

## **Canadian Obstetrical Pediatric Transfusion Network (COPTN) 2018 Survey Report for Ontario**

### **Introduction**

The Canadian Obstetrical Pediatric Transfusion Network (COPTN) is a sub-committee of the Canadian Society for Transfusion Medicine (CSTM). The committee was founded in 2017 with a mandate to assess, analyze and facilitate the implementation of best practices in pediatric and obstetrical transfusion practice in Canada.

One of the first projects this committee undertook was to distribute a Canada-wide survey in order to obtain information pertaining to current perinatal testing and Rh Immune Globulin (RhIG) administration practices in the perinatal population. The survey was distributed on March 13, 2018.

The objectives of the survey were to determine the current practices nationally and to assess any variability in practices related to perinatal testing. Upon survey completion and analysis, feedback and guidance regarding best practices would be provided. The Canada-wide survey results were released in the spring of 2019 (<https://www.transfusion.ca/Resources/Canadian-Obstetrical-and-Pediatric-Transfusion-Net>). This report contains the Ontario-specific data and provides a comparison with the National survey results (where applicable).

### **Scope**

The survey was distributed to all hospitals and centralized laboratories that perform perinatal testing in all provinces and territories in Canada. For all hospitals, except those in Québec, Canadian Blood Services (CBS) distributed the survey to their contact hospitals and to centralized laboratories that perform perinatal testing for individual hospitals. In Québec, the survey was distributed by Héma-Québec to all hospital contacts. COPTN members and other volunteers followed up with individual sites and regions to ensure completion of the survey in order to maximize the response rate. In Ontario, survey responses were received from all hospitals with a transfusion service.

### **Survey Content**

The survey consisted of five sections:

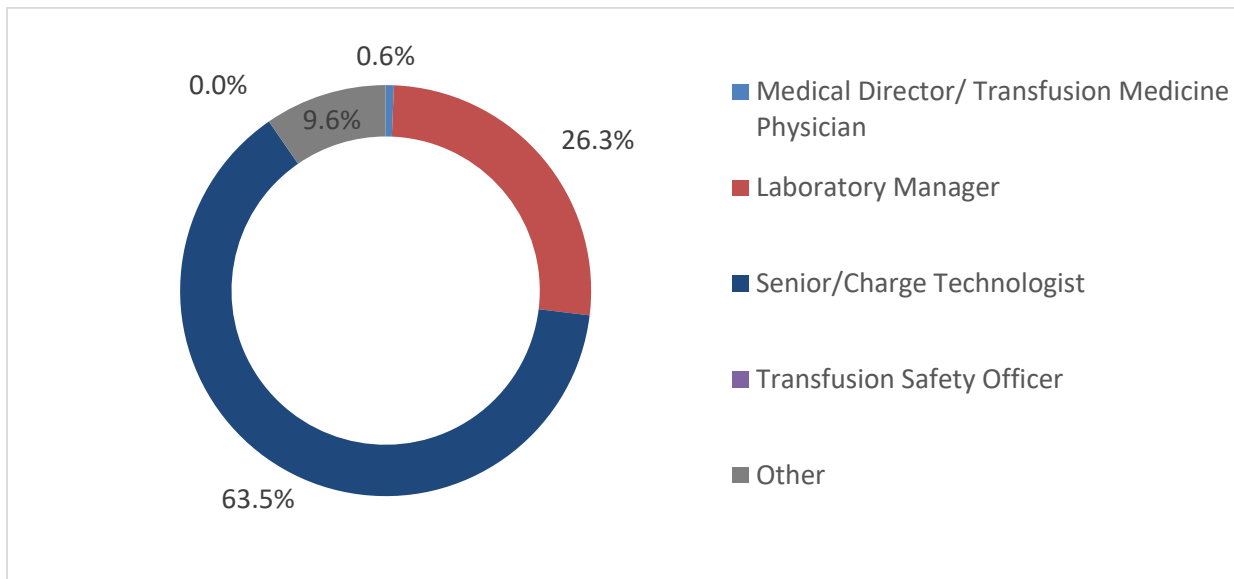
- A. Demographics: five (5) questions;
- B. Antenatal: 35 questions;
- C. Neonates including scenario questions: 22 questions plus three (3) scenarios;
- D. RhIG and fetal-maternal hemorrhage (FMH) assessment: 32 questions; and,
- E. Contact information: five (5) items (name, email, laboratory, city/town and province/territory).

Therefore, the survey consisted of a maximum of 102 questions. Logic was built into the survey so that those respondents that do not perform certain perinatal tests would not need to answer subsequent questions. Respondents with more complex perinatal services had the most questions to answer while the less complex services had fewer questions to answer.

**A. Demographics Highlights**

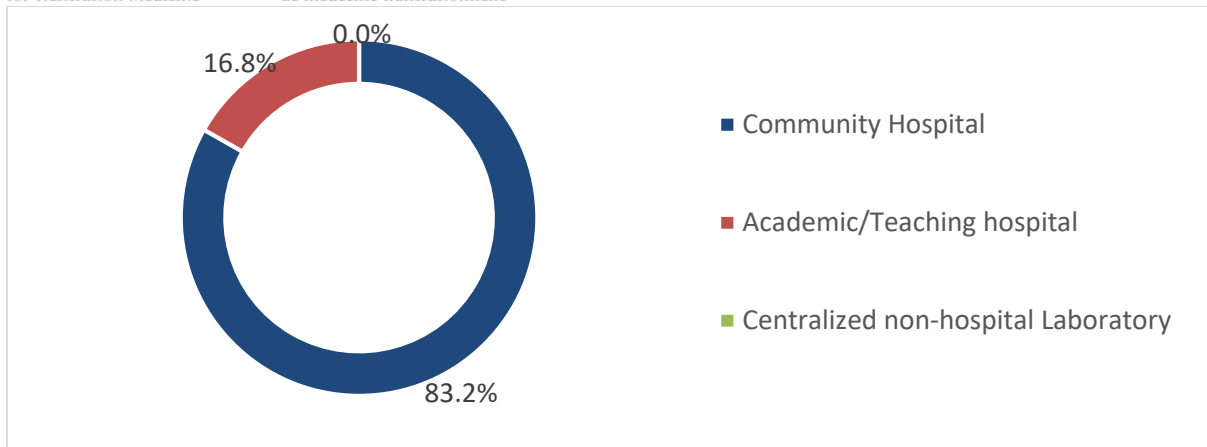
A response rate of 100% (156/156) was achieved by Ontario hospitals with a transfusion service. Ontario’s responses represented 26.9% (156/580) of the responses across Canada.

