25 Summary of Haemopoietic Stem Cell Transplant Errors 2012-2019

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Definition:

Transfusion incidents reported in patients undergoing haemopoietic stem cell transplant (HSCT) are included in this category.

This year, the HSCT-related transfusion errors reported to SHOT from 2012 to 2019 have been reviewed (numbers are counted in relevant error chapters). Solid organ transplants are not included in this analysis.

Key SHOT messages

- Communication is key: clinical teams should ensure the laboratory in both the transplant centre and shared care organisations, are fully informed about the transplant timetable, requirement for irradiated components and duration, and any change in ABO and D blood groups
- Patient involvement in all decision-making is encouraged and should include information about their specific transfusion requirements
- Laboratory staff should ensure the laboratory information management system (LIMS) is updated, and that all laboratory steps are properly checked to detect errors before they result in wrong transfusions

Abbreviations used in this chapter

ABOi	ABO-incompatible
BMS	Biomedical scientist
BSH	British Society for Haematology
CMV	Cytomegalovirus
CNS	Central nervous system
ED	Emergency department
Hb	Haemoglobin
HEV	Hepatitis E virus
HLA	Human leucocyte antigen
HSCT	Haemopoietic stem cell transplant
IBCT	Incorrect blood components transfused
IT	Information technology
JPAC	Joint United Kingdom Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee
LIMS	Laboratory information management system
NHSBT	National Health Service Blood and Transplant
RBC	Red blood cells
SaBTO	Advisory Committee on the Safety of Blood, Tissues and Organs
SCH	Stem cell harvest
Sp-ICE	Specialist Services electronic reporting using Sunquest's Integrated Clinical Environment
SRNM	Specific requirements not met
TAGvHD	Transfusion-associated graft-versus-host disease
UK	United Kingdom

Recommendation

- National guidelines are needed that are suitable for both transplantation and transfusion professionals that cover the procedures necessary for managing transfusions for transplant patients (repeated from the 2016 Annual SHOT Report (Bolton-Maggs et al. 2017))

Action: British Society for Haematology Transfusion Task Force

Introduction

Approximately 40-50% of HSCT are ABO-incompatible (ABOi) (Worel 2008). Such incompatibility may be major, where alloagglutinins in the recipient's plasma have the potential to react with donor red cells (e.g. recipient group O and donor group A), or minor, where alloagglutinins in the donor plasma react with recipient red cells (e.g. recipient group A, donor group O). Bidirectional incompatibility includes both major and minor mismatch, with the presence of alloagglutinins in both the recipient and donor plasma which can react with donor and recipient red cells respectively (e.g. recipient group B and donor group A).

Major and minor incompatibility each occur in approximately 20-25% of transplants, and bidirectional incompatibility in 5% (Worel 2008). The ABO and D group transfusion requirements of these patients change over time with the clinical course of the transplant. Poor communication between clinicians and the laboratory may result in serious errors in transfusion.

The British Society for Haematology (BSH) has published guidance on the irradiation requirements for cellular component transfusion in patients at risk of developing transfusion-associated graft-versus-host disease (TAGvHD). This includes patients undergoing allogeneic and autologous transplant (and their donors to avoid transfusion of viable leucocytes) (BSH Treleavan et al. 2010). In 2016 the Advisory Committee on the Safety of Blood, Tissues and Organs (SaBTO) recommended that transplant patients receive hepatitis E virus (HEV)-screened cellular blood components (SaBTO 2016) and screening of all donors for HEV has been in place across the United Kingdom (UK) since 2017.

