Good practice guidance document for managing indeterminate ABO blood groups to support safe decision-making

What is this document about? This good practice guidance document is based on existing UK guidance highlighting the importance of correctly understanding the reason for an 'indeterminate' blood group, resolving the blood group where possible and making the correct decisions for patient safety. This includes illustrative example cases based on previous reports to SHOT related to this issue.

Who is this for? This guidance document is particularly aimed at hospital transfusion laboratory managers; transfusion IT (Laboratory Information Manageent System/LIMS and Electronic Patient Records/LIMS) providers; haematology medical staff and transfusion practitioners.

Why this document? Indeterminate ABO group on initial testing can lead to delays in transfusion and incorrect decisions in component selection. A UK NEQAS exercise and survey have highlighed gaps in practices and staff knowledge. This guidance document has been drafted to address issues identified. Policies, procedures and processes must consider the impact of communication, leadership, safety culture, human factors and ergonomics on safe decision-making.

How this has been developed? Following a UK NEQAS Blood Transfusion Laboratory Practice (BTLP) exercise in 2023, this guidance document has been developed as a collaborative initiative by Serious Hazards of Transfusion (SHOT), United Kingdom Transfusion Laboratory Collaborative (UKTLC) and United Kingdom National External Quality Assessment Service (UK NEQAS).

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Definition:

An indeterminate ABO group on initial testing includes where the forward group reactions do not match reverse group reactions and/or the forward group shows weak, mixed field or dual populations using manual or automated technology.

Key safety messages (applicable to every transfusion laboratory)

- Indeterminate ABO group on initial testing can lead to delays in transfusion and incorrect decisions in component selection for all patients including transplant recipients
- Policies and procedures in the transfusion laboratory for investigating and resolving indeterminate blood groups in all clinical scenarios should be aligned with UK national/British Society for Haematology (BSH) guidelines
- All discrepant blood group results must be fully investigated with an aim to explain the anomaly and define the blood group. This may require referral to a reference laboratory. A full transfusion history including transplant history is essential when interpreting test results
- The configuration of the LIMS must ensure that ABO incompatible blood components cannot be issued
- Indeterminate blood group scenarios must be included in the competency and training program for laboratory staff
- Assigning a 'safe' (group O) ABO group to a patient for transfusion purposes may have unintended catastrophic consequences for solid organ and haemopoietic stem cell transplant recipients
- Policies, procedures and processes must consider the impact of communication, leadership, safety culture, human factors and ergonomics on safe decision-making

Abbreviations

ABO	ABO blood group system	IT	Information Technology
ABOi	ABO incompatible	ED	Emergency Department
BSH	British Society for Haematology	LIMS	Laboratory Information Management System
CAS	Central Alerting System	EPR	Electronic Patient Records
CNS	Clinical Nurse Specialists	IUT	Intrauterine transfusions
EI	Electronic Issue	FMH	Fetomaternal haemorrhage
HSCT	Haemopoietic Stem Cell Transplant	SOP	Standard Operating Procedure
FFP	Fresh Frozen Plasma		

Recommendation: All transfusion laboratories should review their policies, procedures and processes in relation to the management of samples with indeterminate blood groups on initial testing. This includes testing, release of ABO compatible blood components, IT configuration and communication of results to the end user. Transfusion laboratory managers to bring relevant issues to the attention of IT professionals including LIMS and EPR providers.

Action: Transfusion laboratory managers; transfusion IT (LIMS and EPR providers); haematology medical staff; transfusion practitioners

Introduction

Transfusion laboratories have policies, procedures and processes to support the selection of compatible blood components in all routine, urgent and emergency situations, and the transfusion laboratory information management system (LIMS) should be configured to guide the correct selection as well as preventing the issue of ABO incompatible components that could lead to patient harm. The transfusion laboratory undertakes pre-transfusion tests to provide compatible blood components to named patients. Emergency blood components can be provided pre-hospital, when there is insufficient time to complete testing or if a correctly labelled sample is not available, but the imperative is to establish an ABO blood group as quickly and safely as possible. In some situations, the patient's ABO blood group on initial testing is 'indeterminate' and a full transfusion/transplant history and further serological testing, or referral to a reference laboratory may be required. Where transfusion is required it may be necessary to record an interim blood group for the patient in the LIMS before the final/fully resolved blood group has been determined, this can lead to error.

