranging in age from 1-7 months (see discussion and learning point in Chapter 10, Incorrect Blood Component Transfused (IBCT)).

There were 2 cases of D-positive platelets issued to D-negative patients, one of whom was female and subsequently given anti-D Ig. In 1 case a neonate was accidentally issued cryoprecipitate rather than FFP and one unit was transfused before the error was realised. One child received a red cell unit where the compatibility from a crossmatch was not fully confirmed. One child who was group A received a non-high titre negative group O platelet unit, with no sequelae.

Grouping errors occurred in 3 cases. In 2 of these, non-group O patients received group O red cells, 1 due to a transcription error and 1 due to a technical grouping error. There was also a case of failure to provide red cells that were compatible with both mother and baby ABO group for a baby on ECMO.

Learning point

- Laboratory staff should be fully trained and aware of procedures for pre-transfusion compatibility testing and component selection in infants under 4 months of age, including understanding the need to consider the maternal group and antibody screen. This was highlighted in a recommendation in the 2016 Annual SHOT Report (Bolton-Maggs et al. 2017)

In 1 case a young child was given multiple neonatal red cell split packs because the ward requested 'paediatric units' (instead of a standard full-sized pack as indicated for children from 1 year of age) each via a different giving set. This resulted in significant undertransfusion.

Learning points

- Imprecise terminology around different component types can be confusing, resulting in incorrect ordering and risk of either wastage of components or over transfusion
- Neonatal/infant specifications are recommended for children <1 year of age. From the age of 1 year, children are usually provided with components of the same specification as adults
- Information on the specification of components for neonates/infants and children are available in the British Society for Haematology (BSH) guidelines (BSH New at al. 2016 and 2020)
- Selection of the appropriate component should be the responsibility of the hospital transfusion laboratory taking into account information from the clinical team. This highlights the importance of communication between clinical and laboratory transfusion teams

There was 1 case of a D-positive red cell transfusion to a D-negative patient with sickle cell disease, discussed in Chapter 24, Haemoglobin Disorders (Case 24.6).

IBCT-specific requirements not met (SRNM) n=21 (15 laboratory, 6 clinical)

IBCT-SRNM clinical errors n=6

One clinical communication error resulted in the failure to perform full phenotyping for a child with sickle cell disease.

The other 5 errors were failure to provide irradiated components. The indications for irradiation were: Di George syndrome, previous intrauterine transfusion, SCID, stem cell transplant and ATG therapy.

Case 23.3: Infant with Di George syndrome received non-irradiated components

A young infant was transferred to a cardiac surgical centre for repair of a VSD. Red cells were ordered in preparation for the surgery and the BMS asked the clinicians if irradiated components were required. The conclusion was that there was a low risk of Di George and so non-irradiated units were issued. The next morning the laboratory was informed that genetic testing had confirmed Di George syndrome and that the clinicians wanted components for future transfusions to be irradiated.

Case 23.4: Multiple non-irradiated components given to an infant with SCID

An infant with suspected SCID, on PICU with seizures, diarrhoea and a CMV infection, was given five red cell transfusions before the transfusion laboratory were informed of the need for irradiated blood. The intensive care medical staff were not aware of the need for irradiated components in this patient group.

This case highlights the need for education of all paediatric staff groups regarding the indications for irradiated blood components.

The UK irradiation guidelines have recently been revised (Foukaneli et al. 2020). Irradiation of cellular components for patients with diagnosed or suspected Di George syndrome is no longer required for infants and children <2 years of age *provided* immunological testing has shown sufficient T lymphocytes (both total and naïve), or for older children and adults provided there is no significant history of infection suggestive of severe T-lymphocyte immunodeficiency.

Learning points

- It is important that all clinical staff understand the indications for irradiated components or are aware of how to access this information
- Updated irradiation guidelines are available to support decision making (Foukaneli et al. 2020) and should be reflected in local procedures and policies

IBCT-SRNM laboratory errors n=15

Failure to provide antigen-negative component n=1

A preterm neonate whose mother had documented anti-c received a transfusion of O D-negative red cells (c-positive). The investigation of the mother's previous positive antibody screen had not been recorded clearly in the LIMS.

Inappropriate electronic issue n=4

These cases include an infant with no antibody screen, an infant whose mother had detectable anti-D with no current maternal or infant sample, electronic issue for a child who had had a sibling allograft (there was also no record of this in the blood transfusion laboratory) and a child with HbSD (compound heterozygous haemoglobinopathy) who had blood components issued inappropriately through electronic issue, contrary to local policy.

Failure to perform antibody screen on maternal blood (neonatal transfusion) n=3

See learning point above from IBCT-WCT regarding pre-transfusion compatibility testing.

No valid antibody screen n=2

Two infants under the age of 6 months had no antibody screen performed.

Expired reagents n=1

A young child was identified as part of cohort of patients whose samples had been tested with expired reagents.

K-positive to a female with childbearing potential n=1

A K-negative girl with sickle cell anaemia received a K-positive transfusion.

Non-phenotyped blood for patients with sickle cell disease n=2

In both cases, children received red cells with phenotypes that were not matched. In 1 case the child developed an anti-E. This child had only ever been transfused at one centre and must have received a non-phenotyped unit there.

Non-washed apheresis unit n=1

One child, known to react to platelet transfusions, was due to receive either a pooled platelet unit or a washed apheresis unit. Due to a miscommunication a standard apheresis unit was given instead.

Avoidable, delayed, under or overtransfusion (ADU) n=35

Avoidable n=7

Five of the 7 avoidable transfusions were due to staff acting on erroneous results. One was a duplicate transfusion for a neonate who had already been transfused that day and another involved avoidable use of cryoprecipitate for a child who had plasma exchange.

Delayed n=18

Two children died following multiple delays to transfusion during massive haemorrhage. These have been discussed earlier in this chapter.

In half the cases of delayed transfusion there was an element of communication failure between clinical and laboratory staff. Two delays were due to sample labelling issues, including a neonate whose name had changed from 'baby'. In 3 cases there were delays in multiple steps in the transfusion process. In 1 case there was an IT failure and in 1 case a unit of platelets was left in a taxi.

Overtransfusion n=9

Errors included 2 related to pump programming, and 1 preterm neonate who was accidentally transfused twice in the same 24-hour period. There were also errors in the volume prescribed, 1 due to a miscalculation and 2 due to failure to prescribe in mL for children. Two teenagers were transfused excessive volumes of platelets repeatedly without checking the platelet count in between. The final case is described below.

Case 23.5: Overtransfusion of solvent detergent FFP to a neonate

A bleeding neonate on cardiopulmonary bypass received 105mL of solvent detergent FFP instead of 15mL. The reporter describes that the unit was not clamped after the bolus.

Undertransfusion n=1

One neonate received an undertransfusion due to recurrent issues with a giving set.

Handling and storage errors (HSE) n=14

The most common errors involved time-expired units (n=6). There were issues with pump programming or rate of transfusion in 4 cases. One infant had a 3-way tap turned the wrong way so that the red cells were not entering the patient's circulation but instead going back into the blood pack. There were 3 clinical administration errors; 1 due to concomitant administration of parenteral nutrition, 1 due to an incorrect giving set and 1 due to use of gravity to transfuse (discussed below).

Case 23.6: Use of gravity for red cell transfusion in an infant

A neonate received an emergency red cell transfusion. The unit was administered by gravity rather than via an infusion pump and the child was transferred to another hospital with a nurse escort who had no paediatric training.

Learning points

- Education and training resources should be provided for those administering neonatal transfusions to reduce errors. For example, the SHOT paediatric video which is available on the SHOT website (https://www.shotuk.org/resources/current-resources/videos/, Figure 23.5)
- It is inappropriate to transfuse blood components to neonates by gravity due to the risk of overtransfusion
- Neonatal blood administration sets are available which allow blood transfusions to be delivered by a syringe driver (BSH Robinson et al. 2018)

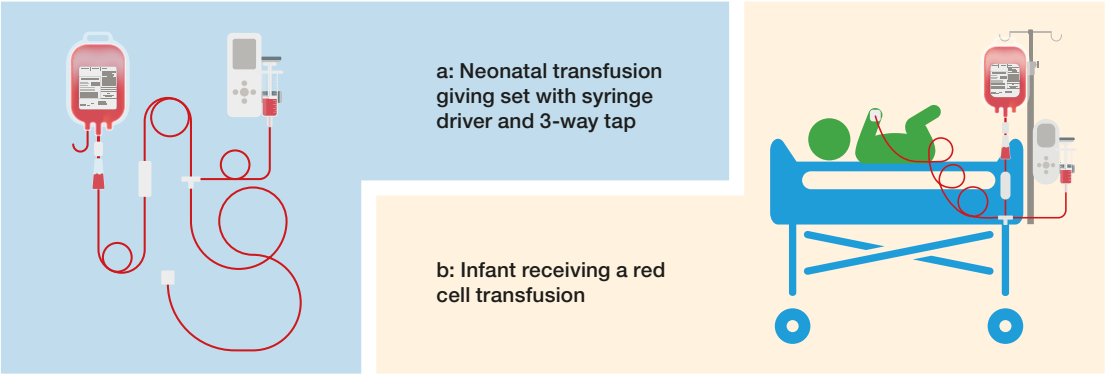


Figure 23.5 (a and b): Transfusion set up for neonates and infants

Anti-D immunoglobulin (Ig) n=5

There were 4 errors of anti-D Ig administration in teenage patients (2 delays, 1 omission and 1 anti-D to a D-positive patient). There was also 1 report of excessive anti-D Ig used for an incompatible platelet transfusion in a neonate.

Case 23.7: Use of anti-D Ig in a D-negative neonate who had received a D-positive platelet unit

A 500g neonate received a transfusion from an adult-specification unit of D-positive platelets due to clinical urgency. Multiple discussions took place regarding the requirement for anti-D Ig for the baby. The baby received 500IU of anti-D Ig via two intramuscular injections. The neonatal team had given the standard adult prophylactic dose of anti-D Ig and the message that haematology and transfusion experts had been consulted had not reached the treating consultant. No harm occurred; however, the team were not aware of the window of time that could be taken before administration and also that an IV formulation was available.

It is likely that the child would have received a maximum of 10mL of platelets, which is approximately 1/5 of a standard neonatal platelet pack volume. However, the anti-D Ig dose given was 10 times the dose that would be advised by the Blood Service to neutralise the red cells in a neonatal platelet pack.

Learning points

- 250IU of anti-D Ig will cover up to five adult therapeutic doses of platelets (approximately 1000mL; BSH Qureshi et al. 2014)
- NHS Blood and Transplant guidance advises 50IU subcutaneous or intravenous (IV) anti-D Ig per neonatal platelet pack transfused (https://nhsbtdbe.blob.core.windows.net/umbraco-assets-corp/14875/inf272v14.pdf)
- Advice from a haematologist regarding prophylactic anti-D Ig dosage should be sought following a D-positive transfusion to a D-negative paediatric female

Transfusion reactions n=61

Febrile, allergic and hypotensive reactions (FAHR) n=54

There was a notable increase in the number of FAHR paediatric reports from 38 in 2019 to 54 in 2020 (Figure 23.6). This is largely due to an unexplained increase in paediatric platelet reactions from 23 in 2019 to 38 in 2020. Paediatric FAHR involving platelets accounted for 38/112 (33.9%) of all platelet reactions reported to SHOT but there has not been a similar increase in platelet reactions in adult recipients (74 for both 2019 and 2020). In the absence of denominator data on the number of paediatric transfusions, we do not know if there has been a change in the rate of paediatric platelet reactions. There were no FAHR cases in patients less than 1 year of age.

The 38 platelet FAHR reports were mostly allergic (31) or mixed (5), with only 2 febrile alone. Of these, 14/38 (36.8%) caused major morbidity, including one of the febrile reactions. The majority (26/38, 68.4%) involved apheresis platelets, with 10 pooled and 2 not known. The proportion of paediatric reactions to apheresis platelets is lower than in the past, consistent with anticipated changes to transfusion practice: since September 2019 it is no longer recommended that patients born after 1995 receive apheresis platelets where possible (BSH New et al. 2020). This change in practice was expected to reduce the total number of paediatric FAHR reports because pooled platelets suspended in PAS are associated with a reduction in allergic response (BSH Estcourt et al. 2017). SHOT has previously recommended that hospitals should consider preferential use of pooled platelets in PAS for patients with a history of allergic reactions (see Chapter 17, Febrile, Allergic and Hypotensive Reactions (FAHR)), and this is the case for children as well as adults.

For red cells, 10/14 reactions were febrile (1 causing major morbidity), 3 allergic, and 1 was a moderate hypotensive reaction. Seven of the patients had sickle cell disease or thalassaemia and all these patients had febrile reactions.

There were 2 moderate plasma reactions: 1 to MB-FFP during a plasma exchange procedure, and 1 to MB-cryoprecipitate for a teenager following major trauma.