Findings from the 8-year analysis

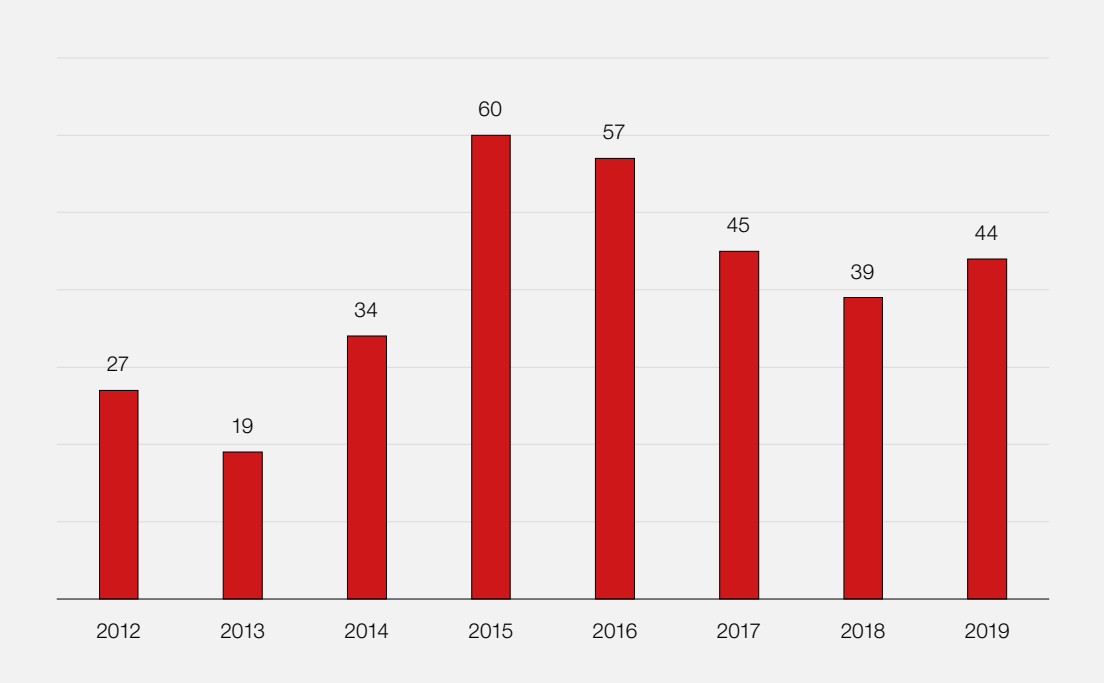
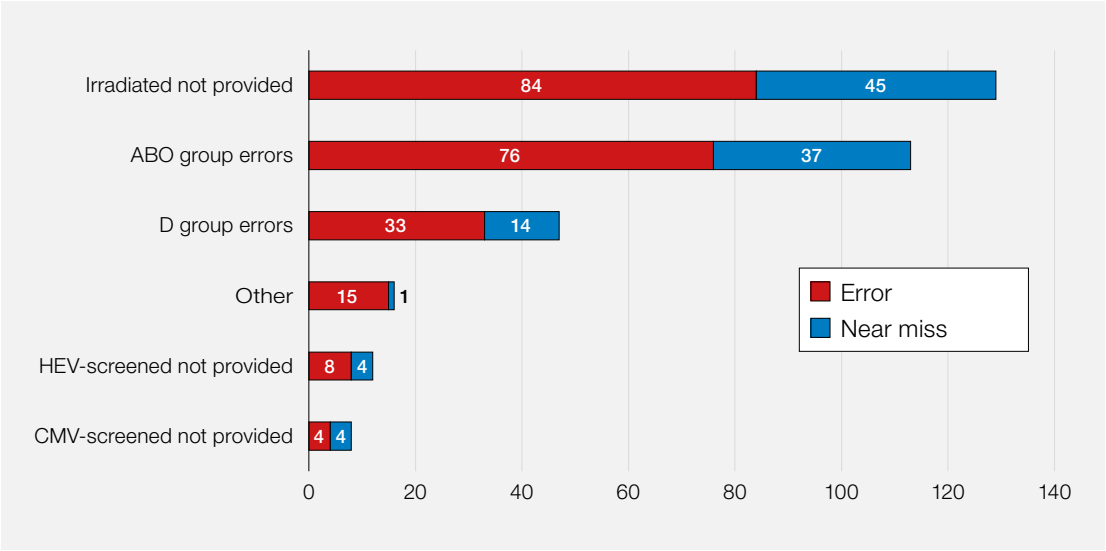


Figure 25.1: Total cases of incorrect ABO, D and specific requirement not met (SRNM) HSCT-related transfusion errors reported to SHOT 2012-2019; n=325

Most transplant-related errors result in incorrect blood components transfused (IBCT), or SRNM. Near miss errors are those detected prior to transfusion of the component. The most common errors are failure to provide irradiated cellular components and transfusion of the wrong ABO group, Figure 25.2.

Figure 25.2: Numbers of errors according to type 2012-2019 (including near miss) n=325



HEV=hepatitis E virus; CMV=cytomegalovirus

'Other' includes inappropriate electronic issue, failure to supply human leucocyte antigen (HLA)-matched components and a case where a neonate was given the wrong component