In Ontario, the majority of survey responders, 63.5% (99/156) were Senior or Charge Technologists and 26.3% (41/156) of survey responders were Laboratory Managers. (Figure 1)



**Figure 1: Percentage of the various roles responding to the survey in Ontario**

Community hospitals represented the highest survey respondent with 83.2% (129/155) of survey responses, followed by academic/teaching hospitals with 16.8% (26/155) of survey responses. (Figure 2)



**Figure 2: Percentage of healthcare facility types that responded to survey in Ontario**

The number of beds “under 100” represented 54.3% of Ontario hospitals with a transfusion service with 9.9% of hospitals falling into the “over 500” category. Respondents were asked if the laboratory performs antenatal testing:

- 58.3% (91/156) perform testing; and,
- 41.7% (65/156) do not.

It should be noted that even though some facilities do not offer antenatal testing, some corresponding antenatal transfusion activities occur there, such as RhIG administration.

**B. Antenatal Highlights (for the 91 respondents indicating “YES” to antenatal testing)**

The survey inquired about all of the perinatal guidelines used to guide testing practices at their hospital with transfusion services (respondents selected all that applied):

- 60.4% had no guidelines or were unsure;
- 28.6% use the Society of Obstetrics and Gynecology Canada;
- 9.9% use the British Committee for Standards in Hematology;
- 5.5% indicated “Other”; and
- 0.0% use the Australian Blood Authority

Hospitals were asked which tests are performed during the initial antenatal assessment. ABO grouping, Rh(D) typing (98.9%; 90/91) and antibody screen (96.7%; 88/91) were identified as the top tests performed by responding transfusion service laboratories. Weak D testing by Indirect Antiglobulin test (IAT) as a routine antenatal test was identified by 28.6% (26/91). For Rh(D) testing of females with childbearing potential, 52.7% (48/91) of the transfusion service laboratories stated they repeat weaker than normal Rh(D) tests with another reagent or method (Table 1).

<b>Table 1. Which of the following describe Rh(D) testing performed for prenatal patients and/or females of child bearing potential in your laboratory?*</b> n (%)	<b>Ontario</b> n=91	<b>National</b> n=243
Either a strong or weaker Rh(D) in the routine test are reported and/or treated as positive without additional testing	39 (42.9)	74 (30.5)
A weaker than normal Rh(D) in the routine test is reported and/or treated as negative without additional testing	2 (2.2)	21 (8.6)
Either a strong or weaker Rh(D) in the routine Rh(D) test, is repeated using a 2nd reagent and/or technique	21 (23.1)	51 (21.0)
A weaker than normal Rh(D) in the routine Rh(D) test, is repeated using a 2nd reagent and/or technique	48 (52.7)	124 (51.0)

\* respondents selected all that applied

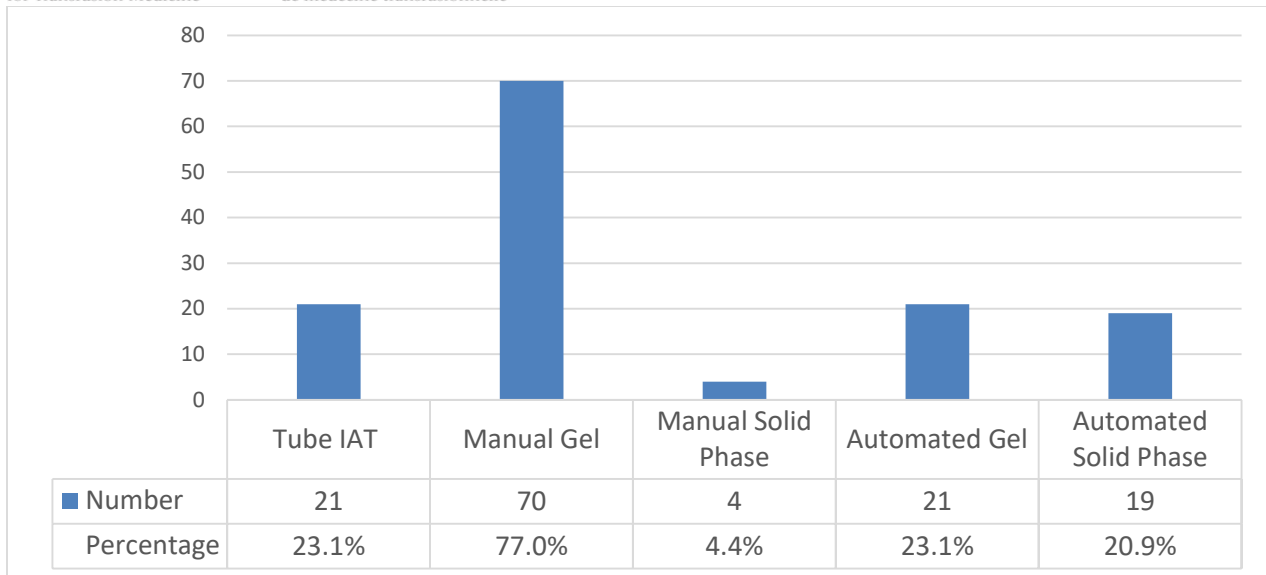
Genotyping on all Rh(D) negative mothers was indicated by 2.2% (2/91) of the respondents, 62.6% (57/91) perform genotyping when there is a weak reaction with one or more anti-D reagents, 45.1% (41/91) perform genotyping when there is a discrepancy from the previous testing, 33.0% (30/91) genotype when there are discrepant reactions between two or more reagents, and 30.8% (28/91) do not perform genotype testing at all. Respondents answered all that applied.

