

DIAGNOSTIC SERVICES

ONTARIO

YEAR IN REVIEW

JANUARY – DECEMBER (2021)

Diagnostic Services “Year in Review” statistics are based on a January to December calendar year. The calendar year provides better correlation with Health Canada birth statistics.

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RED CELL SEROLOGY REFERENCE LABORATORY

The Red Cell Serology Reference Laboratory, Ontario Diagnostic Services provides testing for hospitals in the Central Ontario Region and Hamilton Region, and for private laboratories. Hospital patients who are repeatedly transfused may develop red cell antibodies and as a result may have difficulty in tolerating transfusions. Diagnostic Services has specialized and experienced technologists that assist and provide consultation to hospital transfusion medicine laboratories. The Reference Laboratory identifies red cell antibodies and provides transfusion recommendations. Diagnostic Services has a varied selection of specialized procedures and rare reagents to resolve more difficult red cell antibody cases. Staff within our department may collaborate with other reference laboratories such as the National Immunohematology Reference Laboratory (NIRL), Grifols Clinical Laboratory & Immunohematology Center and the New York Blood Center.

Diagnostic Services Red Cell Antibody Investigations

In 2021, hospitals have referred 2,674 requests for red cell antibody identification.

Referring hospitals have different capabilities and expertise in resolving red cell antibody investigations. Some hospitals have limited reagents for antibody identification or phenotyping of patient or donor units. Others have access to a wider variety of reagent red cell panels and methods as well as on site immunohematology expertise. A few hospital transfusion medicine laboratories have the resources to resolve the majority of serological problems and send only complex investigations for additional serological or genotyping studies.

Canadian Blood Services, Diagnostic Services provides consultation and testing support including antibody investigation, advanced or alternative techniques where required, and recommendations for compatibility testing methods and selection of appropriate donor unit phenotypes if necessary.

Reporting may include interim, final and supplemental reports, depending on the urgency of the testing, the need for patient transfusion and the complexity of investigation.

Testing Performed

The Red Cell Reference Laboratory routinely performs the following tests:

- ABO/Rh blood type and discrepancy investigations (if required)
- Screen for red blood cell antibodies
- Antibody Identification, if antibodies are detected
- Phenotyping (patient)
- Direct Antiglobulin Test
- Elution and Adsorption
- Other tests and techniques, as required.

Serological samples submitted for testing are categorized into either “Prenatal Samples” or “Patient Samples”.

Antibody Screening and identification is routinely performed using a Gel Card testing methodology. A combination of Gel Card testing methodology and indirect antiglobulin tube testing using saline, enzymes or PEG enhancement are the most common antibody identification methods.

The laboratory also coordinates Red Cell Genotyping referral through the Canadian Blood Services National Immunohematology Reference Laboratory (NIRL). The Brampton laboratory is also responsible for maintaining the Central Ontario Sickle Cell Registry.

1.1. Specimens Tested

The data in this report reflects a calendar year period to enable better correlation to other government statistical data (Statistics Canada birth statistics).