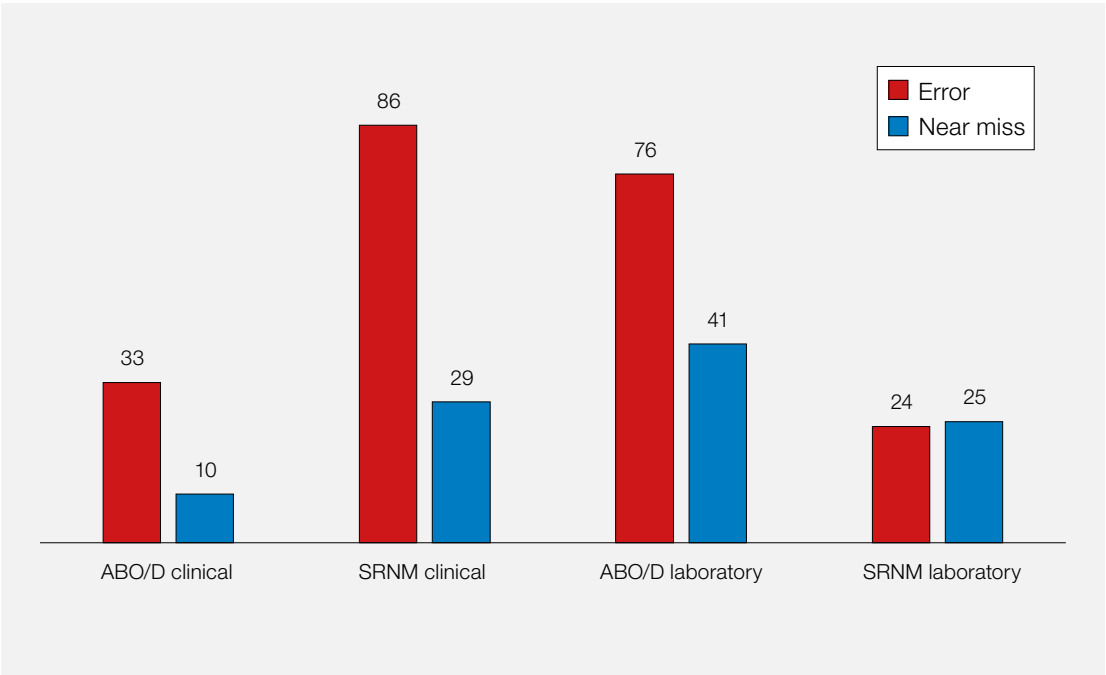
Of irradiated not provided errors, 6 included failure to also supply HEV (1 of these was near miss); 2 included failure to also supply CMV-screened products (1 of these was near miss)

ABO and D errors

Source of error (laboratory or clinical)

Errors occur in the clinical area and/or the transfusion laboratory. Most ABO and D errors originate in the laboratory, whereas failure to meet specific requirements is mostly caused by clinical error, particularly failure to inform the laboratory that irradiated cellular components are required (Figure 25.3). This pattern is also reflected in near miss events. Figure 25.4 indicates what kinds of errors were made. It is important to note that several ABO and D incidents were detected prior to transfusion often by vigilant clinical staff at the bedside.

Figure 25.3: Source of the HSCT-related error n=324*



**Excludes 1 case of wrong component transfused to a neonate*

SRNM=specific requirements not met

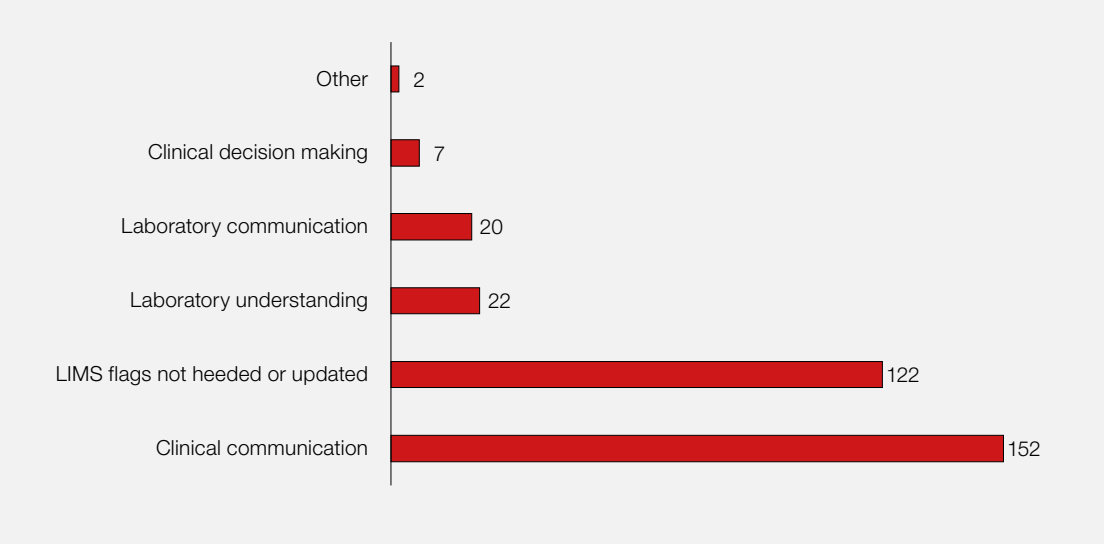


Figure 25.4: Types of error, includes ABO/D and SRNM n=325

LIMS=laboratory information management system

Laboratory errors are caused by inappropriate use of the LIMS, either failure to update the LIMS, or failure to heed LIMS warning flags.

