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INTRODUCTION

This survey was a voluntary web-based educational survey. Two case studies were presented focusing on 1) Electronic (computer) crossmatching and computer downtime, and 2) Hemolysis due to IVIG.

The survey was offered to all TMED A survey participants.

- 80 of 89 (90%) participants submitted responses.

CASE 1

A 30-year-old male is brought to your facility's Emergency Department with injuries as a result of a motorcycle accident. His condition is stable, but he may be scheduled for orthopedic surgery. Your laboratory receives a sample for a blood group and antibody screen.

The sample types as O Rh positive. The antibody screen is negative. The patient has never been hospitalized before and has never received a blood transfusion.

1. What method would your laboratory use to perform a crossmatch for this patient, if necessary?

		Count	%
a.	Immediate spin method	44	55
b.	Antiglobulin method	4	5
c.	Electronic/computer	31	39
No response		1	1

The Operating Room has just informed your laboratory that the patient has been scheduled for surgery and may need two units of blood. You have also just discovered that your laboratory's LIS has crashed and is unavailable to you.

2. Does your laboratory have an alternate system that ensures continuous operation in the event of computer downtime?

		Count	%
a.	Not applicable our laboratory records are paper-based; we do not have an LIS (proceed directly to Case 2)	3	4
b.	Yes, paper-based	49	61
c.	Yes, stand-alone backup computer system	12	15
d.	**Yes, other (explain)**	**15**	**19**
	Stand alone computer for historical record check	17	–
	Paper-based	13	–
	Computer for back-up product chart copies and tags	1	–
No response		1	1

3. Does your laboratory have an alternative records system that allows tests to be reported and blood or blood products to be released for transfusion in the event of computer downtime?

		Count	%
a.	Yes, paper-based	74	96
b.	**Yes, other than paper-based (explain)**	**2**	**2**
	All paper-based records of testing and issue of blood products are then back-entered into the LIS when the downtime has been resolved.	1	–
	Data Warehouse for historical blood type and transfusion history	1	–
	Patient history on a separate server.	1	–
	We have a back-up file which is downloaded to a file from our LIS daily which contains the record of all our patients since we went Live with this LIS in 2002. We can pull this up during down times so it is available. We also have another File that is backed-up daily of all our patients between 1984 and 2002	1	–
No response		1	1

4. How would your laboratory complete the request for crossmatch for this patient during this LIS downtime?

		Count	%
a.	Issue uncrossmatched blood	1	1
b.	Wait until the LIS is functioning again	0	0
c.	Perform serological crossmatch	61	79
d.	**Other (explain)**	**14**	**18**
	Perform immediate spin crossmatch.	5	–
	Process as normal; document on downtime requisition; all documentation retained and entered in LIS when system functioning	4	–
	Regroup patient's ABO/Rh and perform Immediate Spin crossmatch	3	–
	Perform IS XM on the first unit to be dispensed. Subsequent units may be dispensed as ABO/D compatible (same as the first unit going to patient)	2	–
	Give uncrossed blood if urgent.	2	–
	Confirm negative screen result and patient history in back up module.	2	–
	If the results of the current sample are unavailable in one of the backup files, or written on the current worksheet, the testing would be repeated and documented on paper	2	–
	Group and screen would need to be repeated on paper and serological crossmatch be performed.	1	–
	Request second sample for ABO confirmation and then perform serological crossmatch	1	–
	IS crossmatch for specimens with a negative antibody screen; patients with clinically significant antibody(ies) require an IAT crossmatch	1	–
No response		1	1

The following questions apply to those facilities that perform electronic/computer crossmatching.

5. How do you know that your laboratory's LIS will prevent the release of ABO incompatible blood components? Check all that apply.