Table 1: Specimens Tested

Ontario

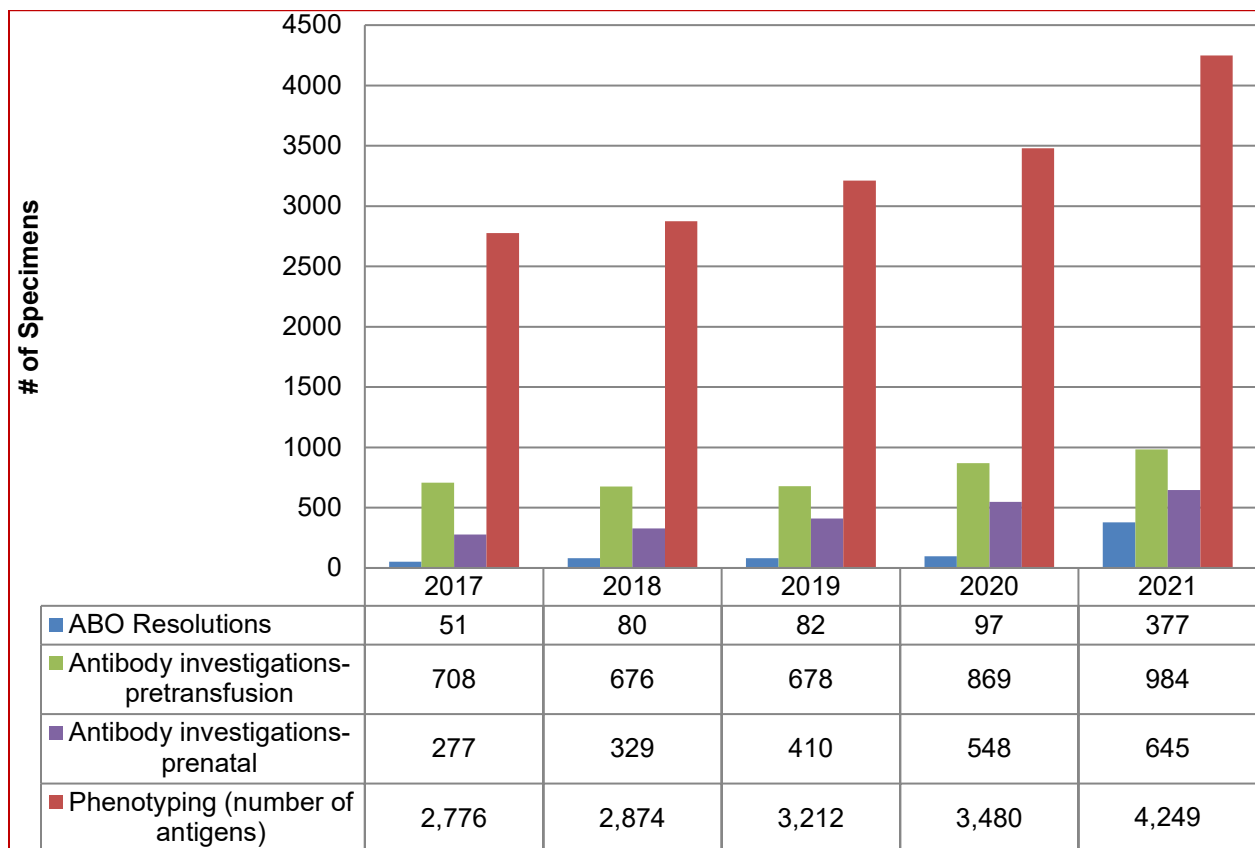
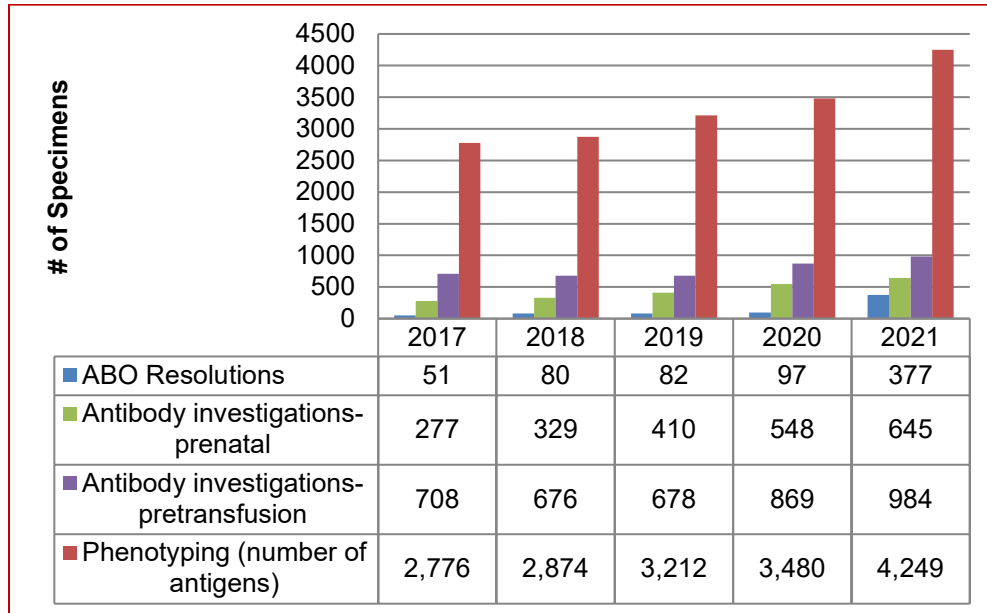
Specimen Type	Test Type	2017	2018	2019	2020	2021
Patient Samples for Red Cell Serology Reference and Prenatal Samples	ABO Resolutions	51	80	82	97	377
	Antibody investigations-pretransfusion	708	676	678	869	984
	Antibody investigations-prenatal	277	329	410	548	645
	Phenotyping (number of antigens)	2,776	2,874	3,212	3,480	4,249
Total # of Specimens Tested		3,812	3,959	4,382	4,994	6,255
Total # of Patients Tested		716	670	987	1,107	2,674