Case 25.1: Incorrect ABO group transfused: failure to heed LIMS flag

A transplant protocol was received by the transfusion laboratory lead on Day -9 stating that the patient was scheduled for allogenic stem cell transplant on Day 0. A flag was set on the LIMS on Day -9 to indicate the transfusion requirements. The patient's blood group was A D-negative and the donor was O D-negative. In this case, the patient should have been transfused with group O D-negative red cells to match the donor group. The specific requirements flag was changed according to the protocol, so that the patient would immediately start receiving the appropriate group blood components if required. On Day +6, a request for red cells was received. The biomedical scientist (BMS) did not check the specific requirements correctly and ordered group A D-negative blood, instead of O D-negative. A second BMS performing the crossmatch failed to check the specific requirements, which clearly stated the red cell blood group for transfusion. The patient grouped as A D-negative and, as the crossmatch was compatible, a unit of red cells (group A) was issued to the patient. This was transfused to the patient without any noticeable reaction.

Most clinical errors are caused by communication failures. Errors also occur due to lack of understanding by transfusion laboratory staff.

Case 25.2: SRNM: failure by clinical team to update the specific requirements form

On Day +9 following an autologous HSCT for primary central nervous system (CNS) lymphoma, a patient's blood transfusion status form was found to incorrectly state that the patient did not require irradiated cellular components. This form should have been updated with the 'irradiated' status flag 1 week prior to the patient's peripheral stem cell harvest (SCH) 3 months earlier. Consequently, in the 7-day period prior to SCH the patient was transfused with two units of non-irradiated red cells. When stem cells were reinfused on Day 0 the patient was put at risk of TAGvHD. The patient received further units of non-irradiated red cells post transplant before the error was detected.

Shared care

Communication failure between hospitals which share the care of transplant patients is a recurring theme over the last 8 years. For example, when a patient is transplanted at a transplant centre, the information about the transplant, changes in ABO/D group and specific transfusion requirements may not be communicated to the local hospital or its transfusion laboratory. The transplant may have taken place several months or years before and specific transfusion requirements in the post-transplant period may vary. It is also important to keep the primary care team informed.

Case 25.3: SRNM due to poor communication as a result of shared care between hospitals

A patient had received a HSCT in August. In September, the patient attended a different hospital and a request was made for red cell and platelet transfusion from the emergency department (ED) due to low haemoglobin (Hb) and platelets. Details of the previous transplant were not provided to the laboratory and irradiated blood components were not issued for this patient; one unit of non-irradiated blood was transfused to the patient before the requirements were known by the laboratory. The patient also had HLA antibodies and required HLA-matched platelets; standard platelets were issued (but not transfused) due to lack of information available at the time of the request.

Wrong ABO-group transfusions

Tables 25.1 and 25.2 show transfusion of the wrong ABO or D group reported in 2018 and 2019.

Table 25.1: ABO and D transfusion errors in HSCT patients 2018 n=18

	ABO/D	Component	Gender	Patient group	HSCT donor group	Component group transfused	Error
Clinical	ABO	RBC	M	A D-positive	O D-positive	A D-positive	Laboratory not informed
	ABO	RBC	M	A D-positive	O D-positive	A D-positive	Laboratory not informed
	ABO	RBC	F	A D-negative	O D-positive	A D-negative	Laboratory not informed
	ABO	RBC	F	A D-negative	O D-negative	A D-negative	Laboratory not informed
	ABO	Platelets	M	O D-positive	A D-positive	O D-positive	Transplant protocol not available to laboratory staff
	D	Platelets	M	O D-positive	O D-negative	O D-positive	Laboratory not informed and shared care
Laboratory	ABO	RBC	F	A D-negative	O D-negative	A D-negative	Wrong component selected in laboratory and not detected at check nor at bedside
	ABO	RBC	F	A D-positive	O D-positive	A D-positive	BMS did not heed patient history
	ABO	RBC	NK	A D-positive	O D-positive	A D-positive	BMS did not heed patient history; 4 years post transplant. Group A units were crossmatch compatible
	ABO	RBC	M	A D-positive	O D-positive	A D-positive	BMS did not heed patient history on LIMS
	ABO	RBC	M	A D-negative	O D-negative	A D-negative	BMS missed LIMS flag
	ABO	RBC	F	B D-negative	O D-positive	B D-negative	LIMS not updated
	ABO	RBC	M	AB D-positive	B D-positive	A D-positive	Failure to heed patient record
	ABO	RBC	F	A D-positive	B D-positive	A D-positive	Selection error by locum BMS
	ABO	RBC	M	B D-positive	O D-positive	B D-positive	Failure to heed LIMS and inappropriate electronic issue
	ABO	Platelets	M	B	O	O D-positive	Data entry on LIMS
	D	RBC	F	O D-positive	O D-negative	O D-positive	Data entry on LIMS
	D	RBC	M	O D-positive	O D-negative	O D-positive	Communication error in shared care

