



Guidance for Prenatal, Postnatal and Neonatal Immunohaematology Testing in Canada: Consensus Recommendations from a Modified Delphi Process

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PII: S1701-2163(25)00334-2

DOI: <https://doi.org/10.1016/j.jogc.2025.103088>

Reference: JOGC 103088

To appear in: *Journal of Obstetrics and Gynaecology Canada*

Received Date: 18 February 2025

Revised Date: 29 April 2025

Accepted Date: 9 May 2025

Please cite this article as: Lieberman L, Walsh CM, Barty R, Callum J, Yan MTS, VanderMeulen H, Robitaille N, Fung Kee Fung K, Ng E, Hume H, Barrett J, Berman R, Colpitts M, Dowe E, de Vrijer B, Ellis S, Fam PN, Grabowska K, Grundland B, Harrold J, Khurshid F, Massey E, McAuley C, Naik N, Okun N, Osepchook C, Pai M, Parsons M, Price V, Rujuis D, Ryan G, Shuman M, Somerset D, Stewardson J, Taillefer C, Tehseen S, Thorne J, Vlachodimitropoulou E, White H, Wilson A, Clarke G, Guidance for Prenatal, Postnatal and Neonatal Immunohaematology Testing in Canada: Consensus

Recommendations from a Modified Delphi Process, *Journal of Obstetrics and Gynaecology Canada* (2025), doi: <https://doi.org/10.1016/j.jogc.2025.103088>.

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Submission Cover Page

Journal of Obstetrics and Gynaecology Canada

Title

Full title: Guidance for Prenatal, Postnatal and Neonatal Immunohaematology Testing in Canada: Consensus Recommendations from a Modified Delphi Process

Short title (max 50 characters): Guidance regarding transfusion testing during pregnancy

Keywords

Enter 3–6 MeSH subject headings that represent the topics covered in this manuscript

prenatal diagnosis, pregnancy, newborn and perinatology, isoimmunization, hemolytic disease of the newborn, Rho(D) Immune globulin

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Disclosures

List all author disclosures, including all funding sources (as documented on the COI forms you submitted), or the statement “The authors declare they have nothing to disclose.”

Dr. Lieberman – Medical advisory Board funding from Werfern, Contracted by Children’s Hospital of Eastern Ontario as a medical advisor for Ontario’s prenatal screening program (BORN Ontario), Leadership role – Chair of the pediatric subcommittee of the Association and Advancement of Blood and Biotherapies, Chair of the Canadian Obstetric and Pediatric Transfusion Network

Dr. Callum – Research funding from Canadian Blood Services and Octapharma and Medical advisory board funding from Octapharma, participation on data safety monitoring board (FEIST trial), Board member of the Canadian Hematology Society

Dr. Colpitts – honorarium from Muskoka Algonquin Healthcare for providing grand rounds 2022

Dr. VanderMeulen – Consulting fees from CSL Vifor, payment for lectures from Ontario local groups, participation in data safety monitoring board for the Canadian Drug Agency

Dr. Barrett – speaker fee from Ferring, payments for expert testimony to CMLA and Plaintiff law firm

Dr. deVrijer – Contracted by the Children’s Hospital of Eastern Ontario as a medical advisor for the Ontario prenatal screening program (BORN Ontario)

Dr. Naik – Leadership role- Ontario Health West, clinical lead

Dr. Theodora Ruijs – Other- Ontario Regional Blood Coordinating Office, clinical project coordinator

Dr. Gwen Clarke – Contracted by the Children’s Hospital of Eastern Ontario as a medical advisor for Ontario prenatal screening program (BORN program), Supported as a board member of the International Society of Blood Transfusion (ISBT) to attend meetings (congresses) annually, advisory board member to J&J related to HDFN and FNAIT, Secretary general of the ISBT (non- funded)

Ethics

Ethical approval was not required as individual patient data was not assessed nor included.

Acknowledgements (optional)

Enter a statement of acknowledgements below, if applicable.