Rh(D) testing results scenarios where the hospital would administer RhIG antenatally (Table 2) for those who do not genotype samples.

<b>Table 2. Rh(D) testing results determining RhIG antenatal administration*</b> n (%)	<b>Ontario</b> n=28	<b>National</b> n= 57
Both Rh(D) direct testing and IAT testing are negative	24 (85.7)	41 (71.9)
Rh(D) direct testing negative and IAT testing weakly positive	11 (39.3)	20 (35.1)
Weaker than expected Rh(D) testing with one or more reagents or techniques	6 (21.4)	9 (15.8)
Discrepant Rh(D) test results in two or more reagents or techniques	4 (14.3)	8 (14.0)
Discrepancies with previous testing	6 (21.4)	9 (15.8)
Other	3 (10.7)	8 (14.0)

\* respondents selected all that applied

Antibody screening methods varied across the laboratory spectrum, but the technique used by most Ontario hospitals with a transfusion service was the manual gel method. (Figure 3)



**Figure 3: Antibody screening methods used in Ontario hospitals with a transfusion service**

If the antibody screen was positive, 56.0% (51/91) of the laboratories indicated that the antibody identification was performed on site. The most common method used for antibody identification when the screen was positive was by manual gel technique (62.7%; 32/51). (Table 3)

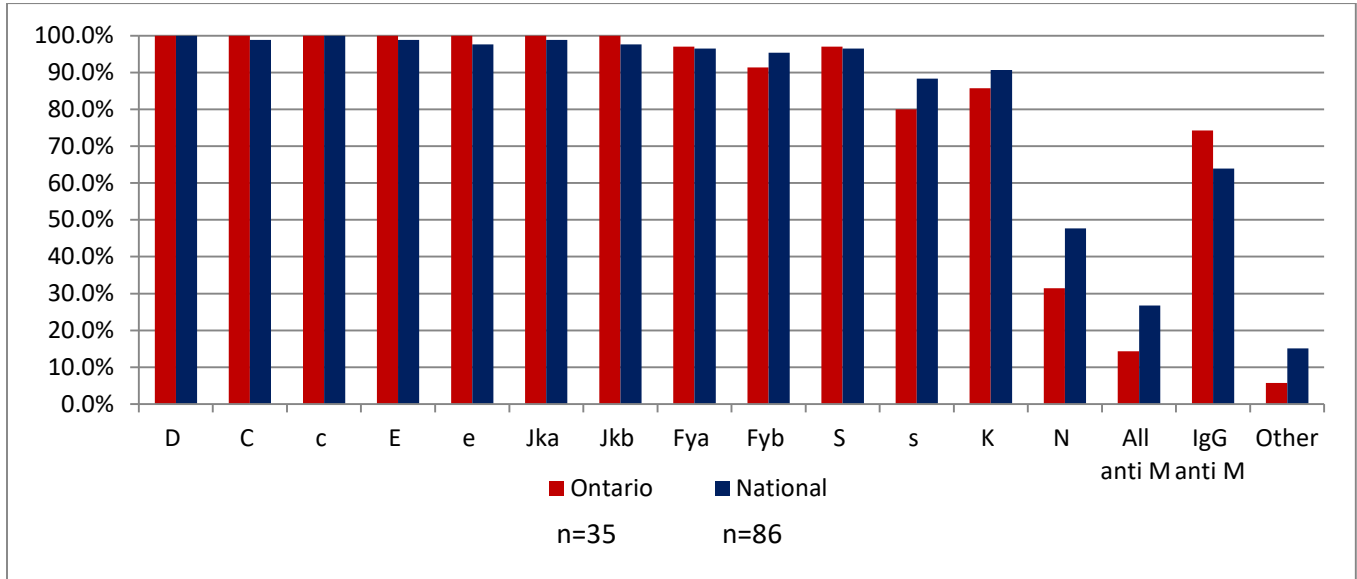
<b>Table 3. Primary method used for antibody identification n (%)</b>	<b>Ontario n=51</b>	<b>National n=145</b>
Tube IAT	1 (2.0)	4 (2.8)
Manual gel	32 (62.7)	100 (69.0)
Manual solid phase	0 (0.0)	5 (3.4)
Automated gel	5 (9.8)	11 (7.6)
Automated solid phase	13 (25.5)	25 (17.2)

When sites were asked if they titrate clinically significant antibodies on site, 68.6% (35/51) responded that they do and use the following techniques:

- 88.6% (31/35) use saline tube; and,
- 11.4% (4/35) use manual gel.

Of the sites that perform antibody titrations on site, 100% (35/35) of the laboratories surveyed indicated that the following RBC alloantibodies would be routinely titrated: anti-D, -C, -c, -E, -e, -Jk<sup>a</sup>, -Jk<sup>b</sup>, and -S. Ninety-seven percent (97.1%; 34/35) for anti-Fy<sup>a</sup> and 91.4% (32/35) indicated that anti-Fy<sup>b</sup> would be titrated. Fewer sites reported they perform titration (between 80-86%) for anti-s and anti-K and even

fewer reported that they would perform titration (5-75%) for anti-N, anti-M, IgG anti-M and “other” (Figure 4).