RBC=red blood cells; NK=not known

	ABO/D	Component	Gender	Patient group	HSCT donor group	Component group transfused	Error
Clinical	ABO	RBC	M	A D-positive	O D-positive	A D-positive	Laboratory not informed
	ABO	Platelets	M	O D-positive	B D-positive	O D-positive	Transplant protocol not available to laboratory staff
	D	RBC, Platelets	F	B D-positive	O D-positive	O D-positive	New blood status form not completed (second transplant)
	D	RBC, platelets	F	B D-positive	B D-negative	B D-positive	Incorrect donor blood group on allograft form
Laboratory	ABO	RBC	F	B D-positive	O D-positive	B D-positive	Blood group misinterpreted post allograft leading to selection and issue of the incorrect group red cells
	ABO	RBC	F	B D-positive	O D-positive	O D-positive	Incorrect interpretation of blood group by BMS
	ABO	RBC	M	A D-positive	O D-positive	A D-positive	Selection error
	ABO	Plasma	M	O D-positive	Not known	O D-positive	Failure to heed LIMS
	ABO	Platelets	M	O D-negative	A D-positive	O D-negative	Failure to heed LIMS
	ABO	Platelets	M	O D-positive	O D-positive	A D-positive	Failure to heed patient history
	D	RBC	M	O D-positive	O D-negative	O D-positive	Incorrect interpretation of blood group by BMS
	D	RBC	M	B D-negative	B D-positive	B D-positive	Failure to follow post-transplant transfusion protocol on LIMS (patient had partial engraftment post transplant)
	D	RBC	F	A D-positive	A D-negative	A D-positive	Failure to heed LIMS
	D	RBC	M	B D-negative	B D-positive	O D-positive	Failure to heed LIMS
	D	Platelets	M	A D-positive	O D-negative	A D-positive	Failure to heed LIMS
	D	Platelets	F	A D-positive	A D-negative	A D-positive	Selection error

Table 25.2: ABO and D transfusion errors in HSCT patients 2019 n=16

Impact of errors

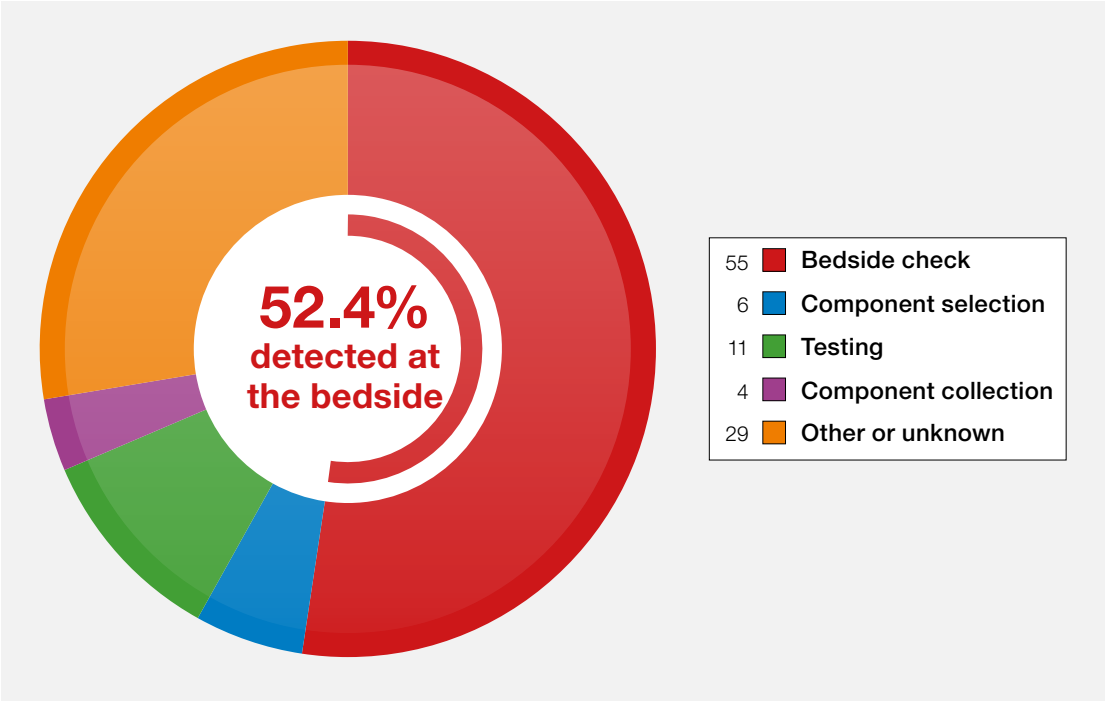
A single adverse reaction was reported as a result of transfusion-related incidents. A mild haemolytic reaction probably associated with passenger lymphocyte syndrome was followed by full recovery. The patient was transfused group A red cells (original recipient group) instead of group O (HSCT donor group) 10 days following HSCT. The error was attributable to the LIMS not being updated with blood group changes.