		Count	%
a.	LIS validation performed prior to implementation of electronic crossmatch	39	93
b.	LIS tested periodically	13	31
c.	**Other (explain)**	**11**	**26**
	LIS issues an Exception when someone releases ABO incompatible blood products.	1	–
	Quality assurance checks are built in the software to catch possible errors.	2	–
	LIS prevents the Electronic Crossmatch on ABO incompatible units	1	–
	LIS tested with each software change/upgrade	5	–
	Audits (one week) monthly, and one month quarterly. Test when criteria not met for an electronic crossmatch.	1	–
	2nd blood group must be in history and donors must be tested before electronic crossmatch is allowed in LIS system	1	–

6. In your facility, how would the second determination of a patient's ABO group be performed? Check all that apply

		Count	%
a.	Retest the same sample	33	78
b.	Collect a second sample for testing	17	40
c.	Historical Record	34	81
d.	Second determination of ABO group not required	1	2

7. If "a." was selected for the previous question (Retest the same sample), how would this be performed?

		Count	%
a.	By the same technologist	4	12
b.	By another technologist	9	27
c.	Either a. or b	20	61

8. Is the ABO group of donor red cells confirmed serologically?

		Count	%
a.	Yes	41	98
b.	No	0	0
	No response	1	2

CASE 1: COMMENTS

1	7. ABO Rh repeat also tested by a different method
2	ABO Rh repeat testing done by secondary method.
3	Case #1 patient has no history and we would perform a second blood grouping. Two determinations of ABO are required - one can be historical.
4	Conditions for eligibility for CAC are: 1)current ABO/D plus second testing of ABO/D (historical or same sample) 2) current negative antibody screen 3) no history of atypical antibody 4) ABO/D confirmed on unit of RBC.
5	For 7. the retesting is the same sample but a different suspension with a different specimen number.
6	Historical record for second grouping must have been performed by our Health Authority
7	If historical blood group present no secondary grouping is performed.
8	Question # 1: We would perform an immediate spin crossmatch until a second sample for ABO confirmation was sent to blood bank. Then we would perform an electronic crossmatch
9	Question # 3: Even though we have a paper based reporting system and also a paper based system for releasing blood products in the event of LIS system downtime, we do have an alternate Blood Bank History backup system which is fed by our LIS to view all previous results for each patient which is backed up daily.
10	Question #1..My response is electronic/computer crossmatch provided that an ABO group confirmation sample had been received and tested, otherwise, uncrossmatched blood would have to be offered with attending physician's consent and a variance form accompanying the uncrossmatched blood issued for the physician to sign and return a copy to blood bank.
11	Question 6: Our policy is to have 2 samples collected for each crossmatch order. The 2nd sample is for the second ABO testing if required.
12	Question 7. If a second technologist is not available to do the second ABO, an immediate spin serological crossmatch is performed on the first unit.
13	Question 7. Second ABO determination performed by another technologist, unless only one technologist is on duty (i.e. Midnight shift).
14	Re question 6 a. Retest the same sample only if the sample was collected using positive patient identification technology.
15	Re: #6. Our lab tries to collect 2 samples for every group and screen order and then does an ABD grouping on each of the 2 tubes. If only 1 tube is received, ABD testing is repeated on the one tube. We also do an "ABO check" via a quick spin method by setting up known A or known B cells versus the patient's plasma for every non Group O patient, whenever the patient does not have a historical ABD type in the BB database in Cerner computer system and when only one technologist has performed both ABD typings on the current specimen(s). #7: There is only 1 tech assigned to TM, and so most of the 2 ABD determinations end up being done by one technologist. However, during day shift hours there is the possibility that another tech will take over the testing during break times, change of shift, etc. and then it is possible that the 2 ABD groupings end up being tested by 2 different technologists.
16	Regarding 6a, sample is tested by different method
17	Retesting is performed preferably by a second technologist, if possible.
18	Second determination of patient blood group is nearly always performed by another technologist.
19	Second determination of patient's ABO group is performed by a second technologist whenever possible. If there is only one technologist on duty and release of red cells cannot wait, then the same technologist will retest the same sample.
20	TM is paper-based. LIS used for patient demographic information only.
21	We confirm PRBC units ABO upon receipt from CBS.
22	We do not do electronic cross match but our LIS still does a delta check between the donor group and the patient group. We test all group "O" blood to be ready to issue as uncrossed. I addition we are confirming compatibility of all groups by doing the Immediate Spin cross match.

CASE 1: DISCUSSION

Performing a crossmatch is required before red cell transfusions unless unmatched group O blood is issued in an emergency situation. The most important function of the crossmatch is to detect ABO incompatibility between the recipient plasma and donor red cells. In the absence of known clinically significant antibodies, laboratories may perform immediate spin crossmatch or electronic/computer crossmatch.