Figure 23.6: Trend in paediatric FAHR reports 2011-2020

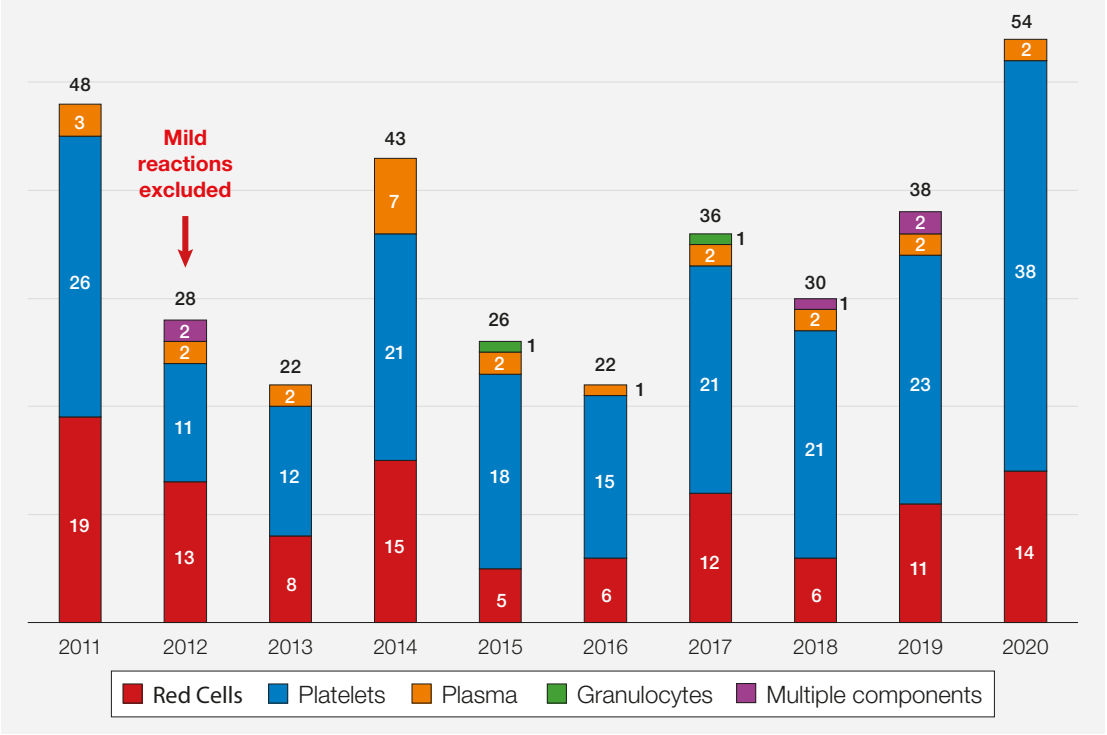
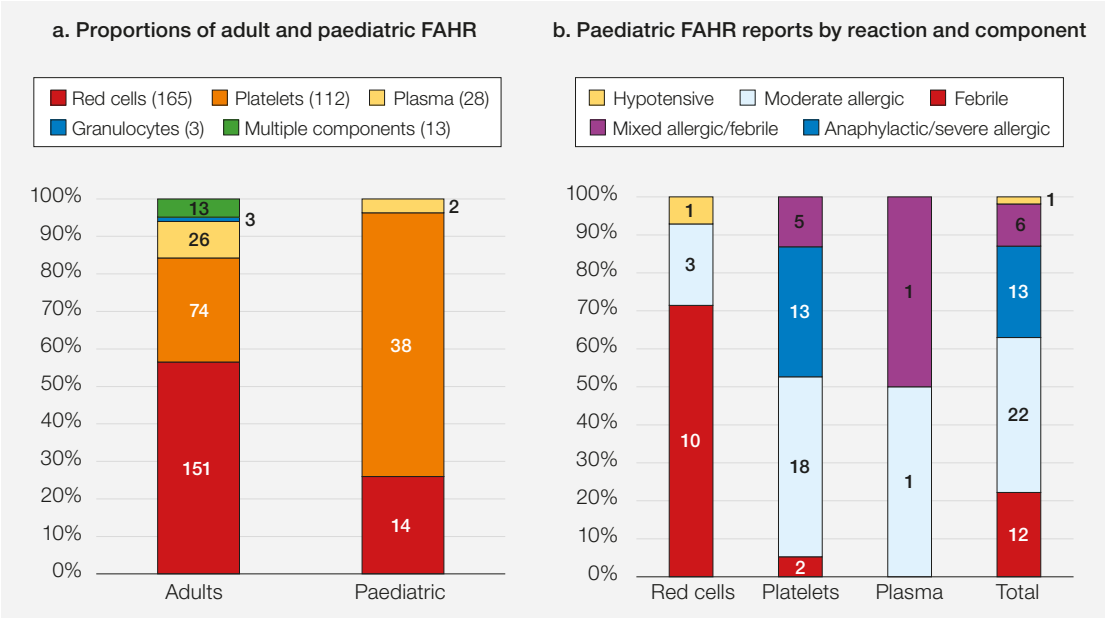


Figure 23.7 (a and b): Paediatric FAHR reports in 2020 (n=54)



Haemolytic transfusion reactions (HTR) n=3

There were 3 HTR in children. One was a case of possible hyperhaemolysis in a child who had antibodies to S, Jk^b and e antigens identified prior to transfusion. The other 2 were DHTR; 1 involving anti-S in a child who historically had an anti-Fy^a and the other was a child who had an exchange transfusion with non-phenotyped red cells and subsequently developed an DHTR due to anti-C and anti-E. This caused major morbidity.

Pulmonary complications of transfusion in neonates and children

There were no cases of TRALI in patients <18 years reported in 2020.

Transfusion-associated circulatory overload (TACO) n=2

There were 2 cases which met the criteria for TACO, 1 in a child and 1 in a neonate. The neonatal case is discussed below.

Case 23.8: Incorrect blood results viewed for a child resulting in overtransfusion and TACO

A stable neonate whose Hb had been between 140g/L and 160g/L for several days was accidentally given a 10mL/kg transfusion based on the Hb results from a different child. Following the transfusion, the neonate became hypertensive and desaturated. The Hb post transfusion was 211g/L on the gas machine and 177g/L in the laboratory. The child underwent venesection/dilutional exchange and recovered. During incident investigation, it was noted that the electronic records of several neonates were open at the same time, the hospital uses an electronic system which means a laptop on wheels is taken to each cot space. The margin of error for looking at the wrong screen for the wrong patient is therefore quite high.

Every effort must be made to avoid patient identification errors. This case of TACO highlights some of the issues around accurately accessing electronic patient records. Having multiple electronic patient records open at the same time can potentially increase the risk of misidentification.

Learning point

- When using electronic patient records, only a single patient record should be displayed on the screen at once to avoid misidentification and prevent serious transfusion errors. Patient records should be closed when leaving the bedspace and the new patient record opened when entering the next bedspace
- In the event that multiple patient records are open, care should be taken that the correct record is viewed when using electronic patient record systems. This may be a particular risk on neonatal units

Transfusion-associated dyspnoea (TAD) n=1

One case of TAD was noted in an infant under 6 months of age following a red cell transfusion.

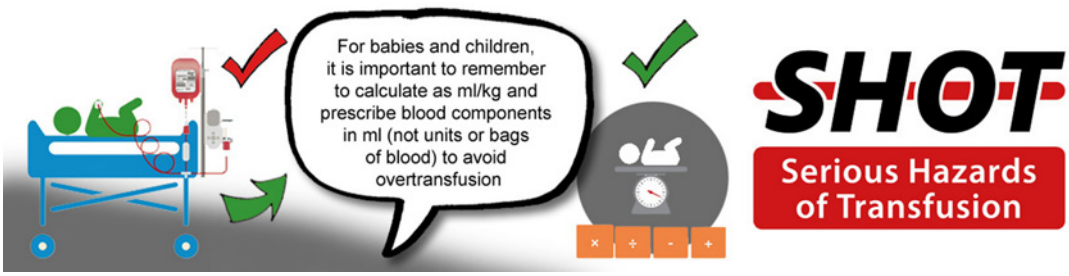
Uncommon complications of transfusion (UCT) n=1

There was 1 case of TANEC in a young infant who had been born at 26-weeks gestation. The baby had multiple co-morbidities. NEC, with pneumatosis on X-ray, developed 6.5 hours after the red cell transfusion was completed.

There were no cases of TTI or cell salvage errors in patients <18 years reported in 2020.

Near miss cases n=52, NM-wrong blood in tube (WBIT) n=44, right blood right patient (RBRP) n=15

The number of cases of near miss/no harm reported to SHOT were the same as last year.



References

Bolton-Maggs PHB (Ed), Poles D, et al. on behalf of the Serious Hazards of Transfusion (SHOT) Steering Group. The 2016 Annual SHOT Report (2017). https://www.shotuk.org/shot-reports/ [accessed 28 April 2021].

BSH Estcourt L.J, Birchall J, Allard S, et al. Guidelines for the use of platelet transfusions. *Br J Haematol* 2017, **176(3)**:365-394.

BSH Foukaneli T, Kerr P, Bolton-Maggs PHB, et al. Guidelines on the use of irradiated blood components. *Br J Haematol* 2020;**191(5)**:704-724. https://doi.org/10.1111/bjh.17015 [accessed 28 April 2021].

BSH New HV, Berryman J, Bolton-Maggs PHB, et al. Guidelines on transfusion for fetuses, neonates and older children. *Br J Haematol*. 2016;**175(5)**:784-828.

BSH New HV, Stanworth SJ, Gottstein R, et al. British Society for Haematology Guidelines on transfusion for fetuses, neonates and older children (Br J Haematol. 2016;175:784-828). Addendum August 2020. *Br J Haematol*. 2020;**191(5)**:725-727. https://doi.org/10.1111/bjh.17109 [accessed 28 April 2021].

BSH Qureshi H, Massey E, Kirwan D, et al. BCSH guideline for the use of anti-D immunoglobulin for the prevention of haemolytic disease of the fetus and newborn. *Transfus Med* 2014;**24(1)**:8-20. https://doi.org/10.1111/tme.12091 [accessed 28 April 2021].

BSH Robinson S, Harris A, Atkinson S, et al. The administration of blood components: a British Society for Haematology Guideline. *Transfus Med* 2018;**28(1)**:3-21. http://onlinelibrary.wiley.com/doi/10.1111/tme.12481/full [accessed 25 March 2021].

Haemoglobin Disorders n=57

24

Author: Joseph Sharif

Key SHOT messages

- Transfusion remains a key treatment for individuals with haemoglobinopathies, particularly in sickle cell disease (SCD), and this remains complicated by the significant risk of red cell alloimmunisation
- The decision to transfuse in SCD requires careful consideration, taking into account the indications and goals of transfusion and balancing these against the risk of alloimmunisation and haemolytic transfusion reactions
- Patients should be involved in every decision to transfuse and be fully informed of the potential risks and benefits. Patients should be educated on the importance of safe transfusion practice and be issued with a transfusion card highlighting their specific requirements

Abbreviations used in this chapter

ADU	Avoidable, delayed and under/overtransfusion	**IBCT**	Incorrect blood component transfused
BMS	Biomedical scientist	**LIMS**	Laboratory information systems
BSH	British Society of Haematology	**NHSBT**	National Health Service Blood and Transplant
DAT	Direct antiglobulin test	**SCD**	Sickle cell disease
FAHR	Febrile, allergic or hypotensive reactions	**Sp-ICE**	Specialist Services electronic reporting using Sunquest's Integrated Clinical Environment
Hb	Haemoglobin	**SRNM**	Specific requirements not met
HTR	Haemolytic transfusion reactions	**WCT**	Wrong component transfused
IAT	Indirect antiglobulin test		

Recommendations

- Processes should be in place to ensure a detailed transfusion history is obtained in all sickle cell disease (SCD) patients requiring transfusion. It is important that the transfusion history of a patient including antibody status is communicated between clinical and laboratory teams, including any specialist tests from reference laboratories (BSH Davis et al. 2016)
- Individual transfusion decisions in SCD patients can be challenging, and advice from haemoglobinopathy specialists is recommended
- For patients with complex transfusion requirements a multidisciplinary approach is recommended with representation from haemoglobinopathy and transfusion medicine specialists. Where possible a transfusion plan should be agreed in advance of an anticipated transfusion

Action: Hospital transfusion teams, clinical teams looking after patients with haemoglobin disorders, laboratory management

Introduction

There were 57 cases reported this year in patients with SCD or thalassaemia. Of the 43 cases in SCD the most frequently reported event was HTR, occurring in 15 cases, followed by IBCT-SRNM in 14 cases. There were 14 cases reported in patients with thalassaemia which were distributed across the categories with the most common being 4 cases of FAHR.

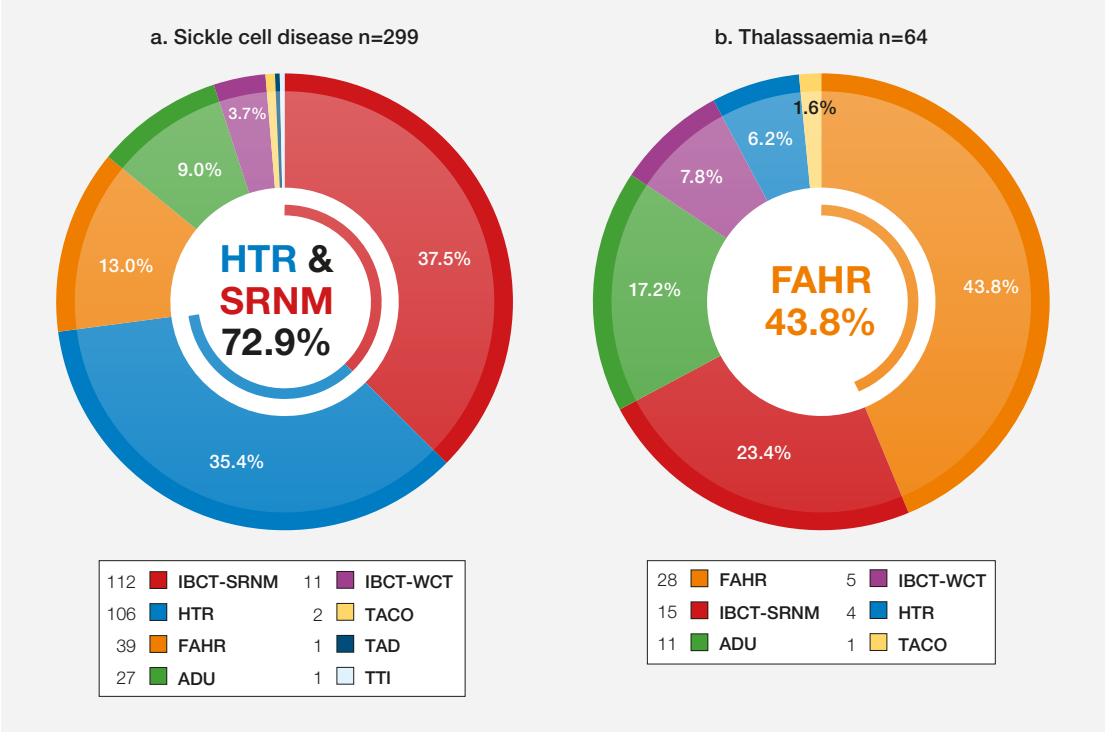
Deaths n=0

There were no deaths related to transfusion in any of the patients with haemoglobin disorders.