This good practice guidance document from SHOT is based on existing UK guidance highlighting the importance of correctly understanding the reason for an 'indeterminate' blood group, resolving the blood group where possible and making the correct decisions for patient safety. Illustrative example cases reported to SHOT demonstrate errors in transfusion decisions related to 'indeterminate' ABO groups. These can arise due to lack of knowledge regarding reasons for indeterminate groups, accessibility to correct policies/procedures but also highlight that the configuration of the LIMS and the wording of the report in the clinical record can lead to unintended consequences. Note that, unlike other blood group antigens, ABO anomalies may not be resolved by genotyping methods, due to the genetic complexity of ABO and the lack of appropriately validated tests, hence some may remain unresolved.

This document does not cover indeterminate D groups. However, the same principles described here should be applied to manage both ABO and D indeterminate grouping in the laboratory.

Scope and purpose of the guidance

This document will cover, with the use of illustrative cases and in reference to the relevant human factors' methodology:

- The reasons for indeterminate ABO groups on initial testing
- Signposting relevant national guidelines for dealing with indeterminate ABO groups
- The impact of human factors, communication and assumption on safe practice
- The correct and timely communication of the interim result and the final result to the clinical area (what appears in the electronic/paper record)
- The configuration of the LIMS (with reference to BSH IT guidelines) and the decision about entering and/or transmitting interim and/or indeterminate blood group ***(Note: Results may be used to select organs for donation to suitable recipients- 'safe' group for red cell transfusion is not the same for allocation of organs)***

Learning Point

- Gaps in staff knowledge and understanding, poor communication between teams especially clinical and laboratory staff, IT issues, assumptions and other cognitive biases are the main contributory factors identified in these error reports.

Table 1: Potential reasons for initial indeterminate ABO groups*

Mixed field or dual population	Acquired serological anomalies	Inherited serological anomalies
Post-transfusion of ABO mismatched red cells, including emergency group O red cells	Acquired B	A and B subgroups
Post-ABOi HSCT transplant	Malignancies	Chimera
Post-IUT (note that these may change the ABO group entirely)	Cold reacting autoantibodies	Bombay phenotype
Post-exchange transfusion of non-identical ABO red cells	Cold reacting alloantibodies (e.g., anti-M or anti-P1)	
Post-large FMH	Transfusion of plasma components (e.g., plasma exchange)	
Sample quality (e.g., clots, lipemic, haemolysed)	Treatment with intravenous immunoglobulins	

**Note that this is not an exhaustive list of causes, and does not cover D and other blood group anomalies*

Case 1: Allocation of a 'safe' blood group on LIMS leads to inappropriate FFP issue (Investigation of anomalous ABO group leads to miscommunication)

A trauma patient received 4 units of emergency group O red cells in ED following a road traffic collision which was not communicated to the laboratory. A group and screen sample was taken post-transfusion, when tested in the laboratory a mixed-field ABO group was obtained with the forward group anti-A reagent. Local policy states that when blood group is not determined a 'safe group' of O needs to be entered onto LIMS to allow issuing of blood components. The BMS entered group O onto the patient's record and added a note stating to give 'Only group O until blood group confirmed'. Later in the day patient continued to bleed post-operatively and a request for 4 FFP was received. The BMS checked the patient's record, and without realising there was a note, issued 4 units of group O FFP according to the blood group attributed to the patient.

Narrative on case

ED staff did not communicate the transfusion requirement to the laboratory staff. Miscommunication between ED and the laboratory, or between laboratory staff, both verbal and written, are often contributory to SHOT reportable errors. Use of LIMS notes must be clearly defined in SOPs to ensure standardisation of comments. These comments must clearly define the requirements for both red cells and plasma components.

Human factors

Ambiguous comment on the LIMS and assumption that 'group O' related to all blood components led to issue of ABO incompatible FFP. Where notes are required in LIMS this requires individuals to know, and remember, that they need to read them.

Laboratory and IT issues

Limitations of LIMS rules and algorithms lead to organisations relying on the use of the 'notes' sections on the patient record. These are often free text and are not always on the screen at the time of component allocation. Use of 'notes' can lead to incorrect blood components being issued, as they do not have alerts and flags associated and do not prevent issue of incompatible units. In this case, the notes stated to issue group O units, and did not specifically define that this was related to red cells only, and that group A plasma should be issued. LIMS should be configurable to prevent the release of ABO incompatible blood components.

Communication

A written miscommunication led to the incorrect ABO FFP being selected for thaw and issue.