Thirty-nine per cent of participants responded that they perform electronic/computer crossmatch compared to 60% that perform serological crossmatch (immediate spin or antiglobulin method).

In response to procedures for issuing blood during computer downtime, the majority of participants that have electronic crossmatch in use would perform serological crossmatch. Two participants would perform immediate spin crossmatch on the first unit to be dispensed with subsequent units dispensed as “ABO/D compatible (same as the first unit going to the patient)”. Based on this response these two laboratories would only be confirming ABO compatibility by immediate spin crossmatch of the first issued unit but not the subsequent issue, which would not meet current standards of practice. Participants are reminded that ABO compatibility must be based on a serological crossmatch if not performed by computer crossmatch.

Validation of all laboratory processes is integral to ensuring safe and proper laboratory results. Thorough validation of the computer system is especially important for the electronic crossmatch to prevent incompatible donor red cells from being issued. Validating the electronic crossmatch includes testing the system prior to implementation by challenging the system with all possible scenarios, especially those that are not acceptable, to ensure the system will not proceed with the electronic crossmatch unless proper criteria are met. Continued audits post implementation further contributes to the validation and safety of the procedure.

To meet the requirements for performing an electronic crossmatch a determination of the recipient’s ABO must be made on a current specimen as well as a second ABO determined by retesting the same specimen, testing a second current specimen or comparing historical records for a previous ABO. All but one participant responded that they would require a second determination of ABO for the electronic crossmatch. This one laboratory should review the requirements for performing an electronic crossmatch (CSTM Standards for Hospital Transfusion Services 5.3.7.3). Most (78%) participants retest the same specimen but 40% of participants would collect a second specimen for testing. Only 81% of participants would refer to historical records for the second ABO determination. The other participants are reminded that comparing historical records is a safe and acceptable practice, as well as being cost and time effective.

When correctly implemented the advantages of an electronic crossmatch include: decreased workload, reduced specimen volume required for testing, reduced exposure of personnel to blood specimens and better use of blood inventory.[1]

References

1. Fung MK, Grossman BJ, Hillyer C, Westhoff CM, editors. AABB Technical Manual. 18th ed. 2014.
2. Canadian Society for Transfusion Medicine. CSTM Standards for Hospital Transfusion Services, Version 3; February 2011.
3. Institute for Quality Management in Healthcare (IQMH), Centre for Accreditation. Accreditation Requirements, 2013 Version 6.0. Ontario (Canada): IQMH; 2013.

CASE 2

A 25-year-old male has arrived in your facility's Emergency Room feeling lethargic and generally unwell. He is a neurological patient who was recently treated with intravenous gamma globulin (IVIG). The dose he received was 2 g/kg over two days. His hemoglobin level at the start of treatment was 110 g/L. He received the last infusion five days ago. He has never received any other blood products or components.

Today his hemoglobin level is 60 g/L. There are spherocytes on his blood film and his LDH and bilirubin are elevated. A sample is sent to the Transfusion Medicine laboratory because of the low hemoglobin and possible need for a transfusion.

The results of the blood group and antibody screen are shown below:

ABO/Rh Typing

ABO Antisera		ABO Cells		Rh Antisera		Interpretation
-A	-B	A_1	B	-D	-D Control	ABO? Rh Pos
4+	0	2+	4+	4+	0	

Antibody Detection

Cell	Rh	Rhesus								Kell						Duffy		Kidd		Lewis		P	MNSs				Lu		Results
		D	C	E	c	e	f	C^w	V	K	k	Kp^a	Kp^b	Js^a	Js^b	Fy^a	Fy^b	Jk^a	Jk^b	Le^a	Le^b	P_1	M	N	S	s	Lu^a	Lu^b	CAT
1	R1R1	+	+	0	0	+	0	0	0	+	+	0	+	0	+	+	0	0	+	0	+	+	+	0	+	0	0	+	0
2	R2R2	+	0	+	+	0	0	0	0	0	+	0	+	0	+	0	+	+	0	+	0	0	+	+	+	+	0	+	0
3	rr	0	0	0	+	+	+	0	0	0	+	0	+	0	+	+	+	+	+	0	+	+	0	+	0	+	0	+	0

CAT = Column Agglutination Test (Gel)