The authors would like to thank Dr. Nadine Shehata, Dr. Michael Sgro, Dr. Lucinda Whitman, Michael Angers (MLT), and Barbara Silveri (MLT), for their contributions as voting panelists. Additionally, the authors would like to acknowledge Tracy Cameron, Sheena Sanders, Alison Wendt for their administrative support.

Notes (optional)

Enter below any other information the Editorial Office should know concerning the production of this article (e.g., other statements to include, including co-first authorship).

I am pleased to submit this manuscript for your consideration. Along with this submission, we would like to request that two related manuscripts be linked and potentially published in the same volume. The manuscripts explain the rationale for the low risk or routine tests and for high risk pregnancy testing and are intended to complement the current submission by elaborating on the reasoning for the statements. The first article is titled: Transfusion Testing during Routine Pregnancies: Consensus Recommendations from the Modified Delphi Process - (Corresponding author Dr. Yan – Manuscript # D-25-00103) and the second is titled (in preparation – will be submitted by early March): National Consensus Statements for the Prevention and Management of Alloimmunization during Pregnancy: A Modified Delphi Process (Corresponding author Dr. Nancy Robitaille).

We believe that publishing these articles together would provide readers with a more comprehensive understanding of the subject and enhance the impact of the research. We would like to ensure that all articles are offered through OPEN ACCESS (supported by University of Toronto) to ensure it reaches all practitioners involved in caring for these patients.

Thank you for your time and consideration. We look forward to your response.

**Guidance for Prenatal, Postnatal and Neonatal Immunohaematology Testing
in Canada: Consensus Recommendations from a Delphi Process**

Guidance: Immunohaematology testing during pregnancy

Abstract

Objective: Blood Group, antibody screen, fetal-maternal hemorrhage (FMH) tests and Rh(D) immunoglobulin (RhIG) administration are interventions during pregnancy that aid in the prevention of haemolytic disease of the fetus and newborn (HDFN). The timing, frequency, and nature of testing varies across centres due to limited data to inform standards development. Using Delphi methodology, this study aimed to establish guidance for Canadian practice related to prenatal, postnatal and neonatal immunohaematologic testing, and RhIG administration, to reduce risk and improve diagnosis of HDFN.

Methods: A national, multidisciplinary Delphi panel rated their agreement with potential guidance statements related to prenatal, postnatal and neonatal immunohaematology testing on a 5-point Likert scale during iterative rounds of voting. After each round, responses were analyzed and statements were re-sent to the panel for further ratings until consensus was achieved, defined as Cronbach's alpha >0.95 or a maximum of three voting rounds. At the conclusion of the Delphi process, statements rated $\geq 4/5$ were included.

Results: Forty-six experts voted on 49 proposed statements. Consensus was achieved after 3 survey rounds (Cronbach's alpha = 0.94), with a 100% response rate throughout. Forty-four statements reached consensus. Statements focused on prenatal immunohaematology testing (N = 21 statements), FMH testing and RhIG administration during pregnancy (N = 15), and testing of neonates for surveillance of hyperbilirubinemia secondary to HDN (N = 8).

Conclusion: This Canadian consensus guidance aims to optimize the surveillance of pregnancies at risk of HDFN and the dosing and timing of RhIG administration. It provides actionable recommendations to harmonize practice and support safe, timely, and cost-effective care.

Résumé

Objectif : Le groupe sanguin, la recherche d'anticorps, les tests d'hémorragie fœto-maternelle (HFM) et l'administration d'immunoglobulines anti-D (Ig anti-D) sont des interventions pendant la grossesse qui contribuent à la prévention de la maladie hémolytique du fœtus et du nouveau-né (MHFN). Le calendrier, la fréquence et la nature des tests varient d'un centre à l'autre en raison du manque de données pour l'élaboration de normes. Utilisant la méthodologie Delphi, cette étude visait à établir des directives cliniques canadiennes relatives aux tests immunohématologiques prénataux, postnataux et néonataux, et à l'administration d'Ig anti-D, afin de réduire les risques et d'améliorer le diagnostic de la MHFN.