Major morbidity n=12

There were 12 cases of major morbidity related to transfusion in this cohort of patients: 10 HTR (9 hyperhaemolysis), 1 IBCT-SRNM and 1 FAHR.

Figure 24.1: Cumulative data for adverse transfusion events in patients with haemoglobin disorders 2010 to 2020



TTI=transfusion-transmitted infection; TAD=transfusion-associated dyspnoea; TACO=transfusion-associated circulatory overload; HTR=haemolytic transfusion reactions; FAHR=febrile, allergic and hypotensive reactions; HSE=handling and storage errors; IBCT-SRNM=incorrect blood component transfused-specific requirements not met; IBCT-WCT=IBCT-wrong component transfused; ADU=avoidable, delayed and under/overtransfusion

Avoidable, delayed and under/overtransfusion (ADU) n=4

There were 3 reports of delayed transfusion; 2 occurred in patients presenting with sickle cell crisis and 1 was for a routine transfusion in a patient with thalassaemia. There was 1 report of overtransfusion for a child with SCD attending for routine transfusion. There were no avoidable transfusions reported this year for patients with haemoglobin disorders.

Case 24.1: Delay due to inappropriate sample rejection

A young male with SCD was admitted with a sickle cell crisis and was deemed to require transfusion. During sample processing, the laboratory inappropriately rejected the group and screen sample. A further sample was requested however the second sample was appropriately rejected due to being incorrect. A senior BMS noticed the original sample was in fact acceptable for processing. These delays resulted in the transfusion being administered over 8 hours after initial bloods were taken. No harm to the patient was reported.

Case 24.2: Infusion pump set up incorrectly

A young female with SCD attended for routine transfusion. The infusion pump was set up incorrectly resulting in overtransfusion. The staff member was not familiar with the local policy and the prescription was not checked. The error occurred during transfusion when the pump was reprogrammed. The patient was reviewed following the incident and no harm to patient was reported as a result of this overtransfusion.

IBCT-specific requirements not met (SRNM) n=15

There were 15 reports of specific requirements not met, 14 of which occurred in patients with SCD and 1 in a thalassaemia patient.

Case 24.3: Failure to merge report from the reference laboratory with historic report on local hospital system

A young female with SCD received a two-unit episodic transfusion. Following transfusion, the laboratory staff noticed there was a discrepancy between the genotyping result available on Sp-ICE and the phenotyping results on the LIMS transfusion record. A sample had been tested by the reference laboratory and the patient found to have Rh variant C and e antigens. These genotyping results had been uploaded to Sp-ICE but the local laboratory had not been informed via a letter. Prior to the discrepancy being noted the patient had received red cells matching the phenotype and subsequently developed anti-C and anti-e.

Red cell genotyping is useful for detecting Rh variants not evident on serological phenotyping. Such specialised tests are only available in certain laboratories and it is therefore important that these results are communicated to the requesting team as well as being available on the national Sp-ICE record.

Case 24.4: SCD patient receives antigen-positive blood despite informing clinical team of his specific requirements

A patient with SCD admitted to a hospital outside his local area with acute pain episode was transfused due to fall in Hb. The patient was aware he had red cell antibodies and asked the medical team to ensure he got appropriate blood. The laboratory team did not see the clinical information on one of two group and antibody screen request forms, indicating the patient had historic alloantibodies, and therefore the patient did not receive antigen-negative units.

This is an interesting case whereby the patient himself was aware of the importance of informing the medical team of his specific requirements for blood and despite this the hospital failed to provide him with appropriate antigen-negative units. Although this was categorised as a laboratory error, the clinical and laboratory teams have a shared responsibility to ensure the patient receives correct blood and, in such cases, where the patient is not known to the local hospital it would be safer for the medical team to talk directly with the laboratory. This further highlights the importance of patient involvement to ensure safe transfusions.

Case 24.5: Ambiguity in the diagnosis and indication for transfusion in SCD

A young child with SCD was transfused. The Hb was 71g/L and the indication for transfusion was documented as anaemia. The request form stated '? sickle cell disease'. The laboratory team failed to flag this potential diagnosis and therefore patient did not receive Rh and Kell matched units.

This case highlights a lack of understanding, from both clinical and laboratory teams, of the relevance of SCD in transfusion practice. The patient's baseline Hb was unknown, nor whether there was a clear indication for transfusion, particularly as the requester did not seem to be clear of the diagnosis. Although the diagnosis on the request form was ambiguous, the laboratory team should have contacted the clinical team for clarification if there was any uncertainty to ensure specific requirements were met.

Febrile, allergic or hypotensive reactions (FAHR) n=9

There were 4 reported incidents in children with transfusion-dependent thalassaemia who each developed fever, rigors, and pain in back, chest or loin. All were thought to be non-haemolytic transfusion reactions.

There were 5 reports of non-haemolytic transfusion reaction reported in patients with SCD with symptoms reported include fever, rash, and pain. In all cases there were no reports of serological incompatibility.

IBCT-wrong component transfused (WCT) n=2

Case 24.6: An example of a D-variant leading to difficulties with matching

A young child with sickle cell disease was admitted to a hospital outside of the local area overnight with a sickle crisis and Hb of 51g/L. Blood grouping for D showed a dual population of red cells and the group was misinterpreted as D-positive as the population of D-positive cells looked greater. The D-group could not be easily confirmed with standard phenotyping, however, the BMS thought the patient was D-positive and issued two such units of red blood cells, both of which were D and E-positive. The laboratory policy is that where D-status cannot be determined D-negative red cells are given. The following day the Sp-ICE record was checked, which confirmed the patient to have a D-variant and according to the Blood Service report, and should have received D-, E-, e+ blood. In addition, only one of the two red cell units given was HbS negative. The child was followed up for development of an antibody.

Despite extended Rh matching, alloimmunisation is further complicated by significant genetic heterogenicity in this blood group system in individuals from Black African or African Caribbean ethnic backgrounds. Variant RHD and RHCE alleles can result in altered D, C and e antigen expression which may be incorrectly identified as positive or negative on serological phenotyping. In such cases genotyping is useful to confirm an Rh variant. This may not however, fully negate the risk as the donor could also have an Rh variant that may not be apparent.

Case 24.7: ABO-incompatible transfusion in SCD

A patient group O with SCD was inadvertently administered the blood intended for a different patient. Two units for two different patients were incorrectly checked only against their electronic prescriptions. The nurse set up the blood transfusion for the SCD patient using group A blood that had been collected for the other patient. Following infusion of 3mL of blood the cannula failed causing the pump to alarm and at this point the nurse noticed the wrong blood was being transfused and stopped administration. No adverse outcome to the patient was reported.

In this case the nurse checked the electronic prescription for two units for two different patients at the same time and did not perform checks at the patient's side as recommended. This ABO-incompatible transfusion could have resulted in a serious acute haemolytic transfusion reaction and risk of significant morbidity and death.

Haemolytic transfusion reactions (HTR) n=15

There were 15 incidents of HTR reported, all occurring in patients with SCD. Nine of the cases were reported as hyperhaemolysis, 5 were delayed HTR and 1 was an acute HTR. These cases are analysed in Chapter 19, Haemolytic Transfusion Reactions (HTR).

Case 24.8: Hyperhaemolysis in a child with prior alloimmunisation and an e antigen variant

A child with SCD and a history of alloimmunisation including anti-S, anti-Jk^{b} and e antigen variant was listed for an elective splenectomy and therefore had preoperative transfusion. She presented 2 days following transfusion with flank pain and dark urine. There was a decline in Hb from 104g/L immediately following transfusion to 67g/L. The patient was treated with immunoglobulin and steroid. The DAT was positive and pan-reactive anti-e was demonstrated in the eluate.

This case highlights the difficulties that can arise with Rh variants which can result in patients receiving blood which appears Rh compatible based on serological phenotyping and the patient subsequently

develops red cell alloantibodies. In some cases, an alloantibody may be misdiagnosed as an autoantibody.

Case 24.9: Case of further antibody development in a patient with previous alloimmunisation

A young male with SCD and a history of anti-Fy^a underwent an elective exchange transfusion. Twelve days later he presented with fever and abdominal pain and a decline in Hb from 105g/L immediately post transfusion to 78g/L and 55g/L 2 days later. Anti-S was identified post transfusion. The patient made a full recovery.

SCD patients with alloimmunisation are at risk of further antibody development and therefore any subsequent transfusion requires careful consideration.

Case 24.10: A case of poor increment in haemoglobin following blood transfusion

A middle-aged patient with SCD received six units of red blood cells over a 6-day period. The post-transfusion DAT was positive, but antibody screen remained negative. Indications listed for transfusions included sickle cell crisis, anaemia, and poor increment in Hb following blood transfusion. Once a HTR was suspected the patient received steroids and made a full recovery.

Case 24.11: HTR not initially recognised

A middle-aged female with SCD had recently received transfusion for an acute painful episode affecting legs, and then presented with a further painful episode affecting arms. A decline in Hb was noted and a decision was made to further transfuse. This resulted in further decline in Hb to 38g/L and dark urine. The patient was discussed with the regional specialist haemoglobinopathy team and treated with immunoglobulin and steroid for post-transfusion hyperhaemolysis.

In the 2 cases above a poor response to blood transfusion was not initially recognised as a potential HTR and further blood given in both cases resulted in hyperhaemolysis. Following transfusion in SCD, poor increment or decline in Hb should always raise suspicion of a HTR and such cases should be discussed with specialist haemoglobinopathy team as further transfusion may be detrimental.

Case 24.12: Acute HTR in SCD

A middle-aged female with SCD and a history of anti-S had an elective exchange transfusion prior to total hip replacement for avascular necrosis. Within 24 hours of transfusion there was a decline in Hb from 98g/L to 36g/L. Patient's symptoms included dyspnoea, dark urine and jaundice. Anti-Jk^b was subsequently identified.

Alloimmunised SCD patients are at increased risk of HTR. This case highlights the importance of discussing the additional risk of transfusion if required for surgery, which should form part of the discussion on the risks and benefits of surgery so that patients can make a fully informed decision.

Case 24.13: Acute chest syndrome in SCD pregnancy and recurrent hyperhaemolysis

A young female with a history of multiple alloantibodies and previous hyperhaemolysis required a red cell exchange transfusion for acute chest syndrome following a stillbirth. The patient was treated pre-emptively with immunoglobulin and steroids but developed another severe HTR with a decline in Hb to 41g/L, with associated haemoglobinuria and hyperpyrexia. The DAT was positive, but no antibody identified in the eluate.

This case highlights the risk of recurrence of haemolysis following a previous hyperhaemolytic reaction. It is useful to have a multidisciplinary approach for such complex cases including haemoglobinopathy and transfusion medicine representation and to have a pre-emptive transfusion plan.

Conclusion

Despite extended Rh and K matching, patients with SCD remain at risk of alloimmunisation (Coleman et al. 2019). Preventing alloimmunisation must be a priority when managing patients with SCD to reduce the risk of HTR and to avoid future difficulties with blood provision.

The optimum degree of antigen matching remains unclear with international guidance suggesting extended red cell antigen matching (Jk^a, Jk^b, Fy^a, Fy^b, S, s) may provide further protection for alloimmunisation. Red cell genotyping can provide useful information not evidenced on serological phenotyping such as Rh variants and evidence of a GATA mutation (Chou et al. 2020).

A national collaborative termed HAEM-MATCH* has recently been formed, to better define a process of extended matching of patients to donated red cell units for transfusion, to improve outcomes for patients with SCD. The hypothesis is that extended donor and patient antigen typing will enable routine timely and cost-effective, automated extended antigen matching in SCD (and other difficult to transfuse cohorts). Other benefits might include a more efficient donor recruitment strategy, reduced delays to transfusion, reduced risks of alloimmunisation, reduced risk of transfusion reactions and streamlined allocation of units for difficult to match patients.

**Thanks to Professor Simon Stanworth who is a haematologist at NHSBT and University of and Dr Sara Trompeter who is a haematologist at University College Hospitals London and NHSBT for the information about HAEM-MATCH.*

For further information please visit http://www.donorhealth-btru.nihr.ac.uk/project/blood-transfusion/

Recommended resources

SHOT Bite No. 15: Hyperhaemolysis
https://www.shotuk.org/resources/current-resources/shot-bites/

HTR and Haemoglobinopathies webinar
https://www.shotuk.org/resources/current-resources/webinars/

References

Chou S, Alsawas M, Fasano RM, et al. American Society of Hematology 2020 guidelines for sickle cell disease: transfusion support. Blood Adv 2020;**4(2)**:327–355.

Coleman S, Westhoff CM, Friedman DF, et al. Alloimmunization in patients with sickle cell disease and underrecognition of accompanying delayed hemolytic transfusion reactions. Transfusion 2019;**59(7)**:2282-2291.