Learning Point

Maximise potential for LIMS rules and algorithms to reduce ABOi errors

Standardise comments in 'notes' sections on LIMS to ensure clear communication

Recommended resources

SHOT Bite No 8: Massive Haemorrhage Delays accessible via this link SHOT Bites - Serious Hazards of Transfusion SHOT Bites (shotuk.org)

British Society for Haematology (BSH) guidelines titled 'Pre-transfusion compatibility procedures in blood transfusion laboratories'

MHRA Central Alerting System alert issued Jan 2022 'Preventing transfusion delays in bleeding and critically anaemic patients'

SHOT bite No 9: Component compatibility accessible via this link SHOT Bites - Serious Hazards of Transfusion SHOT Bites (shotuk.org)

Case 2: Change in group after ABOi haemopoietic stem cell transplant uncovers deficiencies within communication pathways

A group A patient who had received a group O cord blood allograft transplant presented with an anomalous blood group 2 months post-transplant. When laboratory staff investigated the anomaly with the clinical team, they were informed of the transplant, which was confirmed by the local stem cell laboratory. At this point, the patient had already been transfused 10 units of group A red cells.

Narrative on case

When ABO mismatched haemopoietic stem cell transplants occur, patients should receive blood components which are compatible with both the recipient and donor blood groups. This information should be contained in a clearly defined protocol which is made available to all individuals involved in the patient's care, including transfusion laboratories, at primary and secondary treating centres. In this case, no notification was sent to the transfusion laboratory.

Human factors

Both clinical nurse specialists (CNS) were absent on the day the patient was admitted, and the protocol was not emailed to the laboratory, or any other teams involved in the patients care. There was an overreliance on the local stem cell laboratory to detect and inform the CNS of any errors or omissions, which did occur on the day of admission, but this email as also missed by the CNS. Furthermore, none of the blood orders received by the laboratory mentioned the transplant.

Laboratory and IT issues

Of the multiple red cell orders sent for this patent, only 2 mentioned the transplant on the electronic patient record. However, in this hospital the laboratory staff do not have access to information on the EPR. An additional measure on the EPR called a 'patient problem list' was available for the laboratory to identify any specific requirements, but the allograft was not recorded here.

Communication

Multiple errors in communication occurred between the CNS team and both hospital and stem cell laboratories. There were additional omissions on request forms, EPR and patient problem list.

Learning Points

A robust (effective and reliable) system for communication regarding HSCT must be in place to ensure safe care of patients. Email communication is often prone to error and can often provide a single point of failure

A lack of interoperability and access to IT systems can prevent relevant teams viewing critical safety information

Recommended resources

Safe transfusions in hematopoietic stem cell transplant recipients accessed via this link: https://www.shotuk.org/resources/current-resources/

Case 3: Group O granulocytes were issued via electronic issue to a patient despite tests showing an indeterminate ABO group

A lone-working BMS edited a mixed-field anti-A result. The modification was not recorded on the patient's notes and patient was not removed from electronic issue on the LIMS. Granulocytes were requested and a group O component was electronically issued. The LIMS algorithm did not prevent the electronic issue on the edited sample and as there was no record of the modification, the requirement for a serological crossmatch was not identified. The granulocytes were not transfused, and the unit was discarded. Error identified when a new request for granulocytes was received the following day. Limited information available for this case.

Narrative on case

Granulocyte components contain a significant volume of red blood cells and blood group compatibility between recipient and donor must be ensured. As for red blood cell units, a compatibility test is required before issuing granulocytes to a patient. In instances where the patient's blood group has been edited or manually modified a serological crossmatch must be performed and patient removed from electronic issue as per BSH and MHRA guidance (Staves, et al., 2024; MHRA, 2010).

Human factors

The BMS was lone working, covering a busy night shift. The incident occurred on the early hours of the morning. The process for excluding patients from electronic issue required manual input from staff by recording it on a note on LIMS. Although the information was recorded, this did not impact electronic issue and the algorithm set up for electronic issue was for issue of red cells only.

Laboratory and IT issues

The LIMS algorithm did not exclude patients from electronic issue when results have been edited. The process relies on manual input from BMS to remove patients from electronic issue. The LIMS had also limited capability related to audit trail, being difficult to identify when modifications to patient's records have been performed.

Communication

It is important that limitations identified in the IT systems are reported to the supplier to allow a discussion of how errors and incidents can be prevented and the solutions available. IT systems must meet the client's requirements especially when patient safety is at risk. IT systems should comply with recent guidelines and support staff in the daily tasks removing the requirement for human input as much as possible.