Méthodes : Un panel Delphi national multidisciplinaire a évalué l'accord de ses membres par rapport à des déclarations d'orientation potentielles relatives aux tests d'immunohématologie prénatale, postnatale et néonatale sur une échelle de Likert en 5 points au cours de tours de vote itératifs. Après chaque tour, les réponses ont été analysées, puis les déclarations ont été renvoyées au panel pour une nouvelle évaluation jusqu'à ce qu'un consensus soit atteint, défini par un score alpha de Cronbach supérieur à 0,95 ou un maximum de 3 tours de vote. À l'issue du processus Delphi, les déclarations ayant reçu un score de 4/5 ou plus ont été incluses.

Résultats : Dans l'ensemble, 46 experts ont voté sur 49 propositions de déclaration. Un consensus a été atteint après 3 tours de vote (alpha de Cronbach = 0,94), pour un taux de réponse de 100 % tout au long du processus. Au total, 44 déclarations ont fait l'objet d'un consensus. Les déclarations portaient sur les tests d'immunohématologie prénatale (N = 21 déclarations); les tests d'HFM et l'administration d'Ig anti-D pendant la grossesse (N = 15); et les tests des nouveau-nés pour la surveillance de l'hyperbilirubinémie secondaire à MHN (N = 8).

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Conclusion : Ce document de consensus canadien vise à optimiser la surveillance des grossesses à risque de MHFN et à déterminer la dose et le moment d'administration des Ig anti-D. Il fournit des recommandations concrètes pour harmoniser les pratiques et favoriser des soins sûrs, opportuns et économiques.

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Introduction

Pregnancy care for Canada's 350,000 live births/year is provided by various healthcare practitioners including family physicians, emergency physicians, midwives, nurse practitioners and obstetricians.(1) Prenatal immunohaematology testing is an essential part of care, including blood group and antibody screening, fetal-maternal hemorrhage (FMH) screening, antibody identification and titration, and post-delivery neonatal testing for hyperbilirubinemia. These evaluations help determine the timing and need for Rh immunoglobulin (RhIG) prophylaxis and monitor haemolytic disease of the fetus and newborn (HDFN) and immune mediated neonatal jaundice.(2) Currently, no Canadian guidelines comprehensively address both prenatal and postnatal immunohaematology testing, including indications and timing.(3, 4) The lack of such guidance has led to variability in practice, resulting in potential missed RhIG doses and unnecessary RhIG administration,(5) risk of red cell alloimmunization,(6) and need for interventions and follow-up at high-risk obstetric centers, posing challenges, particularly for Canadians outside urban areas.(7)

The paucity of comprehensive guidance is related to several factors. First, the evidence on optimal testing strategies is primarily based on older studies, when testing methods and reagents were less sensitive than those used today. Without up-to-date literature, clinical and laboratory practices often rely on historic local practices. Secondly, as pregnancy care involves various practitioners, recommendations from different clinical societies may be published and implemented without cross-referencing other national guidelines, sometimes leading to conflicting advice. Finally, although some international guidance exists, implementing it in the

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Canadian context presents challenges due to differences in available testing platforms, reagents and RhIG dose formulation.(8)

The objective of this modified Delphi study was to provide consensus guidance on the optimal indications and timing for prenatal, postnatal and neonatal immunohaematology testing for prevention and diagnosis of HDFN, using a multidisciplinary national expert panel.

Methods

A modified Delphi process was used to establish consensus statements related to prenatal, postnatal and neonatal immunohaematology testing in Canada. The Delphi method is a research technique that harnesses the collective intelligence of an expert panel to achieve consensus on a specific topic through a series of iterative, anonymous surveys.(9, 10) It offers valuable evidence based on expert judgement, particularly when high-quality empirical data are lacking to inform standards.(11) Additionally, it allows for a large number of multidisciplinary experts from different locations to vote anonymously in an unbiased manner.(12) In this study, the Delphi technique was modified to include a virtual meeting following initial voting to enable panelists to discuss controversial statements and suggest changes to wording and content.