No deaths in transplant patients were attributable to any transfusion errors.

Near miss errors

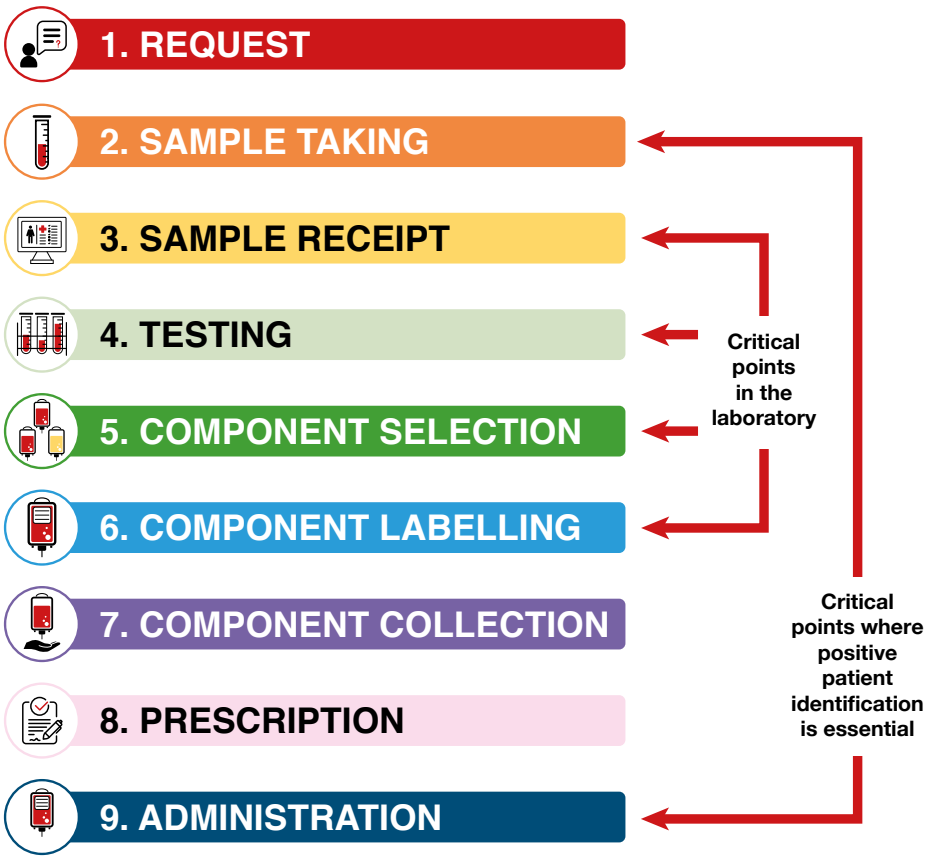
Near miss incidents may be detected at various points prior to transfusion. The most common checkpoint where errors are detected is at the bedside, as shown in Figure 25.5. This illustrates the importance of accurately completing the bedside check and reinforces the need for nursing staff to know about ABO and D compatibility, and for transplant patients to have clear information about which groups are to be transfused at what time point over the course of the transplant period. On 1 occasion the error was detected by the patient.

Figure 25.5: Point of detection of near miss incidents n=105



The nine-step transfusion pathway has several checkpoints where errors may be detected (Figure 25.6). It is notable that where the first error occurred in the laboratory there were several additional steps where the mistake could have been detected either by the BMS at checking within the laboratory, or at the time of transfusion with the bedside checks. In 2018 there was 1 error followed by 3 further opportunities to detect it, 5 cases with 4, and 1 case with 5 opportunities. This demonstrates the importance of each member of staff doing their own checks thoroughly and not relying on the safety of a previous step.