Coleman S, Westhoff CM, Friedman DF, et al. Alloimmunization in patients with sickle cell disease and underrecognition of accompanying delayed hemolytic transfusion reactions. Transfusion 2019;**59(7)**:2282-2291.

Immune Anti-D in Pregnancy n=61 25

Author: Susan Robinson

Definition:

Cases of D-negative pregnant women who become sensitised and are found to have developed immune anti-D, which is detected during pregnancy, either at booking or later in the index pregnancy.

Key SHOT messages

- Cases of alloimmune anti-D found for the first time in pregnancy should be reported to SHOT, and reporters should provide a complete data set after delivery
- Cases of immunisation are still occurring even where current best practice is being followed
- Delivery beyond 40 weeks and obesity continue to be potential risk factors for sensitisation in cases which are otherwise ideally managed
- There are missed opportunities for anti-D Ig prophylaxis where pregnancy management is not ideal
- Interoperability of information technology systems to improve the pathway and outcome for D-negative women in pregnancy and postpartum remains a challenge

Recommendations

- Hospitals should sign up to share access to results on Specialist Services electronic reporting using Sunquest's Integrated Clinical Environment (Sp-ICE) where applicable
- Where an electronic health record is being planned or has been implemented, pathways to support decision-making should be incorporated for appropriate management of D-negative women in pregnancy and post-partum. Hospital staff should work collaboratively with electronic health record providers to support this

Action: Transfusion laboratory management, maternity services, hospital IT departments

Abbreviations used in this chapter

APH	Antepartum haemorrhage	**NHSBT**	National Health Service Blood and Transplant
BMI	Body mass index	**NICE**	National Institute for Health and Care Excellence
BSH	British Society for Haematology	**NPP**	No previous pregnancies
cffDNA	Cell-free fetal deoxyribonucleic acid	**PCR**	Polymerase chain reaction
DAT	Direct antiglobulin test	**PP**	Previous pregnancies
FMH	Fetomaternal haemorrhage	**PSE**	Potentially sensitising event
HDFN	Haemolytic disease of the fetus and newborn	**RAADP**	Routine antenatal anti-D Ig prophylaxis

Ig	Immunoglobulin	**RTA**	Road traffic accident
IT	Information technology	**Sp-ICE**	Specialist Services electronic reporting using Sunquest's Integrated Clinical Environment
IUD	Intrauterine death	**UK**	United Kingdom
LIMS	Laboratory information management system		

Introduction

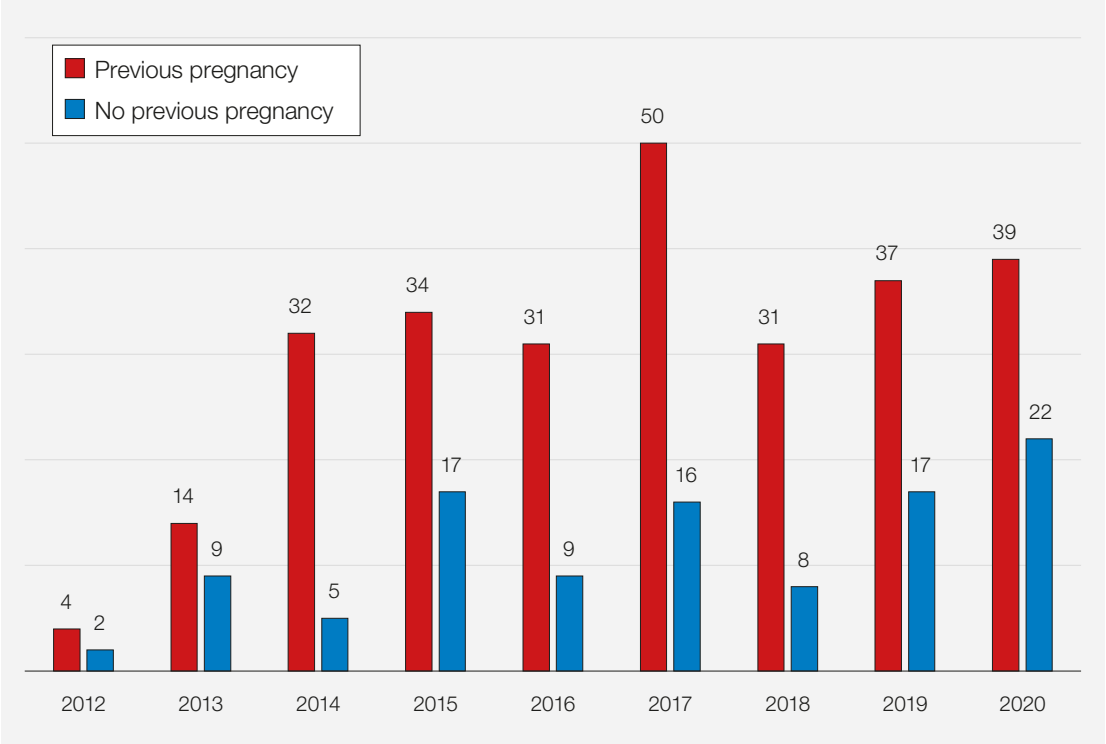
To improve understanding of the causes of continuing anti-D immunisations, SHOT has been reviewing cases where immune anti-D has been detected for the first time in the current (index) pregnancy since 2012. Reporters are requested to provide data on booking weight, management of sensitising events during pregnancy, and the administration of RAADP, both in the index pregnancy and the pregnancy immediately before the index pregnancy (if applicable).

Results

In 2020 a total of 61 cases were reported, 22 cases occurred in women with NPP, and 39 in women with PP. It is reassuring to note that the upturn in 2019 reporting continued in 2020, as the available data would suggest that anti-D immunisation in pregnancy remains under-reported (see the assumptions and calculation provided in the 2018 Annual SHOT Report (Narayan et al. 2019)).

Cumulatively SHOT now has useful data on 105 women with NPP and 272 women with PP.

Figure 25.1: Number of reports of anti-D immunisation in pregnancy by year, 2012-2020



No previous pregnancy (NPP) n=22

For a detailed discussion of the NPP cases, and tables containing similar details to those published in previous Annual SHOT Reports, please see the supplementary information on the SHOT website (https://www.shotuk.org/shot-reports/report-summary-and-supplement-2020/).

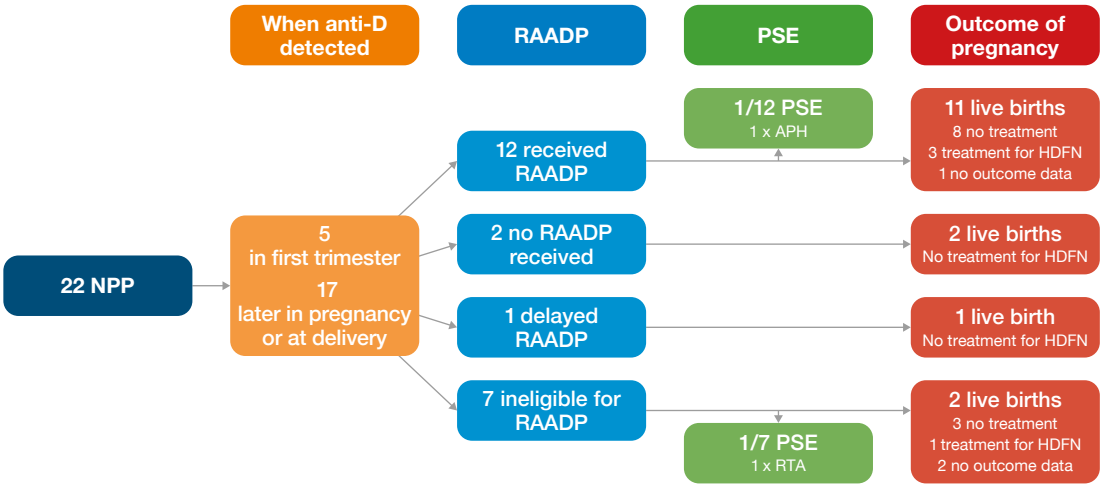


Figure 25.2: Summary of 2020 NPP data (n=22)

NPP = no previous pregnancy; RAADP = routine antenatal anti-D Ig prophylaxis; PSE = potentially sensitising event; APH = antepartum haemorrhage; RTA = road traffic accident; IUD = intrauterine death; HDFN = haemolytic disease of the fetus and newborn

Illustrative cases

Case 25.1: Difficulty in determining whether anti-D detected was due to prophylaxis or alloimmune anti-D in pregnancy

A primiparous woman in her 30s, booked at 10-weeks gestation (booking weight 73kg) and no alloantibodies were detected. A group and antibody screen was taken at 28 weeks and then RAADP was given. The sample was rejected due to incorrect annotation of the label. A further sample was taken the following week, anti-D detected, quantification less than 0.1IU/mL. At the time this was considered most likely prophylaxis. A further sample was taken at 34 weeks, the quantification remained less than 0.1IU/mL and was again considered most likely prophylaxis. No PSE was reported. A D-positive baby was delivered at 41^{+1}. A group and screen sample taken at delivery demonstrated a strong antibody reaction, quantification 4IU/mL, confirming alloimmune anti-D.

The guidelines and pathways for D-negative women in pregnancy are complex and challenging and require close working of the multidisciplinary team. This case highlights issues with logistics in a time-dependent pathway and the need to continue to determine prophylaxis versus alloimmune anti-D. History of anti-D Ig administration, quantification and serial monitoring of antibody levels at increased frequency in ambiguous cases may be useful to help differentiate between passive and immune anti-D (BSH Qureshi et al. 2014).

Case 25.2: Ideal management of twin pregnancy

A primiparous woman in her late 30s, booked at 10-weeks gestation, booking weight of 61kg. She was D-negative, and no alloantibodies were detected. RAADP was given at 28 weeks. This was a twin dichorionic diamniotic pregnancy, delivered at 37^{+4}, both twins were D-positive and anti-D Ig was given post-delivery. Alloimmune anti-D was detected by chance following a preoperative assessment 3 months postpartum 0.8IU/mL and remained persistent after 6 months.

Ideal management may not always prevent sensitisation and further work is needed to explore this, in particular a review of twin pregnancy data in D-negative women is of interest.

Case 25.3: Omission of RAADP

A primiparous woman in her early 20s presented to triage at 37^{+5}, having not attended since booking at 18 weeks. A diagnosis of maternal preeclampsia was made, fetal tachycardia was detected, and a caesarean section performed. A D-positive baby was delivered, DAT positive, and the baby required no interventions for HDFN. This patient was lost to follow up and did not receive RAADP, no PSE were identified retrospectively.

Case 25.4: Presentation of severe HDFN during first pregnancy

A primiparous woman in her late 30s, booked at 12 weeks, booking weight 64kg. Maternal antibody screen at booking and 28 weeks was negative. The mother received RAADP, no evidence of PSE. She presented at 36 weeks with suspected abruption, underwent caesarean section and it was concluded that abruption was unlikely. The baby was D-positive with Hb 40g/L, and a strongly positive DAT. Maternal antibodies anti-D, C and S were detected, and anti-D quantified as 247.9IU/mL. The baby recovered following exchange transfusion for HDFN.

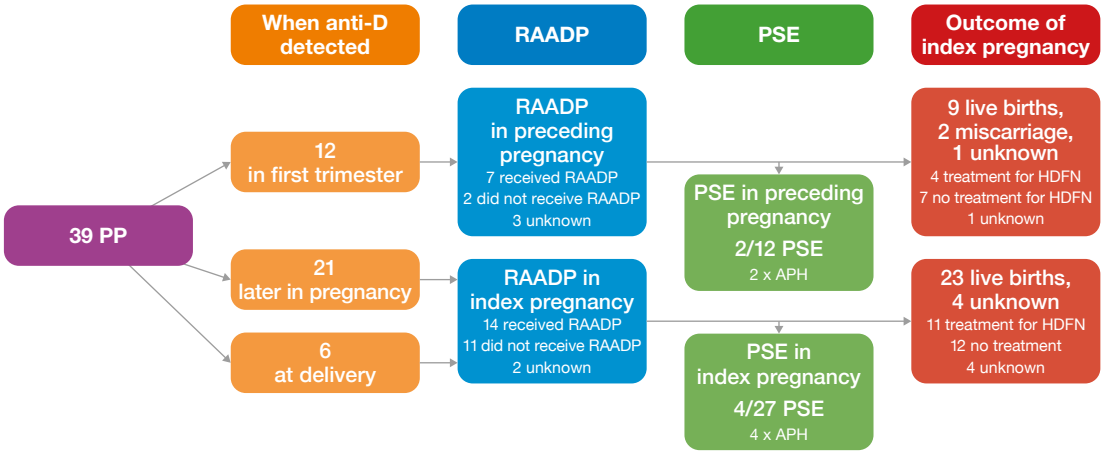
This case is a reminder that in the absence of identification of antibodies at 28 weeks, HDFN may still present in first pregnancies.

Previous pregnancies (PP) n=39

The index pregnancy in these cases refers to the current pregnancy – the pregnancy in which alloimmune anti-D was first detected.

For a detailed discussion of the PP cases, and tables containing similar details to those published in previous Annual SHOT Reports, please see the supplementary information on the SHOT website (https://www.shotuk.org/shot-reports/report-summary-and-supplement-2020/).

Figure 25.3: Summary of 2020 PP data (n=39)



PP = previous pregnancy; RAADP = routine antenatal anti-D Ig prophylaxis; PSE = potentially sensitising event; APH = antepartum haemorrhage; HDFN = haemolytic disease of the fetus and newborn

Illustrative cases

Case 25.5: Sensitisation associated with concealed pregnancy

A woman in her 20s, gravida 2 para 1 (booking weight 67kg) had anti-D detected at 11-weeks gestation with a quantification of 0.1IU/mL, which peaked at a quantification of 4.6IU/mL. A D-positive baby was delivered at 39^{+6}. No neonatal treatment was required. The preceding pregnancy was concealed, and no antenatal care was received. The woman had presented at 40 weeks, and a D-positive baby was delivered vaginally. The FMH estimation was less than 2mL, the woman received 500IU anti-D Ig.