Steering Committee and Delphi Panelists

The steering committee (LL, NS, GC, CMW, JC) assembled a national Delphi panel of content experts representing relevant stakeholders. To enhance content validity of the Delphi process and ensure the participation of the most appropriate experts, panelists were identified in the following ways. Practitioners in high- and low-risk obstetrics, abortion care, transfusion medicine and

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paediatrics were identified as key opinion leaders, as evidenced by their involvement in national and international organizations or their publication record within a related field. Nursing educators involved in RhIG clinics, midwives with large practices, family physicians with an academic interest in obstetrics, and medical laboratory technologists from urban and rural settings were also invited. A patient who experienced an alloimmunized pregnancy was included. Panelists were purposefully selected from both academic and community centers across different regions of Canada.

The objective was to assemble a diverse group of at least 40 experts with broad expertise related to transfusion medicine, thereby enhancing the reliability of the Delphi group's composite judgment. (13) Forty-seven prospective panelists were invited to account for the likelihood that not all would agree to participate, and to ensure broad geographic and disciplinary representation. Panel participation was voluntary and not financially remunerated.

Statement Generation and Knowledge Sharing

Potential statements were drafted by the committee chairs (LL, GC) based on evidence, when available, and on international guidelines, Canadian practice and/or expert opinion when evidence was lacking. Statements were categorized into the following domains: (1) Low-risk - testing focused on routine pregnancies evaluating alloimmunization, FMH and routine RhIG administration; (2) High-risk - testing during alloimmunized pregnancies at risk for HDFN and those with additional RhIG requirements following obstetrical procedures; and (3) Neonatal - testing, including umbilical cord, for surveillance of hyperbilirubinemia related to HDN. Three terms were used when drafting the statements: “*recommend*” was used when there was

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agreement across most international guidelines, “*suggest*” when there was low quality evidence or limited agreement across international guidelines, and “*required*” when national standards mandated a specific action.(14)

To standardize knowledge prior to the Delphi voting process, panelists were provided with publications that reflected the most recent literature and international guidelines on relevant topics (Supplementary Data). Additionally, panelists attended a two-day in-person consensus panel forum. The first day included didactic sessions outlining evidence for each statement, followed by a day dedicated to discussion of each proposed statement. Voting occurred following the in-person forum.

Delphi Survey Rounds

Iterative rounds of electronic Delphi surveys were used to achieve consensus. During the first round of voting, panelists independently rated their agreement with each statement on a 1 (“strongly disagree”) to 5 (“strongly agree”) Likert scale via Research Electronic Data Capture (REDCap), a secure web-based application designed to support data collection and management.(15) Panelists could abstain from voting on any statement for which they felt they lacked expertise. Panelists voted based on their opinion of optimal patient care, rather than on operational feasibility. Additionally, participants were encouraged to provide comments on the wording of each statement, suggest additional statements, and/or offer feedback in free-text fields.

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During subsequent voting rounds, panelists rated each statement again using the same 5-point Likert scale. Panelists were informed of the panel's mean, median score and range for each statement in the previous round. Participants were once again given the opportunity to provide open-ended comments. Iterations of Delphi surveys continued until consensus was achieved among the expert panel, based on the criteria described below.

Data Analysis and Determining Consensus

All statistical analysis was performed using Microsoft Excel. After each voting round, the median score and range for each statement were calculated. The steering committee, blinded to the identities of the participants, reviewed the panelists' ratings and open-ended comments for each statement. Based on feedback from the expert panel, redundant statements were merged, the wording of statements was revised, and new statements proposed by panelists were added to the subsequent voting round.

The Delphi process proceeded iteratively until consensus was achieved. Consensus, defined as homogeneity or consistency of opinion among the expert panelists, was predefined as a Cronbach α of >0.95 or a maximum of 3 voting rounds.⁽¹⁶⁾ The mean response score was imputed for missing data (abstaining votes) when calculating Cronbach's alpha for each voting round.

Once consensus was achieved, the disposition of each statement was determined based on predefined criteria. Statements with a median rating ≥ 4 met the criteria for inclusion, whereas statements with a median rating <4 met criteria for exclusion. For statements where participants

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proposed significant content changes, these changes were reviewed in a follow-up online meeting for discussion and clarification among the panelists. Participant identities and responses were not blinded during the discussion. The meeting was recorded, transcribed and made available to all participants. Statement wording was adjusted if there was consensus during the online meeting, defined as full agreement among participants to adjust a given statement. The Delphi panel then rated their agreement with revised statements in an abbreviated voting round. Subsequently, the final list of statements was circulated to panel members for review and comment.