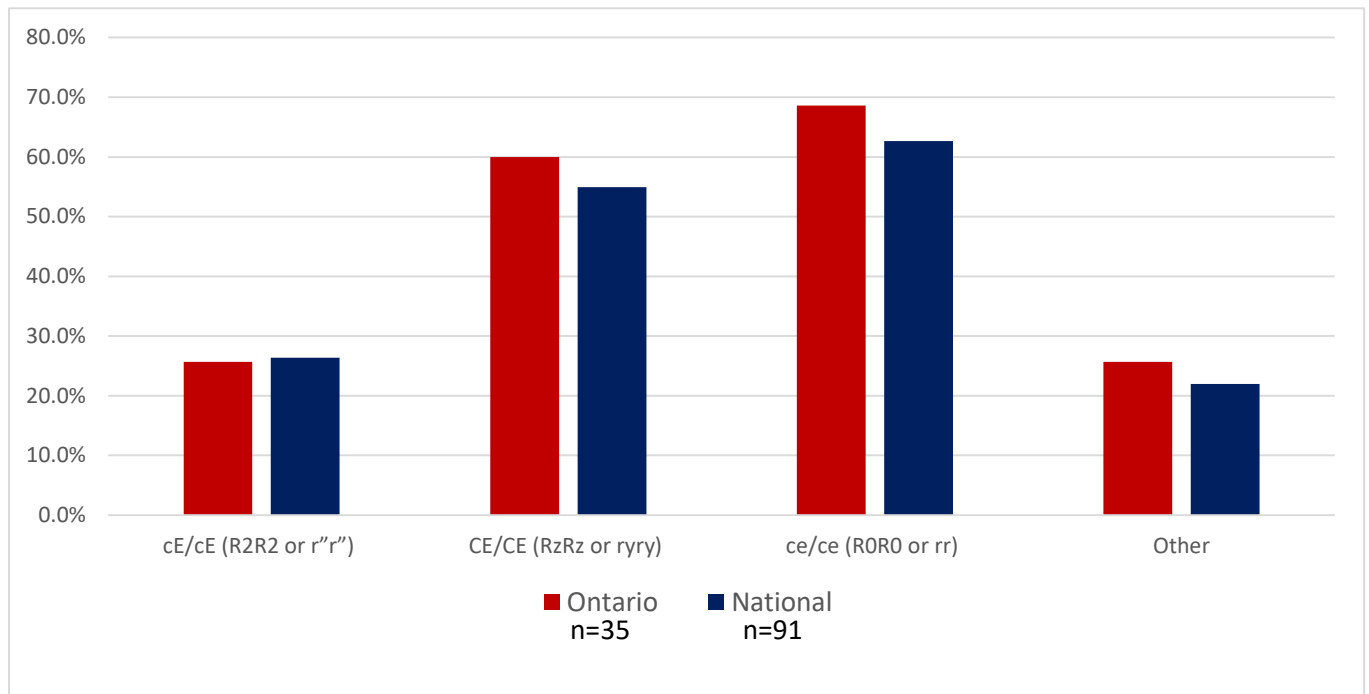


**Figure 4: Percentage of RBC alloantibodies routinely titrated**

The critical titre level identified by the laboratories completing the survey ranged from 8 to 64, with the results as follows in Table 4:

Table 4. Critical antibody titres n (%)	Titre of 8	Titre of 16	Titre of 32	Titre of 64	Other
Ontario n=29	1 (3.4)	9 (31.0)	7 (24.1)	1 (3.4)	11 (38.0)
National n=52	2 (3.8)	18 (34.6)	11 (21.2)	1 (1.9)	20 (38.5)

There were a few case scenario questions in this section. One case that pertained to titration, asked about the phenotype of reagent RBCs that would be used for a prenatal patient with both an anti-c and anti-E. Most laboratories (60-68.6%) demonstrated a single antigen titration approach as opposed to selecting a cell that would provide a combined titre (Figure 5).



**Figure 5: Phenotype of reagent RBCs used for titration of anti-c and –E (sites could choose more than one approach used)**

When asked about performing mid-pregnancy antibody screens, 73.3% (66/90) of the Ontario hospitals with a transfusion laboratory responded that this test is performed on some or all patients. Of those laboratories that do perform this mid-pregnancy antibody screening (respondents selected all that applied):

- 39.4% (26/66) perform it for all patients;
- 54.5% (36/66) perform it for Rh(D) negative patients;
- 34.8% (23/66) perform it for patients with clinically significant antibodies; and,
- 30.3% (20/66) indicated they do not routinely perform mid-pregnancy antibody screens.

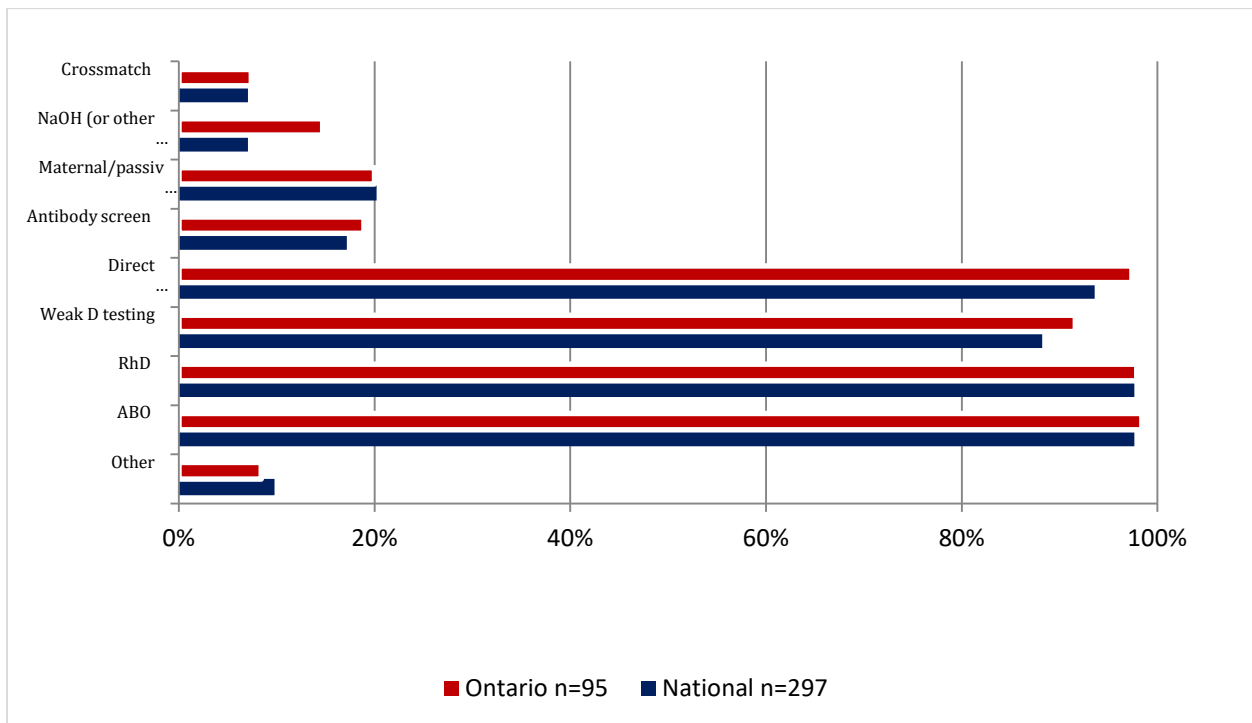
There was variation pertaining to practice for accepting Rh (D) typing and negative antibody screen results from an outside laboratory for the purposes of providing RhIG with 56.7% (51/90) of respondents indicating that this is acceptable practice, but 43.3% (39/90) responded it is not.