1. How would you interpret the ABO group?

		Count	%
a.	Unable to interpret	67	84
b.	A	6	7
c.	O	0	0
d.	**Other (explain)**	**7**	**9**
	Unable to interpret/ Unspecified / Group undetermined Rh Positive	6	–
	Probable A but cannot interpret until discrepancy is investigated	2	–
	Likely this is due to Anti-A from IVIG titre however should rule out subgroup of A, cold reacting antibody, etc to resolve the discrepancy.	1	–
	If we had a historical type on file and it was an A, we would put the patient out as an A.	1	–
	Would follow the ABD discrepancy resolution procedure; in this case we would end up entering the patient's pre transfusion blood type and override the readings obtained, with comments explaining the recent history of IVIG transfusion.	1	–

2. What is the most likely cause of these serological results?

		Count	%
a.	Antibody to antigen not present on Antibody Detection cells	1	1
b.	Passively acquired anti-A	70	88
c.	Cold-reacting antibody	0	0
d.	Subgroup of A with anti-A1	6	7
e.	**Other (explain)**	**3**	**4**
	Anti A found in IVIG	2	–
	At this point you don't know. It could be b,c, or d. We would perform further testing & then decide	1	–
	Based on history provided	1	–

3. What further testing would you do? Check all that apply.

		Count	%
a.	No further testing, refer out	4	5
b.	DAT	70	87
c.	Test red cells with Dolichus biflorus lectin	47	59
d.	Test serum with A1, A2 and O red cells	57	71
e.	**Other (explain)**	**22**	27
	Test eluate against: A1, A2 , O cells; A1, O cells; A, B cells; A1, A2, B cells	8	–
	Perform eluate if DAT is positive.	7	–
	Room temperature screen (A1, A2, B cells/ auto control)	5	–
	Sample would be sent out to our reference lab.	2	–
	Further testing to be done with guidance of hematopathologist/ pathologist/hematopathologist	2	–
	Resolve ABO reverse group discrepancy	2	–
	Serological crossmatch of O Pos units if units required.	1	–
	If a pre IVIG sample was an A we would just do the DAT. A pretransfusion sample should have been complete for ABO, as suggested by the Ministry.	1	–
	Investigate rouleux due to IVIG, perform saline replacement	1	–
	Plasma would be tested against patient cells, (auto)	1	–
	Possible transfusion reaction workup if indicated	1	–
	Test serum against A1 and O red cells	1	–

The ER has added an order for DAT. The results of testing are shown below:

Direct Antiglobulin Test

Polyspecific AHG	Anti-IgG	Anti-C3b/C3d	Saline Control
2	2	0	0

4. Should antibody elution be performed for this sample?

		Count	%
a.	Yes	79	99
b.	No	1	1

You perform an antibody elution and obtain the following results:

Eluate Antibody Identification Panel

Cell	Rh	Rhesus								Kell						Duffy		Kidd		Lewis		P	MNSs				Lu		Results	
		D	C	E	c	e	f	C^w	V	K	k	Kp^a	Kp^b	Js^a	Js^b	Fy^a	Fy^b	Jk^a	Jk^b	Le^a	Le^b	P_1	M	N	S	s	Lu^a	Lu^b	AHG Eluate	Last Wash
1	R1wR1	+	+	0	0	+	0	+	0	0	+	0	+	0	+	+	0	+	+	0	+	+	0	+	+	0	0	+	0	0
2	R1R1	+	+	0	0	+	0	0	0	+	+	0	+	0	+	+	0	+	0	0	0	0	0	+	+	0	0	+	0	0
3	R2R2	+	0	+	+	0	0	0	0	0	+	0	+	0	+	0	0	+	+	+	0	+	0	+	0	+	+	+	0	0
4	Ror	+	0	0	+	+	+	0	0	0	+	0	+	0	+	+	0	0	+	0	+	+	0	+	0	+	0	+	0	0
5	r'r	0	+	0	+	+	+	0	0	0	+	0	+	0	+	+	+	0	+	+	0	+	0	+	+	+	0	+	0	0
6	r"r	0	0	+	+	+	+	0	0	0	+	0	+	0	+	+	0	+	0	0	+	0	0	+	+	+	0	+	0	0
7	rr	0	0	0	+	+	+	0	0	+	+	0	+	0	+	+	+	+	+	+	0	+	0	+	+	+	0	+	0	0
8	rr	0	0	0	+	+	+	0	0	0	+	0	+	0	+	+	0	0	+	0	+	+	+	+	+	0	0	+	0	0
9	rr	0	0	0	+	+	+	0	0	+	+	0	+	0	+	+	+	+	0	0	0	+	0	+	0	+	0	+	0	0
10	rr	0	0	0	+	+	+	0	0	0	+	0	+	0	+	0	+	+	+	0	+	+	+	0	+	0	0	+	0	0
11	R1R1	+	+	0	0	+	0	0	0	0	+	0	+	0	+	0	+	+	0	0	+	+	+	0	+	0	0	+	0	0