Ethics Approval

Ethical approval was not required for this modified Delphi process, as individual patient data was not assessed nor included.

Results

Delphi Panel Participants

Forty-six of 47 (98%) invited panelists agreed to participate. Table 1 details the demographics of the Delphi panel members. The expert panel was comprised of a multidisciplinary group with relevant transfusion expertise, the majority of whom were physicians (36/46; 78%) from academic centers (33/46; 72%). Canadian representation was broad, although there was a gap in participation from northern Canada, with most panelists coming from central Canada (35/46, 76%). A 100% response rate was achieved across all rounds of the Delphi process; however, the denominator for individual statement votes varied as panelists could abstain from voting for any statement if they felt that they lacked relevant expertise.

Delphi Process

The flow of statements through each round of the Delphi process is outlined in Supplementary Figure 1. Forty-seven statements were presented to panelists during round 1 of voting and an additional 2 statements were added based on suggestions from the Delphi panel. During the voting rounds, 8 statements were merged into 3 updated based on feedback. Across all rounds, of the 49 statements, 33 required minor changes which did not alter the meaning of the statement, and 2 required major wording changes.

Cronbach's alpha was 0.89 for round 1 and 0.9 for round 2, with consensus achieved after three rounds (Cronbach's alpha = 0.94). At conclusion of the Delphi process, a total of 44 statements achieved criteria for inclusion, classified into three domains: (1) Routine, low-risk pregnancy: 21 statements; (2) High-risk, alloimmunized pregnancy: 15 statements; (3) Neonatal/cord testing: 8 statements (Table 2). None of the statements met criteria for exclusion. Supplementary Figure 2 presents the distribution of ratings for each statement in Round 3.

Statements Requiring Major Revisions and Discussion During Online Meeting

Two statements underwent major revisions based on panelist feedback. Despite median scores >4 in round 3, extensive commentary prompted revisions and an additional voting round.

The first, statement L2, focused on the need for a routine blood group and antibody screen at 28 weeks gestation. Initially, it stated that this test was '*not suggested*', but following discussion, it was softened to '*may not be necessary*.' In routine, non-alloimmunized low-risk pregnancies, the practice of repeating a 28-week group and screen is controversial, as only 0.01-0.43% of

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pregnancies with a negative first trimester antibody screen develop a new alloantibody later in the pregnancy.(6, 17-22)

Statement L7 originally suggested RhIG for a pregnant individual who experienced an abortion if the gestational age was greater than 8 weeks 0 days. However, a recent publication reported that the size of an FMH between 8-12 weeks did not meet the threshold for alloimmunization (23) and suggested no RhIG before 12 weeks 0 days gestation. (24) As other organizations(3, 25-27) have updated their recommendations on first trimester RhIG requirements and timing in the setting of abortion with reliable pregnancy dating, the statement was revised to align with current evidence and other guidance, and panelists re-voted (L7, Table 2).

Discussion

This modified Delphi consensus process, involving 46 multidisciplinary experts from across Canada, resulted in the development of 44 comprehensive guidance statements on prenatal, postnatal and neonatal immunohaematology testing in Canada. The statements reflect current literature and expert opinion in Canada, offering recommendations on immunohaematology testing for HDFN, FMH testing, RhIG administration during routine and high-risk pregnancies, and the investigation of neonatal hyperbilirubinemia. The goal for these statements is to serve as a foundation for nationally harmonized testing practices in prenatal and postnatal care. While some of the guidance is specific to Canadian practice, to the best of our knowledge, this is the first national consensus document in this area developed by such a large, multidisciplinary group and which encompasses testing practices from early pregnancy to the neonatal period.

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The Delphi technique was chosen as the method to develop these statements due to variability in practice and limited evidence regarding timing and frequency of immunohaematology testing and evidence regarding the need for RhIG during the first trimester. A key strength of the expert panel is its diversity. Panelists represented both rural and urban settings across Canada, including resource-limited and geographically constrained areas, as well as tertiary care settings. In addition, the inclusion of a patient representative who had experienced alloimmunization during pregnancy provided important insights.