When pregnancies are concealed and/or when patients are lost to follow up, opportunities to prevent sensitisation are missed, which can have deleterious effects on subsequent pregnancies.

Case 25.6: Sensitisation associated with obesity and multiple previous pregnancies

A woman in her 30s, gravida 5 para 1(live birth) +3 (miscarriages), booked at 13-weeks gestation, with a booking weight of 92kg. Anti-D was detected with a quantification of 0.1IU/mL. The peak quantification at 31-weeks gestation was 60.4IU/mL. Induction progressed at 36^{+5}, a D-positive baby was delivered and required phototherapy. In the preceding pregnancy the mother had been booked at 10 weeks, with a booking weight of 120kg. RAADP was given, no PSE were identified during the pregnancy, and postpartum FMH estimation was less than 2mL, for which she received 500IU anti-D Ig.

This case is an example where apparently 'ideal' management still resulted in immunisation. Cases in this category included 4 with 3 or more prior pregnancies, 2 of whom were obese in the PP cases where alloimmune anti-D was detected in the first trimester. Potential risk factors include obesity and the number of prior pregnancies. SHOT only collects information about management of the preceding pregnancy, therefore it is not possible to comment on management of the earlier pregnancies.

Case 25.7: Ineffective and sub-optimal clinical decision-making pathways

A woman in her 30s, gravida 3 para 2, booked at 8-weeks gestation, with a booking weight of 83kg. Maternal cffDNA screening test predicted the fetus to be D-positive at 16 weeks. Anti-D was detected at 20 weeks, quantification was not performed. This error was identified at the third trimester antenatal appointment, the fetus was scanned and demonstrated signs of hydrops. The mother was transferred to a fetal maternal unit. A D-positive baby was delivered at 34 weeks requiring exchange blood transfusion. In the preceding pregnancy the mother had been booked at 10 weeks with a booking weight of 63kg, RAADP was given, and there were no PSE identified. Delivery was at 39 weeks and postpartum prophylaxis was adequate (FMH less than 2mL, 1500IU anti-D Ig).

The pathway of D-negative women in pregnancy is complex, involving multi-professional teams, and failure to complete all steps in management risks poor fetal outcome. Electronic systems could be utilised to support good practice and ensure all relevant testing is performed. Electronic health record providers and hospitals who plan to implement or continue to develop an electronic health record should map the pathway for D-negative women in pregnancy and post-partum developing intelligent pathways that support pathway management.

Conclusions

The data this year (detailed on the SHOT website https://www.shotuk.org/shot-reports/report-summary-and-supplement-2020/) demonstrate residual issues around ideal management of D-negative women during pregnancy to prevent immunisation. The 2020 data continue to illustrate missed opportunities where pregnancy management is not ideal. This is demonstrated in the NPP RAADP data by a delay, an insufficient treatment dose and an omission to treat. This is also reflected in the continuing anti-D Ig errors detailed in Chapter 9, Adverse Events Related to Anti-D Immunoglobulin (Ig). Case 25.7 highlights the need for robust processes to ensure steps are completed to ensure appropriate monitoring of antibody levels, to prevent poor fetal/neonatal outcomes. A focused approach to ensure the correct pathway and decision making for D-negative women in pregnancy is necessary.

There are unanswered questions on the ideal management of pregnancies with obesity and/or gestation beyond 40 weeks. These have been identified as potential risk factors previously and data from 2020 shows similar risks. More work needs to be done in this area to improve management and reduce risk.

The data collection on cffDNA highlights ongoing barriers to implementation. IBGRL are currently testing 3,400-3,600 samples per month. These samples come from NHS Trusts/Health Boards, private service providers (minority) and 3 Republic of Ireland Trusts. There are Trusts on hold, which would represent 16,000 samples per annum, due to COVID-19 and the knock-on effect for PCR consumables that resulted in a shortage.

The forecast is that 56% of NHS Trusts and Health Boards will have implemented cffDNA screening by April 2022 (personal communication from International Blood Grouping Reference Laboratory).

One case commented that the pregnancy was booked in another Health Board and no cffDNA data was provided. This highlights the need for more effective information sharing between healthcare organisations, to optimise patient outcomes and quality of care. NHSBT currently report cffDNA results via the online NHSBT database Sp-ICE. At present this is the only way to receive these results. Midwifes can be trained and added as users by the Sp-ICE laboratory administrator and can look up results in this system. Not all Trusts agree to share their data on Sp-ICE, which prevents other UK Trusts and Health Boards from being able to view these results. NHSBT are also developing an electronic data interchange between the NHSBT and hospital LIMS to enable interoperability. This is an example of work that will contribute to the digital transformation of care driven by NHSX, https://hospital.blood.co.uk/diagnostic-services/red-cell-immunohaematology/service-developments/.

The 2020 data suggest:

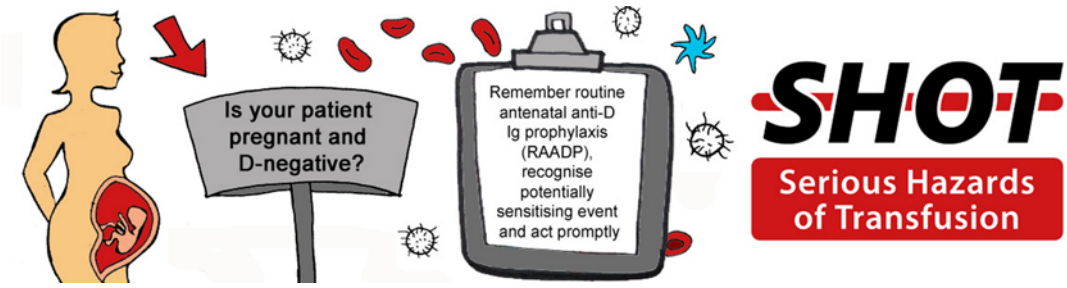
- Ideal management does not prevent sensitisation
- Delivery beyond 40 weeks may be a risk factor for sensitisation even when managed appropriately
- Women who are obese may not be adequately 'protected' by standard doses of anti-D Ig
- There are missed opportunities where pregnancy management is not ideal
- Interoperability of IT systems to improve the pathway and outcome for D-negative women in pregnancy and postpartum remains a challenge

Further work needed

A review of the cumulative data with regards to obesity, delivery beyond 40 weeks, and FMH >4mL, should be undertaken to see if the data provide enough evidence to modify current guidelines.

A focused approach to ensure treatment decisions are right for D-negative women is necessary to prevent sensitisation. The possibility of using electronic applications to support clinical decision making should be considered. Where an electronic health record is being planned or has been implemented, pathways to support decision-making should be incorporated for appropriate management of D-negative women in pregnancy and post-partum. Hospital staff should work collaboratively with electronic health record providers to support this. In the interim, hospitals should align local policies with the BSH addendum which signposts the more recent NICE Guidance 126 and 140 (2019).

The interoperability between Blood Services, reference laboratories, hospital IT systems and wider digital transformation in the NHS needs to progress.



References

Qureshi, H., Massey, E., Kirwan, D., Davies, T., Robson, S., White, J., Jones, J. and Allard, S. (2014), BCSH guideline for the use of anti-D immunoglobulin for the prevention of haemolytic disease of the fetus and newborn. Transfusion Med, 24: 8-20. doi:10.1111/tme.12091 https://b-s-h.org.uk/guidelines/guidelines/use-of-anti-d-immunoglobin-for-the-prevention-of-haemolytic-disease-of-the-fetus-and-newborn/

Narayan S (Ed), Poles D, et al. (2019) on behalf of the Serious Hazards of Transfusion (SHOT) Steering Group. The 2018 Annual SHOT Report. https://www.shotuk.org/shot-reports/ [accessed 28 April 2021].

NICE. Ectopic pregnancy and miscarriage: diagnosis and initial management. NICE guideline NG126 (2019a). https://www.nice.org.uk/guidance/ng126/chapter/Recommendations#anti-d-rhesus-prophylaxis [accessed 28 April 2021].

NICE. Abortion care. NICE guideline NG140 (2019b). https://www.nice.org.uk/guidance/ng140/chapter/Recommendations#anti-dprophylaxis [accessed 28 April 2021].

Acknowledgements

The Steering Group take this opportunity to thank the following individuals and organisations for their contributions without which the publication of this 24th Annual SHOT Report would not have been possible:

- The Blood Services of the United Kingdom for funding and support
- The Royal College of Pathologists to which SHOT is affiliated
- The Blood Services of the United Kingdom for the provision of data relating to the issue of blood components:
  - Central Planning Team, NHSBT
  - Mr James Smith, Senior Information Analyst, SNBTS
  - Mrs Chloe George, Head of Manufacturing & Distribution, WBS
  - Mrs Martina McCalmont, Senior Biomedical Scientist, Hospital Services Department, NIBTS
  - Mr Andy Rowley, Therapy Area Lead, Critical Care - UK and Republic of Ireland, Octapharma Ltd for data relating to SD-FFP (Octaplas®)
- The NHSBT expert group who reviewed TRALI cases:
  - Dr Tom Latham, NHSBT Bristol
  - Dr Peter Davis, Bristol University Hospitals NHS Foundation Trust
  - Dr Rob Webster, Consultant Haematologist, NHSBT Sheffield
  - Dr Andrew Charlton, NHSBT Newcastle
  - Dr Andrew Bentley, Manchester University NHS Foundation Trust
  - Dr Puneet Malhotra, St Helens and Knowsley Teaching Hospitals NHS Trust
- Clinical and scientific staff, in hospitals and reference laboratories, who have contributed to the clinical and laboratory investigation of cases
- Toast Design Consultancy Ltd for maintenance of the SHOT website
- Dendrite Clinical Systems for the maintenance of the online reporting system
- Jenny Leonard for the illustrations
- ARC-UK Technologies for design and production of the report
- Hospital transfusion teams for submitting case reports to the scheme

All collaborators who have contributed to this report

26 MHRA Report on Blood Safety and Quality Regulations (BSQR) in 2020

Author: Chris Robbie

Abbreviations used in this chapter

BCR	Blood compliance report
BE	Blood Establishment
BSQR	Blood Safety and Quality Regulations 2005 (as amended)
BMS	Biomedical Scientist
CAPA	Corrective and preventive action
CATPD	Component available for transfusion past de-reservation
CCE	Component collection error
CLE	Component labelling error
DEE	Data entry error
ECAT	Expired component available for transfusion
EI	Electronic issue
FR	Failed recall
GPG	Good Practice Guide
HBB	Hospital blood bank
HD	Handling damage
HTM	Haemovigilance Team Manager
IAG	Inspection action group
IBCA	Incorrect blood component Accepted
IBCI	Incorrect blood component issued
IBCO	Incorrect blood component ordered
LIMS	Laboratory information management system
NBTC	National blood transfusion committee
PTTE	Pre-transfusion testing error
QMS	Quality management system
RC	Root cause
RCA	Root cause analysis
SABRE	Serious Adverse Blood Reactions and Events
SAE	Serious adverse event
SAR	Serious adverse reaction
SOP	Standard operating procedure
SPE	Sample processing error
UNSPEC	Unspecified

Key MHRA messages

- Hospital transfusion teams must review their own incidents alongside the findings in this chapter to identify their most frequently occurring SAE and RC
- Attention should be made to the SAE and RC highlighted in this chapter to ensure these are being reported consistently and that QMS are reviewed for robustness and effectiveness

Summary

It was a difficult year for everyone coping with the effects of the COVID-19 pandemic. Changes to clinical focus and practice, process affecting the quality and safety of blood and blood components, workloads, staffing levels, skill-mix and education and training mean that comparison of data from 2020 to previous years is difficult. Lower blood usage would inevitably affect the numbers of reports made so this report has been written to try and interpret the data with relevance to the pandemic rather than a comparison to previous data.

Although the number of SAE reports was less than last year, rather than all categories of reports reducing, some stayed the same as the previous year or even increased from previous years. This may indicate that unplanned changes to processes had an adverse effect on quality and safety in some areas. Categories where numbers reduced may be a reflection on lower blood usage but may also be

an indication of the robustness of the processes involved that they were able to cope with the many challenges faced.

SABRE report data

Table2 6.1 and figure 26.1 show the total numbers of reports and the numbers of reports submitted as SAE and SAR for the previous 10 years. Although the total numbers of reports submitted remains similar to last year there has been an increase in the numbers of SAR reported and a decrease in the numbers of SAE reported.