5. What conclusions can you make about the eluate? Check all that apply.

		Count	%
a.	Non-reactive	42	52
b.	Reactive	0	0
c.	**Further testing required (specify)**	**66**	**82**
	Test with A1, A2 and O cells	23	–
	Test with A1 and A2 cells	22	–
	Test eluate/last wash with A1 and B cells	9	–
	Test Last Wash and Eluate against A1, A2 and B cells as well as Screen Cells.	2	–
	Test eluate and last wash against A1 cells	2	–
	Would refer out for further testing if req'd after consulting with hematopathologist	1	–
	The panel cells are gr. O, so if patient has a passive anti-A due to IvIG transfusion, then 3 A1 cells, A2 cell, auto control and a cord cell are to be tested with the eluate.	1	–
	Test eluate with A1 cells, A2 cells, B cells and auto cells	1	–
	Test eluate with A1 and O cells	1	–
	Test eluate with A cells or B cells depending on patient's blood group.	1	–
	Test eluate against A, B, and O cells	1	–
	Test against group A donor cells	1	–
	Test with A1, A2, O cells and auto.	1	–
	Test against A1, A2 cells and auto control	1	–
d.	**Other (explain)**	**4**	**5**
	Eluates not performed here, would be sent out for further testing	2	–
	Test with A1 lectin	1	–
	Since panel cells are group O cells would expect a negative non-reactive result, if suspecting anti-A from the IVIG.	1	–
	No response	14	17

You test the eluate with additional cells and obtain the following results:

Cells	Eluate
A1	2+
A2	1+
O	0

6. What additional testing should be done? Check all that apply.

		Count	%
a.	Test rare group O cells	2	2
b.	Test last wash	55	69
c.	Test auto-control	36	45
d.	**Other (explain)**	**16**	**20**
	Test the last wash against A1 and A2 cells/ A1, A2 and O cells	4	–
	Eluate testing is referred out	3	–
	May check the Anti-A titre of this Lot # of IVIG.	2	–
	No additional work to be performed	2	–
	Sample would be sent out to our reference laboratory.	2	–
	Cord cell to be included	1	–
	Consult with Hematopathologist	1	–
	The eluate is displaying the cells were coated with Anti-A, probably from the IVIG.	1	–
	TM Lab will suggest the following tests: CBC, Retic and haptoglobin	1	–
No response		3	4

7. What conclusions can you make about this case?

		Count	%
a.	Drug-induced hemolysis	0	0
b.	Hemolysis due to IVIG	77	96
c.	No conclusions, refer out	1	1
d.	**Other (explain)**	**2**	**2**
	Possible Passive acquired Anti-A in IVIG	3	–
	Referred to hematopathologist/ hematologist for conclusions.	2	–