Learning Point

IT systems support safe practice, but only when it is configured and designed correctly

LIMS must support electronic issue in accordance with BSH and MHRA recommendations

Limitations to IT systems should be reported to suppliers to ensure that requirements for safe practice are applied

Recommended resources

Using Information Technology for Safe Transfusion
https://www.shotuk.org/resources/current-resources/

Transfusion LIMS Specification
Transfusion LIMS Validation Plan
https://www.shotuk.org/resources/current-resources/script/

Guidelines for the specification, implementation, and management of IT systems in hospital transfusion laboratories
https://doi.org/10.1111/j.1365-3148.2012.01199.x

MHRA Guidance on Electronic Issue
https://www.gov.uk/government/publications/electronic-issue-of-blood-components

Case 4: Incorrect interpretation of weak neonatal blood group reactions by automated analyser

A sample for blood group and direct antiglobulin test for a neonate with jaundice was received in the laboratory. The sample was processed on the automated analyser and returned a weak positive result with the anti-A reagent, strongly positive results were obtained with the anti-B and anti-AB reagents. The blood group was interpreted by the analyser as AB, and this was reported via the LIMS to the EPR. Later visual review of the reactions, by a BMS, noted that the weak reaction with anti-A was a result of a clot in the sample. Manual testing showed that the infant was group B. The results were removed from the EPR and replaced with the correct ABO group.

Narrative on case: ABO antigens may not be fully developed at birth, for this reason the reagent manufacturer instructions stated that weak reactions should be considered as positive results. In contrast, weak reactions with ABO grouping reagents for adult samples are treated as indeterminate and subject to further investigation.

Human factors: The previous automated analyser system had been configured to 'hold' weak ABO results for both adult and neonatal testing for BMS review and further testing. When the new automated system was implemented assumptions were made that it behaved in the same way. Lack of understanding of the analyser ABO interpretation settings and unclear acceptance criteria during validation of the new platform resulted in missed opportunities to configure the system to identify potential 'false positive' reactions.

Laboratory and IT issues: During validation and implementation of the automated analyser system no consideration had been made relating to weak reactions in neonatal ABO grouping. As a result of this incident the analyser middleware was reconfigured to hold back indeterminate neonatal ABO groups for manual review by a BMS.

Communication: Effective communication between the analyser provider and laboratory management could have improved the initial configuration of the system and prevented the error. Validation of new processes, equipment, analyser platforms and IT systems often requires a team of staff with relevant knowledge and skills. Communication of the requirements for testing and acceptance criteria, both verbal and documented, to the team is a critical aspect of the validation process.

Learning Point

Analyser platforms and associated IT systems should be configured to identify weak and indeterminate results for all patients for review and investigation.

Recommended resources

Resources relating to transfusion IT https://www.shotuk.org/resources/current-resources/script/

BSH guideline Transfusion for Fetuses, Neonates and Older Children (b-s-h.org.uk)

Case 5: Incorrect allocation of donated organs based on misinterpretation of ABO group after massive haemorrhage

A patient with polytrauma was resuscitated and received massive blood transfusion support. The patient's actual blood group was A, however no baseline blood group prior to transfusion therapy was available. The blood group of a sample taken post-transfusion in the receiving hospital was uninterpretable and was recorded as group O for purposes of issuing blood components. The patient succumbed to injuries and was identified for organ retrieval. The patient's organs were erroneously allocated to group O recipients following patient demise. Laboratory staff were unaware of the implications of blood group on organ transplantation.

Narrative on case: Blood type determination is one of the most crucial aspects of the process for matching donor organs to transplant candidates. The inability to accurately determine ABO blood type of the donor and/or recipient can have catastrophic consequences for organ transplant recipients. Assigning a 'safe' ABO group on the LIMS to support appropriate selection of ABO compatible components for transfusion can have unintended consequences for organ transplantation.

Hyperacute rejection, development of accelerated or acute antibody mediated rejection in the early period post-transplant can result which may be rapidly progressive with an associated risk of graft loss. Tools such as plasmapheresis and immunosuppressive drugs can successfully prevent and treat this type of rejection. These tools carry significant clinical risks and costs, however, so it is important to prevent such inadvertent antibody incompatible transplants.

Human factors: Staff should also recognise that organ allocation decisions if patients are potential organ donors are distinct from transfusion decisions or decisions about reporting the blood group.

Laboratory and IT issues in the solid organ transplantation setting, a patient/organ donor whose ABO group cannot be clearly established should be labelled as 'AB for the purposes of organ donation', meaning that only recipients of Group AB will be eligible to receive the organs (and as the recipients lack any anti-A or anti-B

antibodies, they will not reject the organs regardless of the true donor blood ABO group). In ABO incompatible solid organ transplantation, the donor to recipient blood group combinations of A to O, B to O, AB to O, B to A, AB to A, A to B and AB to B are incompatible, irrespective of whether the donor is blood group A1 or A2.