The final document reflects practices that are flexible and adaptable to a variety of clinical settings. The exchange of knowledge among the subject matter experts, particularly between patient facing clinicians and laboratory-based transfusion specialists, was essential to the process. Panelists were not generally aware of the limitations of the evidence available to guide testing practice, nor were they initially aware of the variability in immunohaematology testing and management practices nationally. Interestingly, an important manuscript was published during the study period, prompting revision of the statement pertaining to RhIG requirements between week 8- 12 of pregnancy.⁽²⁸⁾ The diversity of ideas from the clinical subspecialists, including high- and low-risk obstetricians, midwives, nurses, and the laboratory team, facilitated an improved understanding of the unique perspective of each group and allowed statement adaptation related to practical and logistical issues.

This consensus project marks a starting point in the process of ensuring a standardized approach. It has fostered a national collaboration aimed at reducing variability in care and optimizing communication between subspecialists, as well as between the laboratory and clinical teams, to

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assure alignment of processes and care plans as evidence and technology evolve. Additional goals of the collaboration include sharing resources and quality measurement tools across provinces and developing a national strategy to facilitate measurement of adherence to these statements and support quality assurance and research.

Future Directions

The evidence reviews and expert panel discussion identified gaps in knowledge necessitating further study. One area concerns the requirement for and benefits of RhIG prophylaxis from 8-12 weeks in specific clinical scenarios including molar and ectopic pregnancies. Additionally, the benefits of anti-K antibodies titration testing and the appropriate titre cut-off remains unclear. Finally, there was no consensus on the necessity of the 28-week type and screen prior to the prophylactic RhIG dose, and further research in the era of targeted RhIG prophylaxis using non-invasive prenatal testing could offer valuable guidance.

Limitations

Despite our national, multidisciplinary panel, not all sites in Canada were represented. Additionally, as with any self-selected group of experts, there is a risk that the recruited panelists had similar opinions. Based on the numerous comments provided and the range of votes, an adequate range of opinions seems likely. The Delphi process has its own limitations as there are no guidelines related to panel size or selection; however, strategies, including *a priori* panel selection criteria, were employed to minimize potential bias. Finally, given the limited high quality published literature in this field, many of the recommendations were based on expert opinion rather than high-quality evidence.

Conclusion

In conclusion, the Delphi technique enabled the establishment of national expert consensus on prenatal, postnatal and neonatal immunohaematology testing. The resulting guidance statements aim to standardize practice related to RhIG administration and immunohaematology testing during and following pregnancy. These aspirational statements encourage care providers and laboratories to choose the best options when possible. While some recommended practices may not be immediately feasible for all jurisdictions, and others will require significant logistic and financial resources for implementation, toolkits will be developed to support knowledge dissemination and translation. Unified Canadian guidance will help policy makers and healthcare providers work toward optimizing antenatal and postnatal care.

Contributors: All of the steering committee members contributed to the study design, data interpretation and reviewed the manuscript and critically revised it for important intellectual content. All of the authors approved the final version to be published and agreed to act as guarantors of the work.

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Supplemental Documents

Key references (and links) related to immunohaematology testing during and following pregnancy (Supplementary Data)

Overview of the modified Delphi process. (Supplementary Figure 1)

Distribution of panelist voting for each statement at final round of voting. (Supplementary Figure 2)

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Table 1: Demographics of expert panelists participating in the modified Delphi consensus process (N=46)

Expert panelists	N (%)
Professional Designation	
Physician ^a	36 (78)
Transfusion medicine specialist	16 (44)
High risk obstetrician	10 (28)
Paediatric hematologist	5 (14)
Family Physician	4 (11)
Paediatrician with neonatology responsibilities	3 (8)
Neonatologist	3 (8)
Low risk obstetrician	1 (3)
Hematopathologist	4 (9)
Medical Laboratory Technologist	3 (6)
Nurse	2 (4)
Midwife	1 (2)
Patient Representative	
Years of Expertise	
0-4.9	4 (9)
5-9.9	4 (9)
10-14.9	8 (17)
15-20	7 (15)
More than 20	23 (50)
Type of Centre	
Academic centre	33 (72)
Community Hospital	6 (13)
Other ^b	5 (11)
Community Office	2 (4)
Region	
Central Canada	35 (76)
Atlantic region	5 (11)
Prairie Provinces	3 (6)
West Coast	2 (4)
North	0 (0)
International	1 (2)