Figure 25.6: The nine-step transfusion pathway



*Note: Once a decision to transfuse is made, the authorisation or prescription may be written at variable times during this sequence, but **must be checked at the final stage.***

Other points of detection include the patient or a relative informing the clinical team of the patient's requirement for irradiated blood.

Recurrent sources of error can be identified for HSCT patients, Figure 25.7. Such errors can be viewed as a cycle where failure to correct one can cause subsequent failures in others. Over time some patients may lose their transplant and the blood group reverts to their original group. Good communication between clinical and laboratory staff is essential.

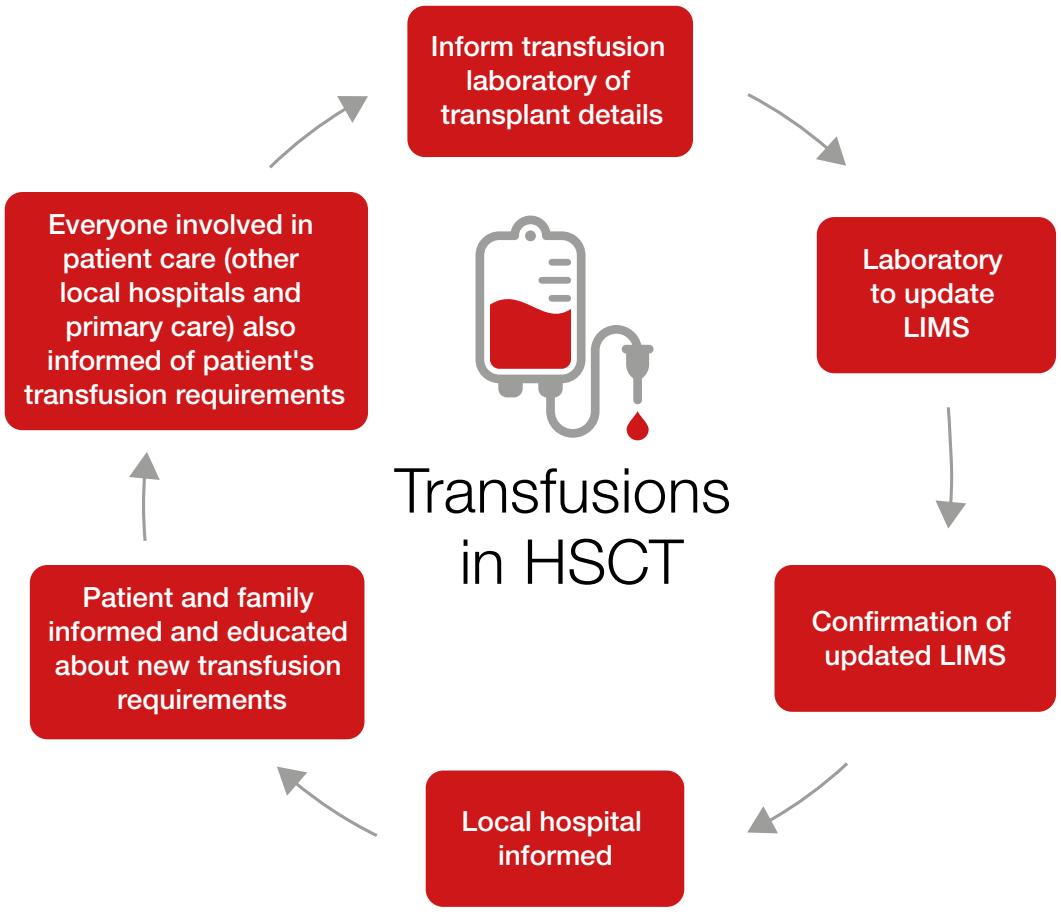


Figure 25.7: Important steps in ensuring safe transfusion practice in HSCT

HSCT=haemopoietic stem cell transplant; LIMS=laboratory information management system

Conclusions

Most transfusion-related errors in HSCT patients are either failure to administer irradiated components putting the patient at risk of TAGvHD, or transfusion of ABO-mismatched red cells. However, whether there are any other short- or long-term effects on the transplant itself are not known. There is evidence to suggest that ABOi HSCT are associated with acute haemolysis, delayed engraftment, and pure red cell aplasia (Staley et al. 2016) and so it is reasonable to question whether ABOi component transfusion in these patients can have similar effects.