### C. Neonatal Intensive Care Unit (NICU) and Baby Highlights

Only 23.2% (36/155) of the sites had a NICU and the distribution across the acuity levels is as follows:

Table 5. NICU acuity level distribution, n(%)	Ontario n=35	National n= 88
I	0 (0.0)	3 (3.4)
II	21 (60.0)	35 (39.8)
III	8 (22.9)	17 (19.3)
IV	2 (5.7)	8 (9.1)
Centralized with multiple sites	0 (0.0)	2 (2.3)
Unsure	4 (11.4)	23 (26.1)

Of the sites that deliver babies, a variety of size of service was demonstrated, ranging from 1-50 deliveries per year to sites that deliver over 1500 babies per year. The type of tests that may be performed on cord blood from these babies is illustrated in Figure 6.



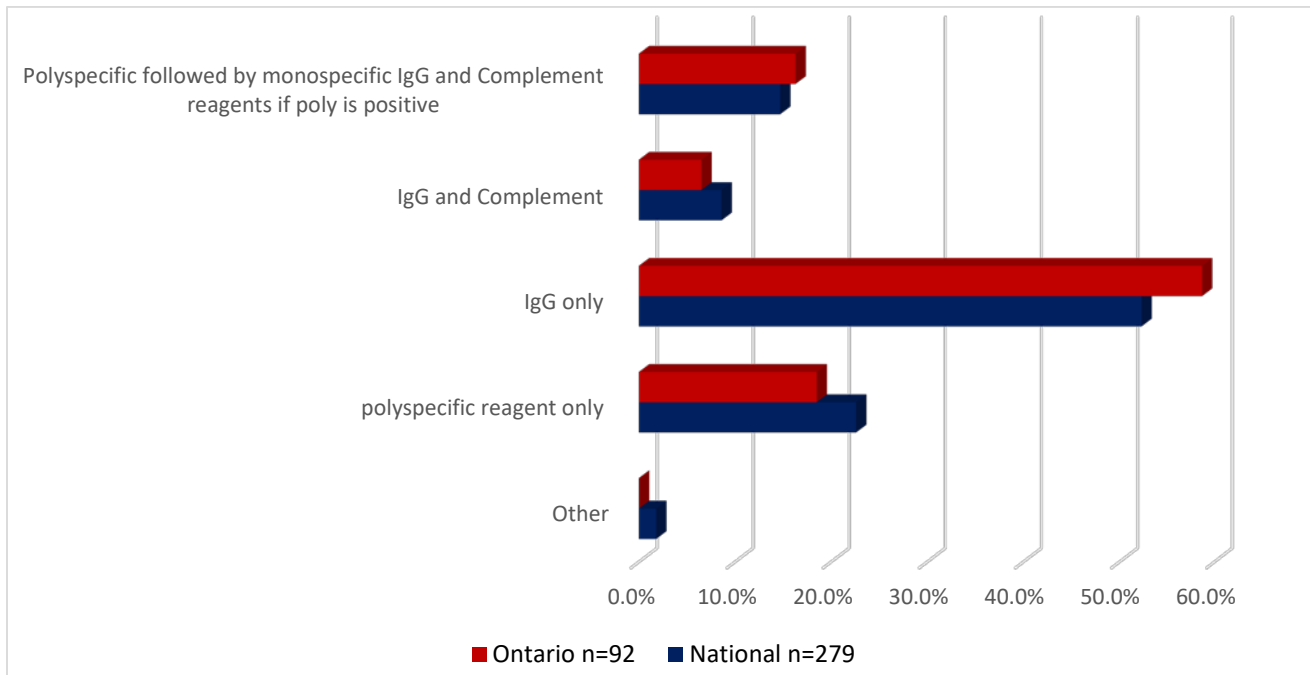
**Figure 6. Types of tests that may be performed on cord blood**

The majority of Ontario hospitals with a transfusion service (80.0%; 76/95) perform cord testing using the tube method for ABO group and Rh(D) type, 25.3% (24/95) use gel method and 7.4% (7/95) use solid phase techniques. Most respondents (72.3%;68/94) indicated that antibody screening is not performed on cord samples. Of the transfusion service laboratories that indicated they perform cord antibody screening the following testing methods were reported: gel method (19.1%; 18/94); tube method (3.2%;



3/94); and solid phase testing (3.2%; 3/94). Cord direct antiglobulin test (DAT) methods used were: tube method (54.7%; 52/95); gel method (37.9%; 36/95); and solid phase (4.2%; 4/95).

When asked what DAT reagents are used, over half of the respondents who perform cord testing (58.7%; 54/92) use monospecific anti-IgG to test their cord samples (Figure 7).



**Figure 7: Type of reagents used for cord DAT in Ontario compared to National**

The next set of questions determined under which circumstances a cord DAT was performed. 28.6% (26/91) of the Ontario transfusion service laboratories responding perform a DAT on all cord samples received. For the 71.4% (65/91) who do not automatically perform a DAT on every cord sample, scenarios were presented that would trigger a DAT order and are illustrated in Table 6. Over a third of the responses indicated they would screen their DAT orders (37.2%; 35/94) before completing the testing.