8. Does your facility have policies/processes/procedures that provide guidance for the administration of IVIG?

		Count	%
a.	Yes	75	94
b.	No	4	5
No response		1	1

9. If “Yes”, does this include guidance on when it may be necessary to have a current pre-transfusion sample?

		Count	%
a.	Yes	45	60
b.	No	30	40

10. If this patient needs a transfusion of red cells, what ABO group would you select?

		Count	%
a.	O	78	98
b.	A	1	1
c.	Avoid transfusion	0	0
No response		1	1

11. Would this event be documented as an adverse reaction to a blood product?

		Count	%
a.	Yes	76	95
b.	No	2	2
No response		2	2

12. If “Yes”, to whom would this event be reported? Check all that apply

		Count	%
a.	TTISS	58	75
b.	CBS	35	45
c.	Attending physician	71	92
d.	Product manufacturer	60	78
e.	Transfusion laboratory medical director	71	92
f.	Transfusion Medicine Committee	48	62
g.	**Other (explain)**	**20**	**26**
	Health Canada/ Health Canada Vigilance Program/ Health Canada Hemovigilance	5	
	Canada Vigilance Office/ Canada Vigilance Adverse Reaction - Health Canada	3	
	Provincial Blood Coordinating Office - Adverse Event reporting	3	
	Transfusion Safety Officer	3	
	Canadian Transfusion Registry/ Provincial Blood Coordinating Office (PBCO)	2	
	PHAC, TSO, Email seniors / supervisors as well	1	
	Technical Specialist/Safety Officer...they would contact TTISS, CBS and manufacturer about the reaction	1	
	Transfusion Medicine Consultant	1	
	We would notify our onsite clinical pathologist. Our reference lab would follow their reporting protocol.	1	

CASE 2: COMMENTS

1	We are in the process of reviewing our current policy i.e. determining when it may be necessary to have a current pretransfusion specimen.
2	The synopsis does not indicate if a pre-transfusion BGRS was drawn and tested before the IVIG infusion.
3	Regarding # 9. Based on information provided on the MOHLTC IVIG Request Form.
4	The Provincial Blood Coordinating office (PBCO) is informed. This agency then reports to Health Canada.
5	SOPs for our site state that the hematopathologist will determine additional testing required in the event of a positive DAT post IVIG transfusion.
6	Our site does not perform antibody elutions nor A1/A2 testing. We would be consulting the hematopathologist due to the positive DAT, the significant drop in Hb post IVIG infusion, and because of the extra reaction in reverse grouping with a hx. of IVIG infusion, prior to any blood transfusion. We would issue serological crossmatch compatible via IAT, O neg rbcs if ABO discrepancy not yet resolved and transfusion required very urgently, and would notify hematopathologist.

CASE 2: DISCUSSION

Case 2 represents a group A patient with passively acquired anti-A due to recent administration of high dose intravenous globulin (IVIG). The passive anti-A in the patient's plasma is reactive with the A_1 cell causing an ABO discrepancy. The direct antiglobulin test (DAT) is positive for IgG. An eluate performed on the patient cells shows anti-A specificity and therefore shows no reactivity with group O panel cells. Appropriate testing of the eluate would include a small panel of group A and O RBCs to prove the specificity. The patient in this case suffered from a hemolytic reaction as evidenced by the decrease in hemoglobin from 110 g/L pre IVIG treatment to 60 g/L at time of presentation to the Emergency Room. Contributing to the diagnosis is the detection of spherocytes on his blood film and an elevated lactate dehydrogenase (LDH) and bilirubin. Due to the circulating anti-A, group O blood should be crossmatched until the patient is no longer exhibiting passive anti-A.

IVIG is a plasma-derived product that contains antibodies that contribute to immunity from a range of diseases. Clinically significant hemolysis is a known but uncommon adverse event of IVIG transfusions. Administration of high dose IVIG per day or cumulatively over a few days in non-group O patients is a known risk factor (particularly group A or AB patients). IVIG related hemolysis is defined as follows: a fall of at least 10 g/L in hemoglobin and a positive DAT with at least two of the following; increased reticulocyte count, increased LDH, low haptoglobin, hyperbilirubinemia, hemoglobinemia, hemoglobinuria or the presence of significant spherocytosis.

Transfusion Medicine laboratories should have policies and procedures for documentation, reporting, evaluation and follow-up of all transfusion reactions. Clinically significant hemolysis attributed to IVIG should be reported to the provincial hemovigilance network and to the IVIG manufacturer. Reporting laboratories may refer to the CBS website https://www.blood.ca/en/hospitals/plasma-products for the most current manufacturer contact list.

References

1. Fung MK, Grossman BJ, Hillyer C, Westhoff CM, editors. AABB Technical Manual. 18th ed. 2014.
2. Canadian Society for Transfusion Medicine. CSTM Standards for Hospital Transfusion Services, Version 3; February 2011.
3. Ontario Regional Blood Coordinating Network. Ontario Intravenous Immune Globulin (IVIG) Utilization Management Guideline, Version 2.0; March 2012.