	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
SAE	810	931	705	762	764	1027	1076	1198	1197	1093
SAR	444	343	345	346	262	464	508	408	497	590
Total	**1254**	**1274**	**1050**	**1108**	**1026**	**1491**	**1584**	**1606**	**1684**	**1683**

Table 26.1: Submitted confirmation reports 2011–2020

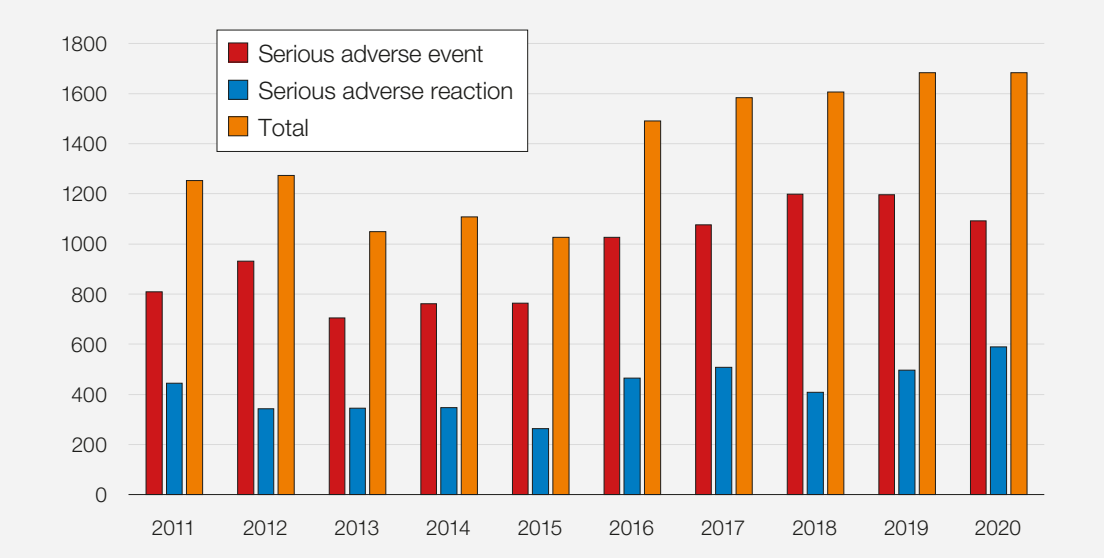


Figure 26.1: Submitted confirmation reports 2011–2020

Figure 26.2 compares the number of reports received by month for 2019 and 2020 to demonstrate the effect of the pandemic on reporting figures. The reporting numbers were comparable, with a slight dip in the peaks of the pandemic, both in the first wave and the second. Increased reporting in the months of September and December, which could potentially reflect easing in the pandemic effect.

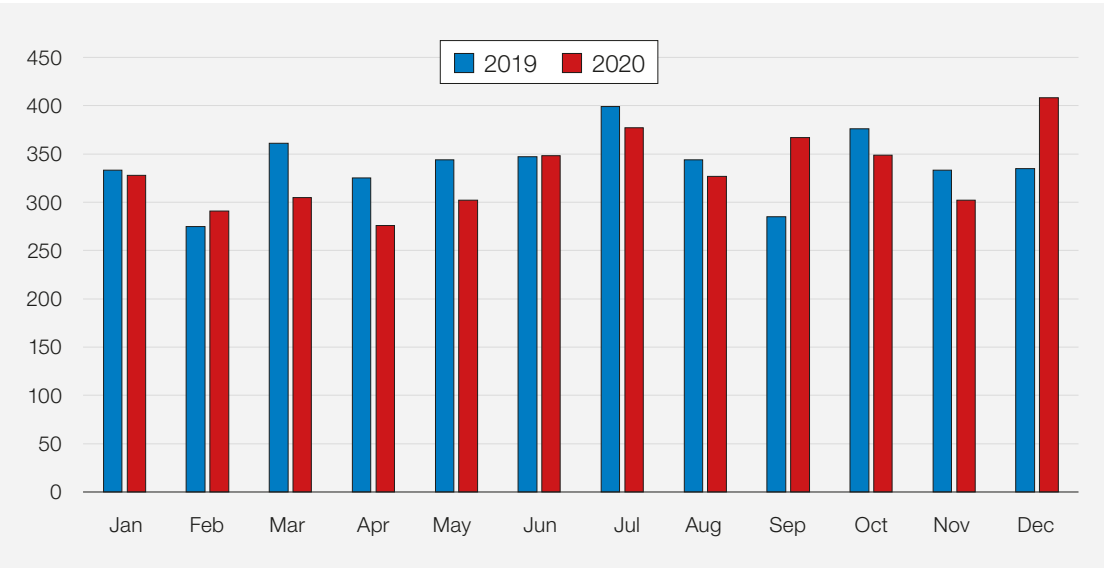


Figure 26.2 Comparison of SAE/SAR reports received by month 2019 and 2020

Serious adverse events n=1093 (-104)

Definition: (BSQR 2005) Any untoward occurrence associated with the collection, testing, processing, storage and distribution, of blood or blood components that might lead to death or life-threatening, disabling or incapacitating conditions for patients or which results in, or prolongs, hospitalisation or morbidity.

Storage data n=274 (-3)

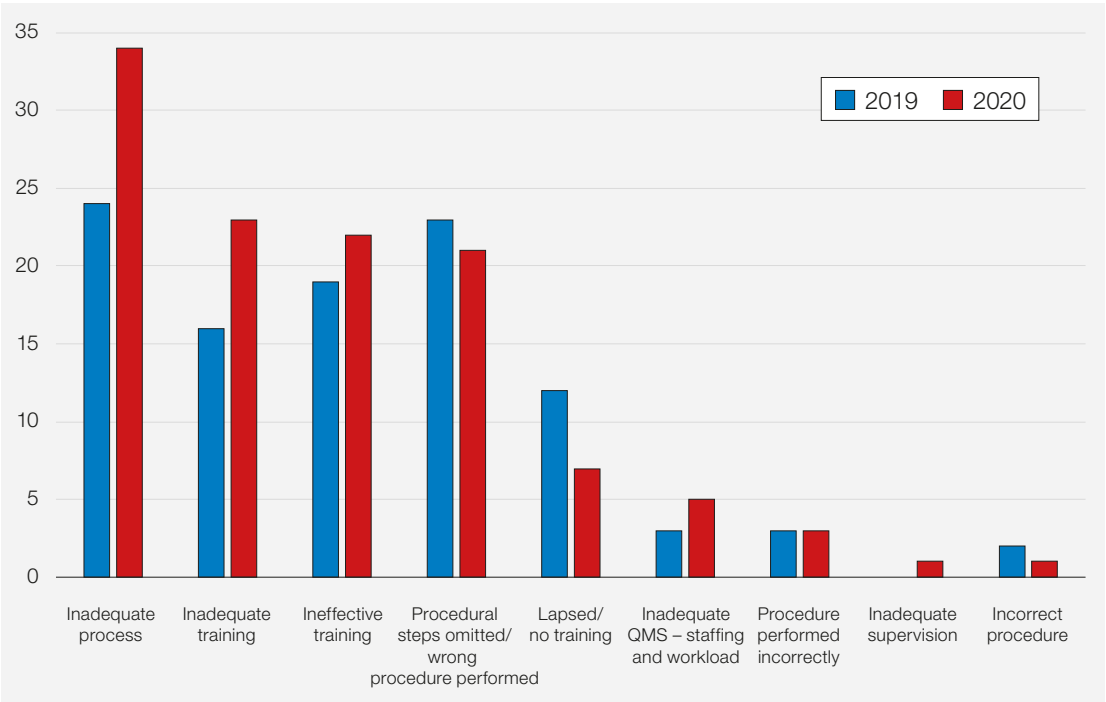
Storage remains the second largest individual error category (after "Other") and comprises of all BSQR reportable Storage SAE in both the laboratory and clinical areas. The MHRA has broken this category down further to try and identify specific storage error sub-types, Table 26.2. For a description of the sub-categories used, see appendix 1.

Table 26.2: SAE storage error sub-classifications

Storage sub-classification	2020 (+/- 2019)	2019 position
Incorrect storage of component	117 (+15)	1
Component expiry	55 (-16)	2
Sample expiry	30 (-9)	3
Return to stock error	21 (-1)	4
Failure to action alarm	16 (+4)	6
Storage temperature deviation	13 (-2)	5
Security	12 (+7)	8
30- or 60-minute rule	6 (+3)	9
Miscellaneous	4 (-4)	7
Total	**274 (-3)**	**not applicable**

Although unofficial data from BE suggest a 30% reduction in blood usage in 2020 during the COVID-19 pandemic, the number of Storage errors remain similar to last year. The reduction in Component and Sample expiry is probably explained by a reduction in the number of units in circulation. There has been an increase in the number of incorrect storage of components and this increase has largely been seen due to a number of factors relating to changes in staffing and practice during the pandemic.

Figure 26.3: Incorrect storage of component by Specification 2019 and 2020



QMS = quality management system

Figure 26.3 compares the RCs of incorrect storage of components for 2019 and 2020. It is notable that there has been an increase in the sub-categories:

- Inadequate process
- Inadequate training
- Ineffective training

There was a subsequent reduction in "procedural" errors noted. As hospitals adapted processes to cope with the effects of the pandemic, storage locations were either moved or became inaccessible as areas of the hospital were adapted into "hot" or "cold" areas. Staff were also redeployed to unfamiliar areas. Therefore, errors in the Incorrect storage of components were likely to be the result of poor business continuity planning, resulting in inadequately planned changes to storage processes, with a lack of thought to how the changes made might affect how components might be correctly stored. Further factors highlighted within the narrative of the reports received demonstrated poor communication of these changes to staff, failure to provide adequate training and ensuring shifts were covered by staff with the correct access to storage locations. It is accepted that coping with the pandemic presented hospital staff with many challenging circumstances and staff should not be criticised for the increase in incorrect storage errors, but it does demonstrate how errors can be prevented using robust change management controls.

Recommendation

- Review business continuity plans to ensure all changes to storage processes are adequately managed, ensuring the new processes are robust, covered with updated SOP and that re-training of staff is adequately planned and delivered

Action: Hospital transfusion teams

Other n=725 (-54)

Table 26.3: 'Other'

Other sub-category	2020 (+/- 2019)	2019 position
Incorrect blood component issued (IBCI)	157 (-33)	1
Pre-transfusion testing error (PTTE)	127 (+8)	3
Component collection error (CCE)	118 (+1)	4
Component labelling error (CLE)	114 (-5)	5
Sample processing error (SPE)	109 (-33)	2
Data entry error (DEE)	60 (+6)	6
Failed recall (FR)	12 (+6)	10
Component available for transfusion past de-reservation (CATPD)	11 (+1)	7
Unspecified (UNSPEC)	6 (-3)	8=
Expired component available for transfusion (ECAT)	5 (-4)	8=
Incorrect blood component ordered (IBCO)	4 (-1)	11
Incorrect blood component accepted (IBCA)	3 (+2)	13
Other – LIMS Failure	2 (N/A)	x
Handling damage (HD)	2 (+1)	12
Total	**725 (-54)**	**not applicable**

Table 26.3 shows the number of reports in the "Other" category of SAE. A reduction in the overall number of reports received is probably a reflection of the reduction in blood usage during the pandemic as can be seen in a reduction of IBCI and SPE error. However, not all categories of SAE have reduced, with some categories remaining similar to last year or even increasing. Although workloads in HBBs reduced as fewer components were used, laboratories were not immune to the effects of the pandemic with

reductions in staffing levels as staff were sick, isolating, or re-deployed. Even without the pandemic laboratories are still affected by other factors including staff vacancies and loss of experienced staff, training of new staff and inexperienced members of staff trying to cope with reduced supervision. Please see appendix 2 for a description of the sub-categories.

Human error category and human factors

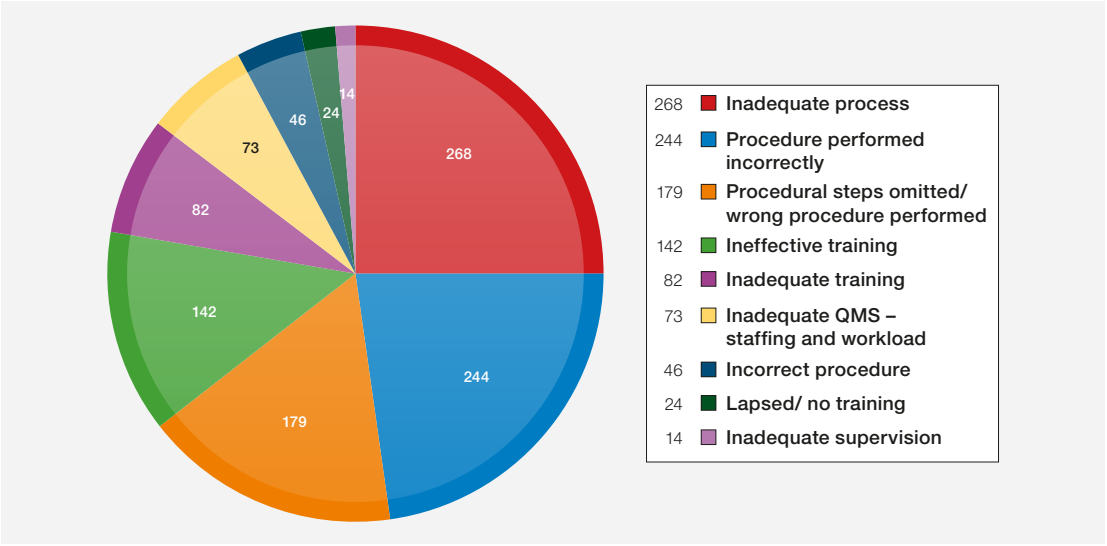
To understand reports in the human error category, the MHRA have continued to use sub-categories which can be applied to the report narratives to help understand the human factors involved. For a description of the categories used, see appendix 3.

Table 26.4 shows the breakdown of reports in the human error subcategories.

Table 26.4: Human error sub-category, 2020

Human error sub-category	Total 2020 (+/- 2019)	2019 position
Inadequate process	268 (-14)	2
Procedure performed incorrectly	244 (-66)	1
Procedural steps omitted/wrong procedure performed	179 (-20)	3
Ineffective training	142 (+2)	4
Inadequate QMS – staffing and workload	90 (-8)	5
Inadequate training	82 (+24)	6
Incorrect procedure	46 (+10)	7
Lapsed/no training	24 (-3)	8
Inadequate supervision	14 (-1)	9
Total	**1072 (-101)**	**not applicable**

Figure 26.4: Human error sub-category



QMS = quality management system

These numbers should be used as guidance only. The quality of this data is limited by a number of factors:

- The RC of incidents are usually the result of many contributory factors. The sub-category chosen reflects the most likely reason for the main SAE category. If multiple factors are involved relating to the QMS, then "Inadequate process" has been chosen as the sub-category rather than choosing a category that best fits the main SAE reported
- The sub-category chosen is based on the information in the report. A limited investigation or a report which does not provide MHRA with enough information may not be sub-categorised appropriately

There were 101 fewer "human error" reports in 2020 from 2019, again a reflection of the reduction in reporting due to the reduction in blood usage. For the first time since this category was sub-categorised, the highest proportion of SAEs fall into the "inadequate process" category. "Procedural errors" account for 40% of all human error reports which is a decrease of 4% from last year. That means that 60% of all human error reports have been reported proposing improvements to QMS within the CAPA. An increase in SAE sub-categorised as "Inadequate training" is likely to be in part a reflection of training regimes that did not adequately reflect changes to processes changed at short notice due to the pandemic.