Table 6. Scenarios prompting DAT cord testing* n (%)	Ontario n=65	National n=190
Cords from all group O mothers	23 (35.4)	34 (17.9)
Cords from all mothers with clinically significant antibodies	49 (75.4)	124 (65.3)
Cords from all Rh (D) negative mothers	45 (69.2)	98 (51.6)
On physician request	61 (93.8)	173 (91.1)
Following a review that indicates hemolysis	18 (27.7)	48 (25.3)

Cords with fetal ABO incompatibility with the mother	9 (13.8)	44 (23.2)
--	----------	-----------

**\*respondents selected all that applied**

A series of scenarios were presented in this section of the survey to determine the type of testing routinely performed in these cases. The first case inquired about the routine cord tests performed for a baby whose mother is Rh(D) negative. The results are summarized in Table 7.

<b>Table 7. Routine cord testing from baby with an Rh(D) negative mother* n (%)</b>	<b>Ontario n=95</b>	<b>National n=297</b>
ABO	92 (96.8)	266 (89.6)
Rh (D)	94 (98.9)	290 (97.6)
DAT	76 (80.0)	196 (66.0)
Antibody screen	2 (2.1)	8 (2.7)
Phenotyping	2 (2.1)	2 (0.7)
No testing	0 (0.0)	1 (0.3)
Other	20 (21.1)	48 (16.2)

**\*respondents selected all that applied**

Another scenario pertained to the routine testing performed on cord samples when the mother is group O. Slightly more than half of the Ontario transfusion service laboratories perform an ABO group, Rh(D) type and a DAT (Table 8).

<b>Table 8. Routine cord testing from baby with a group O mother* n (%)</b>	<b>Ontario n=95</b>	<b>National n=297</b>
ABO	54 (56.8)	170 (57.2)
Rh (D)	54 (56.8)	162 (54.5)
DAT	52 (54.7)	147 (49.5)
Antibody screen	1 (1.1)	2 (0.7)
Phenotyping	0 (0.0)	0 (0.0)
No testing	27 (28.4)	88 (29.6)
Other	17 (17.9)	49 (16.5)

**\*respondents selected all that applied**

The same panel of tests was used in a scenario about cord testing when the mother has clinically significant antibodies (Table 9).

<b>Table 9. Cord testing from baby with a mother having clinically significant antibodies* n (%)</b>	<b>Ontario n=95</b>	<b>National n=297</b>
ABO	83 (87.4)	249 (83.8)
Rh (D)	83 (87.4)	249 (83.8)

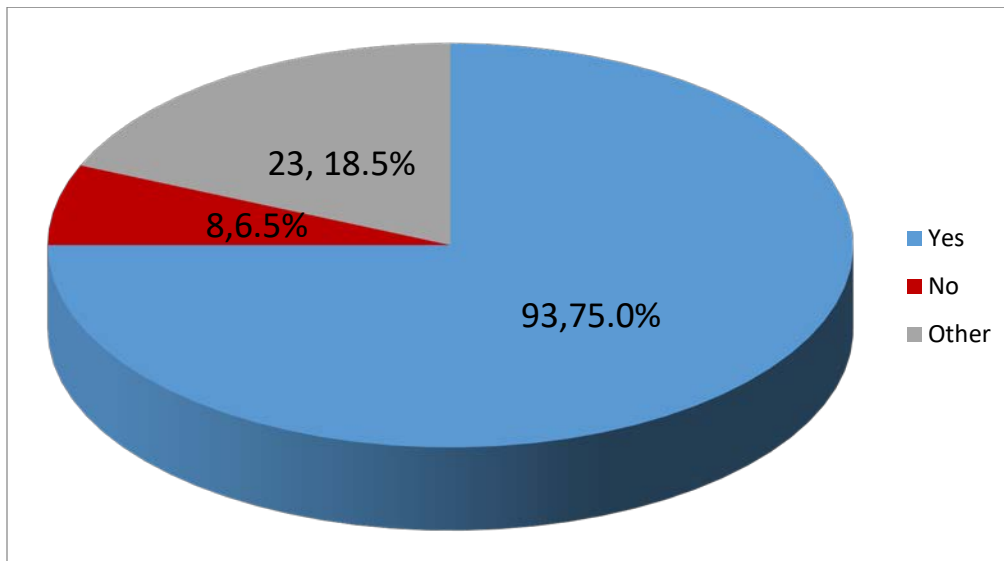
DAT	86 (90.5)	252 (84.8)
Antibody screen	13 (13.7)	31 (10.4)
Phenotyping	39 (41.1)	102 (34.3)
No testing	3 (3.2)	11 (3.7)
Other	25 (26.3)	67 (22.6)

\*respondents selected all that applied

#### D. RhIG and Fetal Maternal Hemorrhage (FMH) Assessment

The majority of the transfusion service laboratories surveyed (83.1%; 128/154) responded that they do dispense RhIG for antenatal or postnatal indications. Most facilities use the 1500 IU (300 µg) size for both antenatal (97.6%; 123/126) and postnatal (85.5%; 106/124) purposes. Ninety-seven (76.4%; 97/127) of the respondents also issue the 1500 IU size for potential immunizing events like trauma, amniocentesis and therapeutic or spontaneous abortions.

The majority of transfusion services laboratories polled perform either a neonatal or cord Rh(D) typing before dispensing postnatal RhIG to the mother (Figure 8).