The two main causes of transfusion errors are poor clinical communication and failure to heed or update the LIMS system in the laboratory. These causes are a common theme in many other areas of transfusion practice, and steps must be taken to reduce such errors. Errors in clinical communication are further compounded by the shared care of patients between the transplant centre and the patient's local hospital, which necessitates the need for effective transfer of information between centres.

Shared care of patients between the local hospital and transplant centre must be improved to ensure ongoing safe care.

Embedded in many transplant protocols is the requirement to inform the laboratory staff of the patient's impending transplant and associated change in transfusion requirements, particularly ABO and D group

changes. Transfusion laboratories are not always informed in a timely manner, resulting in delays in updating the LIMS and failure to follow instructions. More robust procedures are required to ensure this information is appropriately forwarded to the laboratory and updated in the patient's electronic history. This is echoed by The Joint United Kingdom Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee (JPAC), which advises that a clear post-transplant transfusion policy should be developed for all transplant patients and circulated to clinical and laboratory teams involved in their care. JPAC acknowledges previous Annual SHOT Reports which show component selection errors are common for patients who have changed blood group following HSCT (JPAC 2014).

Every transplant programme issued to the laboratory and clinical staff needs to be time specific, such that when ABO changes occur throughout the course of the transplant, all clinical and laboratory teams are reminded of these changes.

Appendix 25.1 gives a proposed checklist for transfusion in transplant patients. The introduction of databases such as Specialist Services electronic reporting using Sunquest's Integrated Clinical Environment (Sp-ICE) by National Health Service Blood and Transplant (NHSBT) in England allows laboratories to access patient transfusion data from hospitals which have opted in and includes warnings for those with red cell antibodies or specific requirements.

There is also confusion in some areas about transfusion in ABO-mismatched HSCT. This is likely compounded by the complex transfusion schedule that exists for ABO-mismatched transplants in relation to changes in the ABO and D group (Schrezenmeier et al. 2019). These SHOT data show that transfusion of the wrong ABO or D group in ABO-mismatched transplants continues to be a problem. The importance of training for both clinical and laboratory teams in centres which perform HSCT should not be underestimated.

How can such errors be avoided?

When a patient is undergoing an ABO-mismatched HSCT, transfusion of red cells of their own ABO group could be contraindicated. For example, if the patient is blood group A D-positive and their donor is O D-negative, the correct group of red cells to transfuse is O D-negative. This group is compatible with both donor and recipient and the red cells will not be haemolysed by either donor or recipient's anti-A or anti-B at any stage of engraftment. Most LIMS cannot prevent issue of components of the patient's own ABO group, so laboratory users must rely on flags or text warnings to state e.g. 'give O NEGATIVE red cells only' (if this LIMS feature is possible) in order alert them to the requirement.

One busy teaching hospital with a large transplant service (more than 100 allografts and more than 200 autologous HSCT in 2018) reported this type of error to SHOT many times. This led them to seek an information technology (IT) solution and they wrote a specification for their LIMS supplier. After working with their developer to discuss and approve the design, they developed a solution and installed it as a LIMS update on their test system for them to configure and validate. The solution enabled them to configure for every permutation of donor and recipient ABO and D group, which groups of red cells can be selected, preventing selection of any other group including the patient's own group where applicable. This improvement achieved three main benefits to patient safety and to their service:

- It prevented further errors of this type
- It allowed safe use of groups other than O when appropriate, therefore conserving group O red cells
- For any of these patients (without alloantibodies) electronic issue became possible and so enabled a more rapid response for day case transfusions

HSCT patients require extensive transfusion support post transplant, and transfusion errors can be avoided with better communication between all the clinical teams and laboratory teams involved in the patient's care. This must include local hospitals involved in the shared care of the patient. Accurate, timely communications, vigilant staff and effective patient education will help ensure appropriate actions and safer transfusions in these patients.

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Action	Tick
Ensure individualised protocol readily available to clinical and laboratory teams regarding the transfusion requirements pre-, peri- and post-transplant	
Check that the transfusion laboratory has received the protocol and confirmation has been received that LIMS has been updated with the changes	
Check that the specific transfusion requirements for each patient are documented and easily accessible to all ward staff (e.g. front of notes, ward office whiteboard)	
Confirm that local hospital/haematology team are informed of change in transfusion requirements in written format	
Ensure that the discharge summary details specific transfusion requirements with an indication for how long these are required and that this information is easily accessible to other departments that may be responsible for the patient's care e.g. emergency departments	
Provide patient with an alert card showing they have received a HSCT and which details their specific transfusion requirements	

Appendix 25.1: Example of a checklist for HSCT to ensure good communication between clinical and laboratory teams