Recommendations

- All reporters must continue to thoroughly investigate all SAE, even those with no actual harm to patients. It is through thorough investigation that improvements can be identified to reduce risks to the quality and safety of blood and blood components and reduce the risk of harm to patients
- Ensure that training regimes adequately cover the process or task being trained
- Ensure that any changes to processes are adequately planned, including the planning and delivery of training programmes

Action: Hospital transfusion teams

Top 5 SAE

SAE deviation sub-category	Specification sub-category
Pre-transfusion testing error (PTTE)	Inadequate process
Incorrect blood component issued (IBCI)	Inadequate process
Component collection error (CCE)	Ineffective training
Incorrect storage of component	Inadequate process
Incorrect storage of component	Inadequate training

Table 26.5: Top 5 SAE with human error sub-category

"Procedural" errors resulting from slips and lapses in concentration from staff are either genuine human error SAE or an indication that the investigation was not thorough enough to identify the true RC and contributory factors involved. This accounts for 40% of all human error reports. The remaining 60% of human error reports demonstrate "System errors". These have been assessed and presented as a "top 5" most commonly occurring SAE and RC.

PTTE – Inadequate process (n=45)

SAEs that fall into this sub-category will typically involve:

- Use of out of date reagents or controls
- Failure to exclude from EI and to manually crossmatch
- Failure to accurately interpret results
- Failure to complete testing or resolve anomalous results

From the report narratives, RCs often involve:

- Inadequate change control where errors in the LIMS were not identified
- Inadequate design of processes that did not direct staff in the correct actions to take under different circumstances

IBCI – Inadequate process (n=43)

SAE that fall into this category will typically involve blood being issued that does not meet a patient's specific requirements.

RCs will often be due to:

- Processes that do not require a BMS to access the NHSBT Specialist Services electronic reporting using Sunquest's Integrated Clinical Environment (Sp-ICE)
- Information from a clinical area not acted upon in a timely or consistent manner
- Poorly kept patient history on the LIMS that is easily overlooked or misunderstood

Although functionality within a LIMS should be used to provide warnings and barriers to issuing the incorrect component, the overall process should focus on the selection of the correct component in the first place, rather than a reliance on systems to detect errors already made.

CCE – Ineffective training (n=35)

SAE that fall into this category will often involve porters, but can also involve doctors, nurses, healthcare assistants as well as laboratory staff if the collection process directly involves them helping or handing over components. Errors can involve electronic tracking systems as well as manual processes.

From the corrective actions proposed to resolve this SAE (re-training of staff involved) the implication is that staff have either not understood the training initially or have forgotten it. Although training packages might be deemed to be "robust", thought must be given to the ability of the staff being trained and the frequency of re-training. Some staff may require more in-depth training than others, and staff that perform the tasks less often may need to be trained more often than other staff.

Storage/ Incorrect storage of component – Inadequate process (n=34)

SAE in this category can involve portering, clinical and laboratory staff. Many of these SAE are a direct result of the effects of coping with the COVID-19 pandemic. Changes that were necessary that affected hospital locations and environments, staffing levels, skill-mix as well as staff sickness and isolation resulted in changes to storage locations, processes, and the availability of trained staff. Changes were often made without thorough planning using change control procedures and considering all the possible factors. As well as poor planning as a whole, often the RC involved multiple factors, including:

- No consideration made to changing storage arrangements
- Inadequate process design
- No or insufficient SOP
- No or inadequate training
- No review of capacity plans to ensure adequate staffing or skill-mix

While these points are to be made, it is not to criticise actions taken under extreme circumstances but should be taken as a learning point that demonstrates the importance of proper change control and change management to ensure quality and safety is maintained.

Storage/ Incorrect storage of component – Inadequate training (n=23)

SAE in this category primarily involve clinical staff but may also involve other staff categories. These SAE typically involve staff that have been trained in the correct storage processes but that the training was not thorough enough to cover the errors made, or is not adequately rolled out to enough staff to ensure trained and competent staff perform the storage tasks. RC often involve:

- Staff who should have been trained but have not
- Untrained staff, who do not have responsibility for component storage being directed to store components instead of trained staff
- Training that does not distinguish between component types or monitored and unmonitored storage locations

Recommendations

Review QMS to ensure the processes involved in the most frequently occurring SAE are robust. Ensure that:

- the process is thoroughly defined
- that procedures are written giving full and clear instructions how to perform the task
- that training is planned, adequate, delivered and understood

Action: Hospital transfusion teams

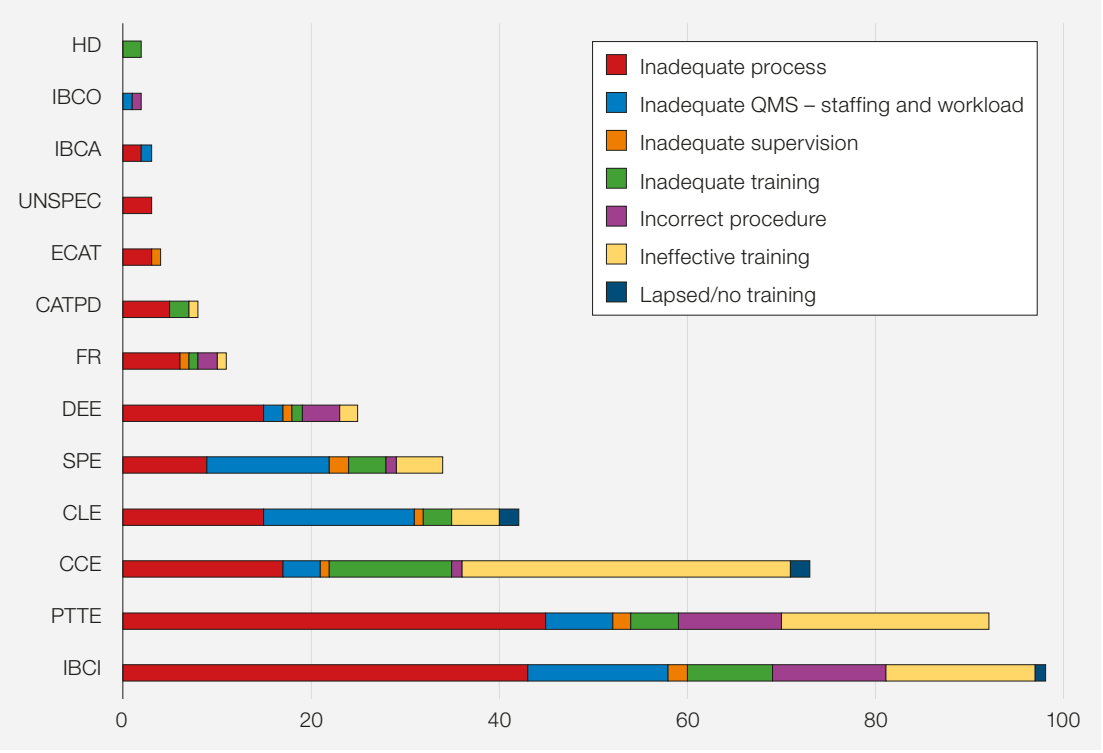


Figure 26.5: Other sub-category and root cause for all SAE other than procedural steps omitted/ wrong procedure performed and procedure performed incorrectly

HD = handling damage; IBCO = incorrect blood component ordered; IBCA = incorrect blood component accepted; UNSPEC = unspecified; ECAT = expired component available for transfusion; CATPD; component available for transfusion past de-reservation; FR = failed recall; DEE = data entry error; SPE = sample processing error; CLE = component labelling error; CCE = component collection error; PTTE = pre-transfusion testing error; IBCI = incorrect blood component issued

Figure 26.5 demonstrates all the most frequently occurring SAEs that fall into the other category and their root causes where the QMS was deemed to have been insufficient.

From January 1st, 2021 MHRA have been assigning human error sub-categories directly on individual reports once they have been reviewed and closed.

Notification

Date of event:	15 Mar 2021
Event involving:	Other
If other, please state here:	PTTE - Pre-transfusion testing error
Specification:	System error / Inadequate process
If other, please state here:	
Implicated Component:	Red blood cells
Blood component transfused:	No

Figure 26.6: Example of a new human error sub-category to demonstrate a system error

Recommendations

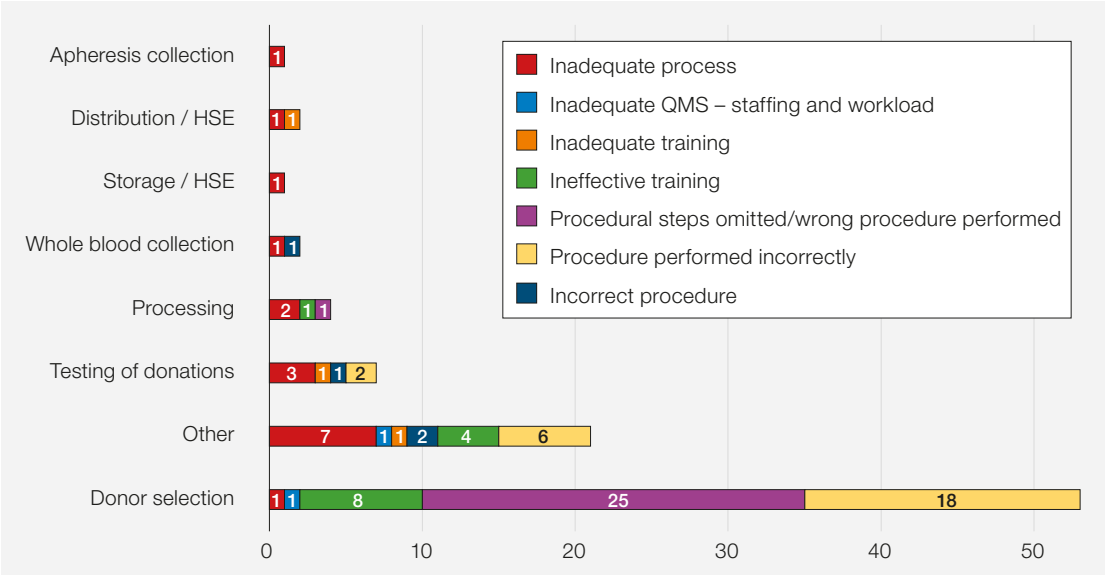
- Review SAE closed by MHRA and take note of the RC sub-category and event sub-category to trend and identify a site's own most commonly occurring SAE and RC

Action: Hospital transfusion teams

Blood establishment reporting n=95 (-28)

Although reports from blood establishments (BE) are included in the main analysis, the specific nature of the SAE reports from BE are lost in the greater numbers of reported hospital transfusion laboratory SAE. Figure 26.8 displays the reported BE SAE in 2020.

Figure 26.7: Blood establishment SAE event category by specification

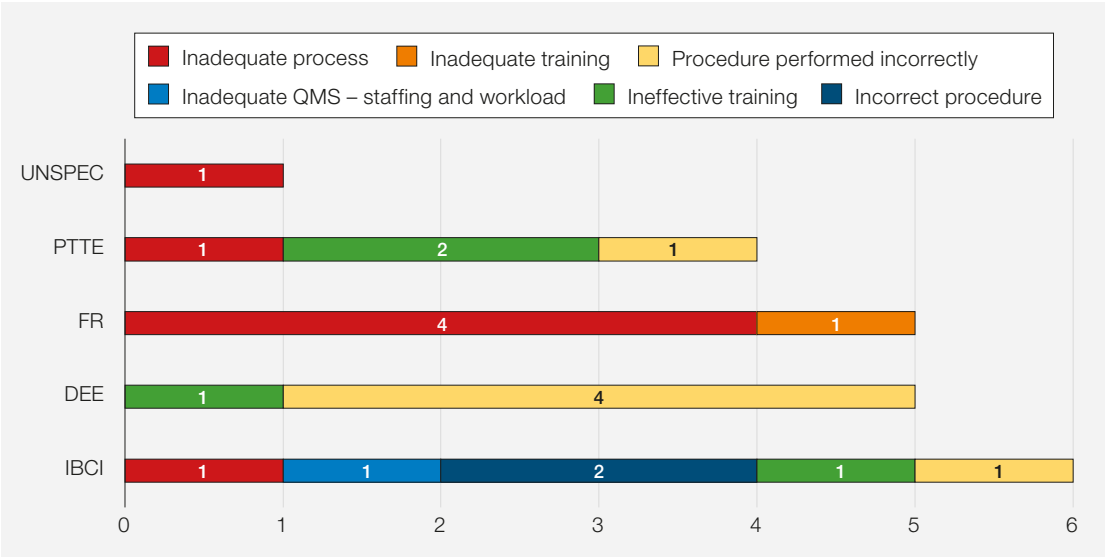


QMS = quality management system; HSE = handling and storage errors

The majority of the reports fall into the donor selection category and typically involve errors where a donor is accepted despite requiring deferral for travel, medical or lifestyle reasons.

Figure 26.9 shows a breakdown of the 21 reports which fall into the "Other" category.