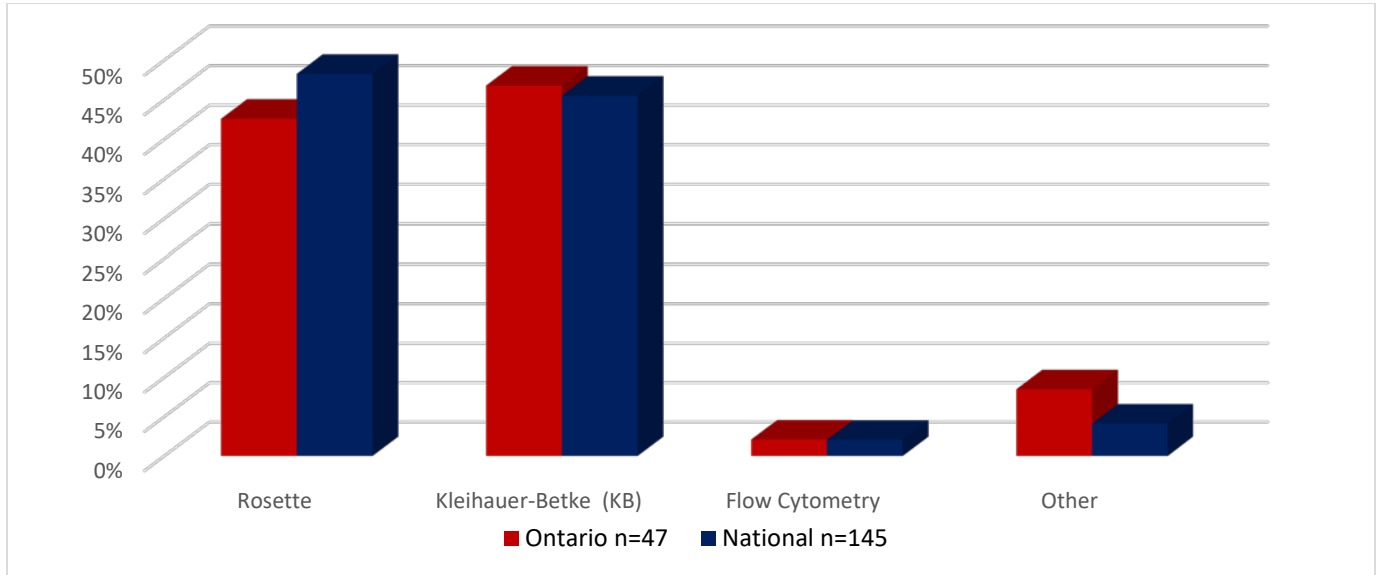


**Figure 8: Neonate/cord Rh(D) testing performed before postnatal RhIG administration**

The 18.5% (23/124) of the transfusion service laboratories in Ontario that responded ‘other’ indicated that deliveries are not done at their site and/or they dispense RhIG for prenatal patients only.

For FMH assessment, 31.4% (48/153) of the facilities perform this testing on site, 33.3% (51/153) refer the samples to another laboratory and the a over a third of the respondents (35.3%; 54/153) do not perform any FMH testing at all. The main screening tests used for FMH by the Ontario hospitals with a

transfusion service were the Kleihauer-Betke (KB) at 46.8% (22/47) (Figure 9), followed closely by the Rosette test at 42.6% (20/47).



**Figure 9: Types of FMH screening tests used**

If a FMH assessment is required for an Rh(D) positive mother, most facilities perform a KB test (90.0%; 18/20), 10.0% (2/20) of the facilities identified that another test was used, and none use flow cytometry. For quantification of a FMH, a number of different tests were used to calculate the appropriate dose of RhIG:80.0% (16/20) use the Kleihauer-Betke (KB), ;20.0% (4/20) selected “other” with further explanation; and none use flow cytometry All sites selecting “other” indicated that FMH are sent out to another laboratory.

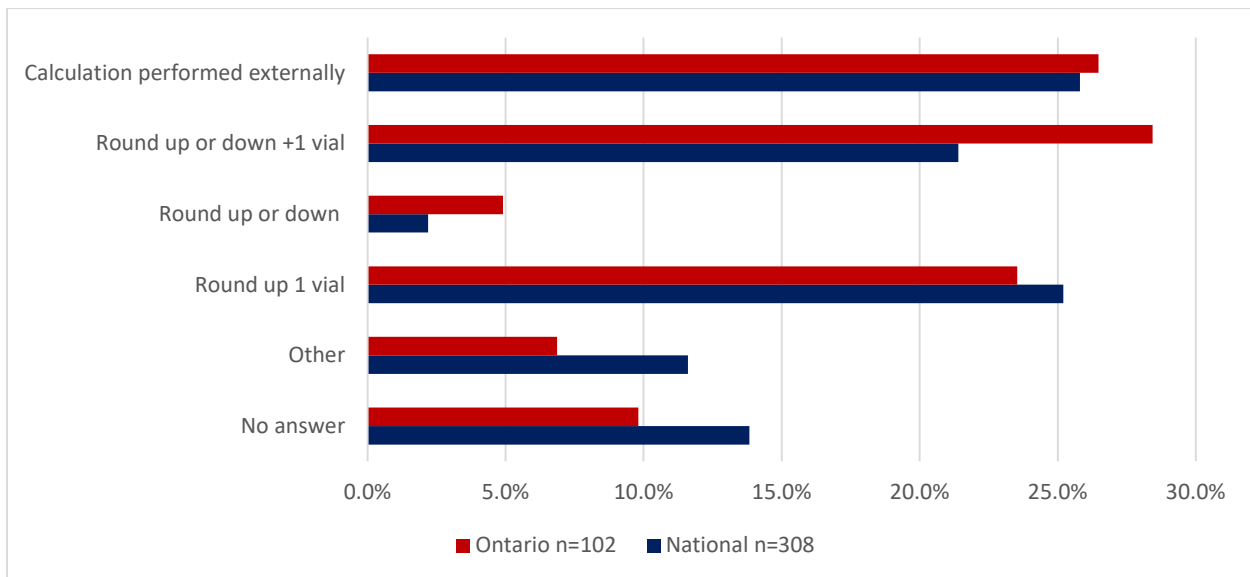
For the KB test, 73.0% (27/37) of respondents use commercial kits and 27.0% (10/37) prepare their reagents in house. Many facilities prepare their KB controls in house: 8.1% (3/37) use commercial controls and 91.9% (34/37) use in house controls. A small number of facilities (13.5%; 5/37) follow up a positive KB test with flow cytometry, but most (86.5%; 32/37) do not.

There are a variety of methods used to calculate the volume of a FMH in the KB as illustrated in Table 10, but the most utilized method is the one described by AABB and CAP (College of American Pathologists).