Communication: While laboratory staff may not always be able to identify when patients are potential organ donors, it is vital that electronic patient records reflect accurate, confirmed blood groups for patients. Any indeterminate blood group must prompt appropriate actions. When contacted by specialist nurses for organ donation, in case of any anomalous blood group that is yet to be fully resolved, this must be clearly communicated to support safe organ allocation.

Learning Points

Labelling a patient/donor whose ABO group cannot be clearly established as 'ABO group not determined – awaiting confirmation' will prevent any inadvertent ABO-incompatible solid organ transplant

Processes for organ retrieval teams should ensure confirmation of the ABO group, including clear questions for the laboratory staff to exclude any ABO grouping anomalies

Recommended Resources

British Transplantation Society guideline https://bts.org.uk/wp-content/uploads/2016/09/02_BTS_Antibody_Guidelines-1.pdf

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Appendix 1: Gap analysis to support compliance with good practice

	Recommendation	Compliant Y/N*	Comment/Further Action
1.	There is a local policy/procedure detailing the process for dealing with indeterminate blood groups which includes identification, investigation, escalation, resolution, reporting and transfusion management of patients with ABO discrepant results in accordance with BSH guidelines. ***These should include dealing with discrepancy of unknown cause, antenatal patients, post-BMT/PBSCT transplant recipients, and organ donors***		
2.	Training and regular competency assessment for all staff working in transfusion laboratories includes awareness of the actions that need to be taken in case of indeterminate blood groups		
3.	The LIMS allows an indeterminant group to be reported instead of forcing use of a 'safe' ABO group to release blood components		
4.	The LIMS supports provision of safe and appropriate blood components where an ABO blood group has not been determined , that does not rely on use of emergency group O red cells		
5.	Laboratory processes are in place to report indeterminate blood groups with appropriate comments to clinical teams. This includes alerting the user to any updates, revisions, or confirmation of the blood group		

**** If the answer is 'no' to any of these, then appropriate actions need to be taken locally to ensure safe transfusions***

Note: This gap analysis is a high-level view of compliance status. Further details for compliance are available in the UK NEQAS, SHOT and UKTLC survey report which can be accessed at this link: SHOT Surveys - Serious Hazards of Transfusion (shotuk.org)

References/Resources

The Blood Safety and Quality Regulations 2005: https://www.legislation.gov.uk/uksi/2005/50/made

The 21st edition of the Guide to the preparation, use and quality assurance of blood components, providing state-of-the-art guidance for healthcare professionals, by the European Directorate for the Quality of Medicines & HealthCare (EDQM) 2023 https://www.edqm.eu/en/blood-guide

UKAS ISO15189:2022 standards https://www.ukas.com/accreditation/standards/medical-laboratory-accreditation/

UK Transfusion Laboratory Collaborative: Minimum standards for staff qualifications, training, competency and use of information technology in hospital transfusion laboratories 2023: https://pubmed.ncbi.nlm.nih.gov/38351636/

British Society for Haematology Guidelines for pre-transfusion compatibility procedures in blood transfusion laboratories 2012 https://onlinelibrary.wiley.com/doi/full/10.1111/j.1365-3148.2012.01199.x

Guidelines for the specification, implementation and management of IT systems in hospital transfusion laboratories Transfusion Medicine. 2024; 34(2): 83-111. Guidelines for the specification, implementation and management of IT systems in hospital transfusion laboratories (b-s-h.org.uk)

Guidelines on transfusion for fetuses, neonates and older children 2016 Transfusion for Fetuses, Neonates and Older Children (b-s-h.org.uk)

CAS Alert SHOT/2022/001Preventing transfusion delays in bleeding and critically anaemic patients CAS-ViewAlert (mhra.gov.uk)

MHRA EI guidance Electronic issue of blood components - GOV.UK (www.gov.uk)

British Transplantation Society guideline https://bts.org.uk/wp-content/uploads/2016/09/02_BTS_Antibody_Guidelines-1.pdf

SHOT BITE no.9 Component Compatibility Educational Resources - Serious Hazards of Transfusion

SHOT BITE No.18 Haemopoietic Stem Cell Transplant Educational Resources - Serious Hazards of Transfusion

UK NEQAS survey report Good practice guidance document for managing indeterminate ABO blood groups to support safe decision-making - Serious Hazards of Transfusion