Figure 26.8: BE reports in "Other" category



QMS = quality management system; UNSPEC = unspecified; PTTE = pre-transfusion testing error; FR = failed recall; DEE = data entry error; IBCI = incorrect blood component issued

Comment from Julie Staves, Chair of the NBTC Laboratory Managers' Working Group

It is pleasing to see that despite all the additional challenges of 2020, the Transfusion Laboratory community continued to ensure appropriate adverse incidents are reported through the correct processes to MHRA and SHOT.

The small reduction in the number of SAE seen is as expected due to the reduction in the number of blood components transfused in 2020. It remains concerning that there are still a high number of incorrect blood components being issued from laboratories. Improvements within the LIMS should be considered to try and help address some of these issues, although in 2020 this was less of a priority due to the ongoing pandemic.

The incorrect storage of components remains at a similar level to previous years which is probably a result of difficulties we've all experienced in both laboratory staffing. The redeployment of clinical staff combined with the difficulties of providing face to face training has also impacted on this area. I am pleased to see an improvement in the use of human factors when investigating incidents and the fact the 60% of all human error reports have proposed improvements to the QMS shows that as a community we are reflecting on our errors and incidents and looking towards improving our process.

Serious adverse reactions (SAR)

Definition: (Ref 2) an unintended response in a donor or in a patient that is associated with the collection, or transfusion of blood or blood components that is fatal, life-threatening, disabling or incapacitating, or which results in or prolongs hospitalisation or morbidity…blood establishments and the person responsible for the management of a hospital blood bank shall notify the Secretary of State (Competent Authority) of any serious adverse reactions observed during or after transfusion which may be attributable to the quality or safety of blood or blood components:

(i) Collected, tested, processed, stored or distributed by the blood establishment, or
(ii) Issued for transfusion by the hospital blood bank

Blood products

Adverse reactions involving blood products (i.e. licensed medicines such as anti-D Ig, Octaplas® (Solvent-Detergent fresh frozen plasma), or coagulation factor concentrates should be reported to the MHRA via the Yellow Card scheme (http://yellowcard.mhra.gov.uk).

Summary of SAR report data

To avoid any confusion, the MHRA will only supply, in this Annual SHOT Report, total SAR figures that qualify for reporting to MHRA under the BSQR, see figure 26.10

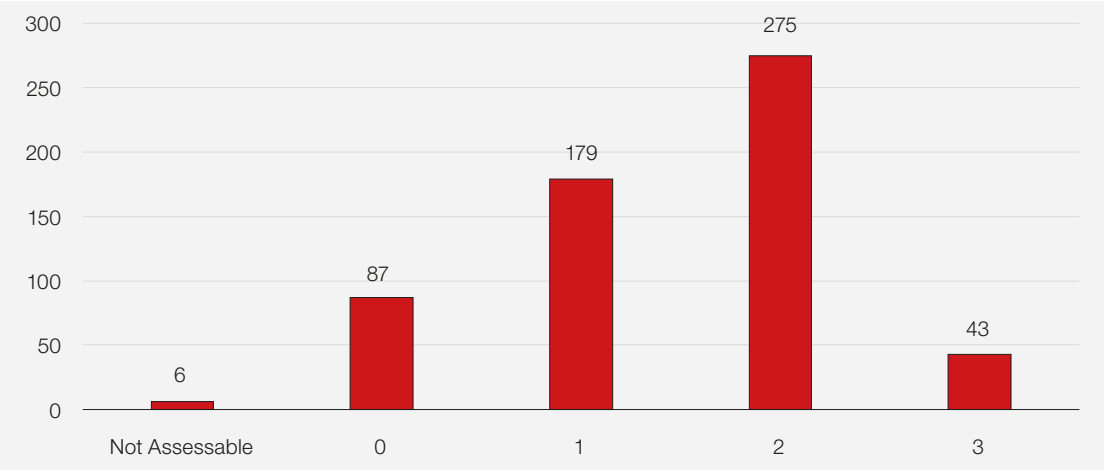


Figure 26.9: SAR reports, by imputability, reported to SABRE in 2020

Haemovigilance team managers (HTM) update 2020/21

Author: Mike Dawe

Over the past year, due to COVID-19, the Haemovigilance Team Manager has been seconded to other areas of the MHRA to support the agency's COVID-19 response. As a consequence, there is very little to report regarding the activity of the role as reported in previous years.

Findings and recommendations

Update to manufacturers not meeting a site need

There have been further concerns raised regarding a lack of meaningful support from LIMS and equipment manufacturers leading to issues where sites are concerned that they may not meet their regulatory requirements.

HBB must comply with the BSQR and part of that responsibility is to ensure that equipment is qualified and computerised systems are maintained in a validated state. This often requires information and support from the manufacturer or vendor and as such sites feel that they are left alone to deal with the regulatory issues that may arise due to poor customer engagement. Part of the HTM role is to liaise with manufacturers to ensure that they understand the regulatory framework that they are placing their product into.

As a consequence, the HTM has made manufacturers aware of the pertinent regulations that they need to provide the relevant support to the customer. The following is an example, but not limited to, of a pertinent GPG requirement that users can highlight, if relevant, to a manufacturer:

9.1.6 Deviations from established procedures should be avoided as much as possible and should be documented and explained. Any errors, accidents or significant deviations that may affect the quality or safety of blood and blood components should be fully recorded and investigated in order to identify systematic problems that require corrective action. Appropriate corrective and preventive actions should be defined and implemented.

As such this is a core part of the laboratory management responsibility. Using this requirement as an example, users can make a manufacturer aware of the regulatory impact as well as the patient safety concerns, from the regulatory perspective, that they may have. This can be reinforced by stating that continued operation as a blood bank is dependent on meeting regulatory and good practice requirements and MHRA has the power to issue cease and desist notices where blood banks are not adequately in control and are experiencing significant and recurring incidents. As a consequence, a lack of cooperation from manufactures can threaten the support of blood banks by MHRA.

If a site finds that this approach does not work please report the incident through the MHRA Yellow Card reporting system, https://yellowcard.mhra.gov.uk/, ensuring that keywords such as, but not limited to, Blood, Blood Components, Blood Transfusion are used. This will alert the Devices Safety and Surveillance Division (DSS) who can then collaborate with the Haemovigilance Team and the Blood Inspectors, if deemed appropriate, and the issue can be raised with the manufacturer directly.

Document retention

Several sites have requested advice on the retention of documents. The relevant GPG requirements are as follows:

5.5.2.2. Traceability data (that allow tracing from donor to recipient and vice versa) should be retained for a minimum of 30 years (Directive 2002/98 Article 14.3).

Whatever system or systems are used the recent infected blood enquiry has shown the importance of maintaining these records, https://www.infectedbloodinquiry.org.uk/. If a site uses a combination of traceability systems, then there must be a method of referencing an individual and or components traceability records between the systems used.

5.5.2.3. Documentation regarding investigations into Serious Adverse Events and Serious Adverse Reactions should be retained for a minimum of 15 years.

5.5.2.4. Quality System documentation and associated records should be retained for a minimum of 10 years.

Sites must consider that any quality system, and associated records, that have been linked to a SAE and/or SAR, then these records must be kept in accordance with section 5.5.2.3.

A site should carry out an audit of archived records against the above requirements before they are destroyed.

Summary

Once travel restrictions are lifted, sites that have previously arranged education days, will be contacted to rearrange a suitable alternative.

If a site has a pressing concern regarding a regulatory issue, we can arrange an online meeting so please do not hesitate to contact us for support regarding advice and help within the regulatory framework. Please contact mike.dawe@mhra.gov.uk or chris.robbie@mhra.gov.uk for further details.

MHRA Inspection activity on hospital blood banks

Author: Shirley Stagg

A total of 300 blood compliance reports (BCR) were submitted for review for the reporting period 01 April 2019 to 31 March 2020. A flexibility was put in place that allowed hospital blood banks (HBB) to request extra time to complete their submission due to the first peak of COVID-19, however, most were submitted on time and only one remained outstanding at the end of May. The BCRs were scored and discussed at a meeting of the BCR Assessment Team (BAT) in September.

The inspection process for this year was delayed due to COVID-19 and therefore some general trends from inspections are discussed rather than numerical data based on deficiencies.

Inspection outcomes

An overview of the compliance management escalation processes used by the good manufacturing practice (GMP) inspectorate, including information on the IAG and CMT referral processes, is available from the MHRA inspectorate blog: https://mhrainspectorate.blog.gov.uk/2017/02/06/overview-of-compliance-management-escalation-processes-used-by-the-gmp-inspectorate/

There have been no referrals to IAG or CMT so far from this cycle of inspections.

Summary of significant issues identified at inspected sites

Management of change

The control of change continues to be a deficiency that is commonly raised at blood inspections. Issues raised include:

- Failure to raise a change control
- Lack of user requirement specification
- Lack of risk assessment and actions to mitigate risks
- Incomplete validation
- Failure to carry out a post implementation effectiveness check
- Additions to validated systems not managed through change control

Management of non-conformances

The management of non-conformances is frequently raised as a deficiency due to the following:

- Failure to classify incidents consistently. This includes issues with considering the potential for harm as well as actual harm
- Lack of detailed investigation - including a lack of justification where human error is identified as a root cause
- No review of previous incident reports or other relevant information to identify recurring problems

The availability of trained and competent staff

Initial training of HBB personnel is generally found to be good. However, issues with staff availability and ongoing competency evaluation are frequently raised as an issue as highlighted by:

- Competence evaluations of laboratory personnel significantly overdue
- Incidents frequently attributed to personnel being too busy
- A lack of capacity management plan or similar document to ensure adequate resources to manage blood transfusion operations and maintain the quality management system

Information and guidance

For further information on MHRA and the Regulation of Blood please refer to the MHRA website: https://www.gov.uk/topic/medicines-medical-devices-blood/blood-regulation-safety

The MHRA Blood forum was launched in June 2016 as a tool to help those involved in blood component collection, processing, testing and distribution to comply with the EU Blood Directives, UK Statutory Instruments and good practice requirements. It provides the ideal opportunity for extended communication between peers and allows users to put forward their comments and get 'real-life' examples of ways in which they can manage robust quality procedures that ensure compliance and which dovetail with their own business needs and resources. http://forums.mhra.gov.uk/forumdisplay.php?60-Blood-Forum

Appendices

Appendix 1: Storage sub-categories

Component expiry	A component has time expired and not been removed from the storage location according to laboratory procedures
Incorrect storage of component	A component has not been stored in the correct location
Sample expiry	A sample has expired and the component has not been removed from the supply chain for the original patient
Return to stock error	A component has been returned to the supply chain in error instead of being quarantined or discarded
Failure to action alarm	A storage location alarm has been activated but not actioned according to the procedure
Storage temperature deviation	The storage temperature has gone out of specification without an alarm being activated
Security	A storage location is accessible to staff or public who are not authorised to do so
30- or 60-minute rule	Red cells are returned to a refrigerator after 30 or 60 minutes have elapsed contrary to local procedures for return of unused red cells
Miscellaneous	Any other storage event affecting the quality and safety of blood or blood components

Appendix 2: Other sub-categories

Incorrect blood component issued (IBCI)	Blood issued which does not meet the patient's specific requirements
Sample processing error (SPE)	Sample incorrectly receipted into the laboratory that should have been rejected
Component labelling error (CLE)	Typically transposition of labels
Pre-transfusion testing error (PTTE)	Any error in the process of testing patient samples and the interpretation of results
Component collection error (CCE)	Any error in the collection of components from storage locations, or the handover of components on collection from the laboratory
Data entry error (DEE)	Transcription errors of data, including both electronic and hand-written data
Failed recall (FR)	Failure to recall components in a timely manner
Unspecified (UNSPEC)	Any error affecting the quality and safety of components not specified elsewhere
Component available for transfusion past de-reservation (CATPD)	Expired components which were incorrectly collected, prior to their scheduled re-stock by the laboratory
Expired component available for transfusion (ECAT)	Any component issued for a patient, where the component expires prior to the planned transfusion
Incorrect blood component ordered (IBCO)	Components ordered from a blood establishment that do not meet the patient's specific requirements
Handling damage (HD)	Damage to a component affecting its quality and safety
Incorrect blood component accepted (IBCA)	Blood accepted into a laboratory for a specific patient where the special requirements have not been matched

Appendix 3: Human error sub-categories

Procedure performed incorrectly	Failure to carry out a step(s) correctly
Procedural steps omitted/ Wrong procedure performed	Missing a key step or not following the procedure
Inadequate process	Inadequate design of a process. Also includes multiple causative factors
Incorrect procedure	Process not properly described in the SOP
Ineffective training	Training not understood by operator
Inadequate training	Training process not fit for purpose
Lapsed or no training	Carrying out a procedure without any formal training
Inadequate QMS – staffing and workload	Staffing levels below the minimum level, or unacceptably high workload has resulted in staff making errors. It is also important to consider an appropriate skill-mix when deciding on minimum staffing levels
Inadequate supervision	Errors have been made by trainees or inexperienced members of staff and should have been noticed by adequate supervision

References

Good Practice Guidelines for Blood Establishment Required to Comply with Directive 2005/62/EC, 15/02/2018 https://www.edqm.eu/en/good-practice-guidelines-blood-establishments

The Blood Safety and Quality Regulations 2005, http://www.legislation.gov.uk/uksi/2005/50/regulation/1/made

If you would like more information on SHOT please contact:

The SHOT Office,
Manchester Blood Centre,
Plymouth Grove,
Manchester
M13 9LL

Telephone: 0161 423 4208
Email: shot@nhsbt.nhs.uk
Website: www.shotuk.org

Printed on paper from responsible sources.

print & plant

A collaborative initiative to restore forests around the globe.
For more information please visit: www.e-arc.co.uk/environment