<b>Table 10. Methods used to calculate FMH volume in KB test n (%)</b>	<b>Ontario n=54</b>	<b>National n=152</b>
AABB/CAP formula	40 (74.1)	87 (57.2)
Mollison formula	1 (1.9)	8 (5.3)

Other	3 (5.6)	35 (23.0)
No Answer	10 (18.5)	22 (14.5)

Most facilities (98.6%; 73/74) did not adjust for individual maternal blood volume. The majority of the laboratories calculate the appropriate dose of RhIG by either calculating the FMH volume and always rounding up a vial or calculating the FMH volume, round to the nearest vial (up or down), and then adding a vial (Figure 10).



**Figure 10: Methods of RhIG dose calculations**

### Discussion

There is variability in practice for maternal and cord testing across Ontario and Canada. Variability in the “types of testing” performed at each site may indicate that unnecessary testing is done and may not add value, wasting valuable time and resources which is not in line with the culture of the Choosing Wisely Canada movement. Other practice variabilities identified in this survey may suggest that practice improvements are needed to maximize efficiencies and benefit patient care.

Unnecessary testing:

- Performing mid-pregnancy screens on Rh(D) positive mothers;
- Testing DATs for all cords received, or from all group O mothers or all Rh (D) negative mothers, regardless of hemolysis indications;
- Anti-N titrations;

- Performing passive anti-A and anti-B testing on cord samples;
- Use of polyspecific DAT reagents for cord testing when anti-IgG will suffice; and,
- Performing antibody screening on cords.

#### Practice Improvement Opportunities

- Implementing perinatal guidelines to guide testing practices;
- Weak Rh(D) (by IAT) testing should NOT be performed on patients except to determine eligibility for RhIG (e.g., weak Rh(D) testing on cord or neonatal samples);
- Interpreting weaker than normal Rh(D) (by direct agglutination) results as Rh (D) positive for female patients of child bearing potential;
- Performing DATs on cord samples from mothers who have clinically significant antibodies;
- Performing phenotyping where possible on cord samples from mothers with clinically significant antibodies;
- Performing Rh(D) testing on the cord/neonatal sample and FMH assessment before RhIG administration to the mother, if possible, to ensure the RhIG is necessary and that the RhIG dose is correct;
- Limiting antibody titrations of anti-K. Any level of anti-K may be clinically significant, so titrations are unnecessary. However, some clinicians use anti-K titration levels as a gauge to determine the frequency of performing Doppler ultrasounds on the potentially affected fetus;
- Always perform an antibody screen on Rh(D) negative mothers at 28 weeks. The RhIG may be administered once the sample is drawn and the antibody screen may be completed later; and,
- Do not use cord samples for crossmatching.

The survey results demonstrate that some sites need to adopt more current perinatal practices to reduce unnecessary testing thereby increasing efficiency, reducing wastage of resources and improving patient care. For some patient safety examples, survey results indicate that some postpartum RhIG is administered without any FMH assessment, so there is no assurance that the RhIG dose is sufficient to prevent Rh(D) immunization in the mother. A few sites answered that they use cord samples for crossmatching, a practice that contravenes transfusion standards and is not recommended.

The majority of the survey results on practices reported by Ontario hospital personnel are comparable to those of hospitals in other provinces with a few exceptions:

#### Antenatal testing

- A higher percentage of Ontario respondents (compared to National) answered that either a strong or weak Rh(D) testing result is reported as Rh(D) positive without additional testing.
- A higher percentage of Ontario hospitals (compared to National) that do not genotype samples reported they would issue RhIG antenatally if both the Rh(D) direct and indirect testing results

are negative. Also more Ontario hospitals would issue RhIG if they obtain weaker than expected Rh(D) results with one or more reagents or techniques compared to National survey results.

- A higher percentage of Ontario hospitals use automated solid phase as their primary method to perform antibody investigation compared to hospitals in other provinces.

### Cord testing

- More Ontario hospitals (compared to National) perform a DAT on cord samples – all group O mothers, mothers with clinically significant antibodies and all Rh(D) negative mothers. Fewer Ontario hospitals perform a DAT for fetal ABO incompatibility for mothers who are ABO blood group A or B.
- More Ontario hospitals (compared to National) use monospecific anti-IgG to perform a DAT on cord samples and fewer use polyspecific reagent.
- When responding on routine cord testing for babies with an Rh(D) negative mother, more Ontario hospitals perform both ABO group and Rh(D) type compared to hospitals in other parts of Canada that reported a higher percentage performing Rh(D) type only. Also, a higher percentage of Ontario hospitals report that they would perform a DAT on cord samples from Rh(D) negative mothers compared to those in the rest of Canada.
- A higher percentage of Ontario hospitals reported they would perform a DAT and phenotyping on a cord sample from a mother with clinically significant antibodies when compared with hospitals in the rest of Canada.

### Fetal Maternal Hemorrhage (FMH) assessment

- 35% of Ontario hospitals reported they do not perform any FMH testing at all (lower than National results at 45%).
- When asked which formula was used to calculate FMH volume when the KB test is performed, a higher percentage of Ontario hospitals reported they use the AABB/CAP formula.

Overall Ontario hospitals testing of antenatal and cord samples appears to be similar to hospitals in the rest of Canada. There are a few areas where the need for practice improvements in Ontario were identified:

1. Weak Rh(D) (by IAT) testing should NOT be routinely performed on antenatal patients. It should only be performed on cord or neonatal samples to determine maternal eligibility for RhIG.
2. Weaker than normal Rh(D) test results should NOT be interpreted as Rh(D) positive in females of child bearing potential.
3. Performing a DAT on cord samples from group O mothers or Rh(D) negative mothers where there is no indication of hemolysis in the neonate is NOT required.

4. FMH assessment is an important test that is required for patient safety to ensure sufficient RhIG is given to prevent alloimmunization of the mother. ALL hospitals where obstetrics is performed need to either perform this test on site or refer it out to another facility.

Refer to the National Advisory Recommendation on RHD genotyping for further guidance.

<https://www.nacblood.ca/resources/guidelines/downloads/RHD-Genotyping-March28.pdf>

What are the next steps?

A perinatal consensus forum is currently being planned for the Spring of 2022. The objective of this event will be to bring together an expert panel from across Canada to develop recommendations on best practices for perinatal and neonatal testing. The event will be held in Toronto around the time of the CSTM Annual Scientific Conference.