^aRespondents could select more than one subspecialty type^bOther responses included: birthing centre; blood supplier (specialized testing); community and academic centre and international work; provincial nursing consultation

Table 2: Guidance statements for prenatal, postnatal and neonatal immunohaematology testing

Statement #	Low Risk Statements
L1	For routine care, prenatal testing for ABO, RhD, and antibody screen is recommended after 8 weeks gestation, preferably between 11 and 14 weeks.
L2	A routine ABO, RhD and antibody screen may not be necessary at 28 weeks gestation for either RhD positive or RhD negative pregnancies.
L3	Antibody screening is suggested for all pregnancies (RhD negative and RhD positive) following a sensitizing event or after maternal RBC transfusion.
L4	Maternal ABO, RhD, and antibody screen at the time of delivery is only recommended when: - there is no prior test during the current pregnancy; and/or - there is a clinically significant antibody; and/or - the risk of maternal transfusion is increased; and/ or - the risk of neonatal transfusion is increased.
L5	RHD genotyping is recommended in any pregnant person with weak or variably reactive RhD typing.
L6	It is recommended that pregnancies with weak or indeterminant RhD and without available RHD genotype results be considered RhD negative until genotyping results are available.
L7	For any pregnancy less than 12 weeks gestational age (12 weeks 0 days) experiencing an abortion (threatened, spontaneous or therapeutic), an ABO, RhD, and antibody screen are not recommended and RhIg is not required.
L8	Informed consent (verbal or written) must be obtained and documented prior to the administration of RhIg.
L9	For RhD negative pregnancies, determination of fetal RhD status by non-invasive prenatal testing (cffDNA testing of maternal plasma) is suggested to avoid unnecessary RhIg administration.
L10	Routine antenatal RhIg at a dose of 300 µg (1500 IU), is recommended for all RhD negative pregnant individuals at approximately 28 weeks gestation.
L11	For sensitizing events in RhD negative pregnancies RhIg dosing varies depending on gestational age of the pregnancy: - less than 8 weeks 0 days: no RhIg required ≥ 8 – 11 weeks: 120 ug (600 IU) for ectopic or molar pregnancies, trauma or invasive prenatal testing (RhIg not required for abortions) ≥12-19 weeks: 300 µg (1500 IU) for all sensitizing events ≥20 weeks: 300 µg (1500 IU) for all sensitizing events with FMH quantification to determine need for additional doses.
L12	If immune anti-D is detected, RhIg is not recommended.
L13	RhIg is recommended for routine prophylaxis and for sensitizing events in RhD negative pregnancies when antibodies other than anti-D are present.
L14	In the setting of ongoing or recurrent antepartum bleeding starting at 20 weeks (≥20 weeks 0 days) gestation in an RhD negative pregnancy, both RhIg and FMH testing are recommended.
L15	Following delivery of an RhD positive neonate in an RhD negative pregnancy, RhIg is required within 72 hours of delivery.

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L16	Postnatal RhIg dosing (300 µg (1500 IU) or 120 µg (600 IU)) may vary depending on access to FMH test results.
L17	Quantitative FMH testing prior to 20 weeks gestation is not routinely recommended for RhIg dose guidance.
L18	Quantitative FMH testing is required starting at 20 weeks (≥ 20 weeks 0 days) gestation for pregnancies with a sensitizing event that may lead to FMH.
L19	For sensitizing events starting at 20 weeks gestation (≥ 20 weeks 0 days), RhIg doses should be based on quantitative FMH assessment with use of a validated calculator.
L20	FMH testing is required postpartum for RhD negative pregnancies with an RhD positive neonate.
L21	Flow cytometry is recommended for confirmation of diagnosis and quantitation of FMH, where feasible.
High Risk Statements	
H1	Communication between the obstetric, neonatal, and transfusion care providers regarding alloimmunized pregnancies is recommended.
H2	Once a clinically significant antibody has been identified, paternal antigen testing is suggested to assess the risk to the fetus, if paternity is assured.
H3	For anti-K antibodies early consultation with Maternal Fetal Medicine is recommended.
H4	For patients with clinically significant antibodies to RhD, C/c, E, or K, non-invasive prenatal testing (cffDNA testing of maternal plasma) is recommended to determine if the fetus is at risk.
H5	Once a clinically significant antibody has been identified, antibody titration is recommended every four weeks until 28 weeks and every two weeks thereafter. If a critical titre is reached, referral to Maternal Fetal Medicine is recommended.
H6	Once a critical titre is reached, further monitoring of antibody titres is not routinely recommended; evaluation by Maternal Fetal Medicine with monitoring by MCA Doppler ultrasound is recommended.
H7	Maternal fetal medicine consultation is recommended for alloimmunized pregnancies with clinically significant antibodies when: • a critical titre is identified, and the corresponding fetal antigen is unknown or predicted positive based on cffDNA assessment. • an anti-K antibody is identified. • a previous fetus or neonate has been affected by HDFN requiring intrauterine or post-natal transfusion and the corresponding fetal antigen is unknown or predicted positive based on cffDNA assessment
H8	Monitoring of alloimmunized pregnancies with antibody titration is <i>not routinely</i> recommended in the following situations: • a critical titre is identified • cffDNA assessment predicts that the fetus is negative for the corresponding antigen • a previous fetus or neonate was affected by HDFN and required intrauterine or post-natal transfusion
H9	Maternal (or cord) antibody titrations are not recommended immediately pre delivery, or postpartum.
H10	RhIg is recommended for RhD negative pregnancies following any fetal intervention, invasive prenatal testing, or maternal abdominal trauma starting at 8 weeks 0 days gestation.

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H11	RhIg is recommended for RhD negative pregnancies starting at 8 weeks 0 days gestation, following an ectopic pregnancy.
H12	RhIg is recommended for RhD negative pregnancies starting at 8 weeks 0 days gestation, following molar pregnancy.
H13	RhIg is recommended for RhD negative pregnancies following amniocentesis.
H14	RhIg is recommended for RhD negative pregnancies following chorionic villus sampling.
H15	When RhIg may have been previously administered and there is uncertainty about whether the antibody detected is passive (due to RhIg) or immune: a. RhIg is recommended for routine antenatal dosing and for sensitizing events. b. ongoing titration of anti-D at usual intervals is recommended. c. repeat antibody assessment is suggested at six (6) months postpartum.
Neonatal Statements	
N1	Samples for pre transfusion testing in the neonate must be collected and labeled in compliance with requirements of the Canadian standards for blood and blood products (Z902-20).
N2	Cord blood sample collection and testing is recommended for all neonates when: a. the pregnant person is RhD negative, RhD indeterminate or RhD unknown; or b. the pregnant person has a clinically significant antibody; c. there is a history of HDFN mediated hyperbilirubinemia requiring transfusion (intrauterine or postnatal) or IVIG therapy for a prior fetus or neonate; d. there are known risk factors for nonimmune neonatal jaundice or anemia (such as G6PD deficiency).
N3	Neonatal RhD typing on a cord or peripheral blood sample is required for all RhD negative or indeterminate pregnancies.
N4	A weak D test is required on a cord or neonatal peripheral sample when the mother and neonate are RhD negative or indeterminate.
N5	For alloimmunized pregnancies, cord phenotyping for the implicated antigen and DAT are recommended.
N6	For neonates with hyperbilirubinemia, investigations, and management according to the Guidelines of the Canadian Paediatric Society are recommended.
N7	A neonatal DAT is not recommended as a single test to screen for an alloimmune cause of hyperbilirubinemia.
N8	If neonatal transfusion is required, a neonatal peripheral blood or maternal blood sample should be used for antibody screen.