Table 2: Samples Received Each Month

Sample Type	January-21	February-21	March-21	April-21	May-21	June-21	July-21	August-21	September-21	October-21	November-21	December-21
Patient	112	180	140	147	133	145	125	130	180	162	101	105
Prenatal	75	53	88	64	114	84	104	65	121	111	82	53

The sample total for antibody investigations is 2,674 samples in 12 months or an average of 223 samples per month.

Figure 1: Specimens Tested



Hospital/Private Laboratory Referrals:

Samples referred into the Brampton Diagnostic Services Laboratory are from:

- 62 Health Care Facilities
- 3 Private Labs (Alpha, LifeLabs and Med-Health)

Private Labs are referring in primarily prenatal samples (94%) with only 6% patient samples for antibody investigation.

Table 3: Total Number Samples sent from Hospital/Private Laboratories

Alpha Laboratories Inc.	Prenatal	73	76	
	Patient	3		
LifeLabs	Prenatal	110	114	
	Patient	4		
Med-Health Laboratories Inc.	Prenatal	22	28	
	Patient	6		
			218	Totals
			205	Prenatal
			13	Patient

The hospital laboratories are referring in a combination of patient and prenatal samples for investigation.

Table 4: Total Number Samples with No Antibodies Detected

Prenatal	Patient	Total
110	90	200

Table 5: Total Number of Antibodies Detected in Prenatal Samples

Multiple Antibody Combinations Identified	Number of Prenatal Multiple Antibody Investigation in (Current Year)
Anti-D, Anti-E	1
Anti-E, Anti-Lua	1
Anti-Fya, Anti-Jka	1
Anti-D, Anti-E	1
Anti-E, Anti-Lua	1
Anti-Fya, Anti-Jka	1
Anti-Jka, Anti-Mia	1
Anti-c, Autoantibody	1
Anti-C, Anti-D	1
Autoantibody, Cold Agglutinin	1
Anti-C, Anti-e	1
Anti-Lea, Anti-M	1
Anti-E, Anti-c	3
Anti-D, Anti-G	1
Anti-D, Anti-G	1
Anti-M, Anti-Wra	1
Anti-Fya, Anti-Lub	1
Anti-c, Anti-E, Anti-Fya	1
Anti-D, Anti-G	4
Anti-D, Antibody to an HLA related antigen	1
Anti-c, Anti-Jka	1
Anti-Wra, Antibody to an HLA related antigen	1
Anti-C, Anti-D, Anti-Jka	1
Anti-E, Anti-K, Anti-M	1
Anti-C, Anti-G	3
Anti-Jkb, Anti-M	

Number of Prenatal Investigation for each Antibody			
Clinically Significant Antibodies - Identified	2019	2020	2021
Anti-D	17	28	47
Anti-C	16	17	14
Anti-Cw	2	4	2
Anti-c	17	22	22
Anti-E	36	48	28
Anti-e	3	6	2
Anti-G	9	8	14
Anti-Fya	6	11	6
Anti-Fyb	1	5	0
Anti-H	0	2	3
Anti-Jka	10	18	15
Anti-Jkb	0	4	5
Anti-V	0	2	0
Anti-Inb	0	4	2
Anti-K	10	21	8
Anti-Jsb	0	1	0
Anti-Lub	5	2	2
Anti-M *	39	32	27
Anti-S	6	11	4
Anti-U	0	12	3
Anti-Ce	0	3	0
Anti-s	0	1	1
Anti-hrB	0	1	0
Anti-hrS	0	1	1
Anti-Lua	0	1	2
Anti-Yta	0	1	3
Anti-Lu14	0	2	1
Anti-Wra	0	6	6
Anti-PP1pk	0	1	0
Anti-Jra	0	2	0
Total	177	277	218

* Note: only IgG anti M is clinically significant in pregnancy

Clinically <u>In</u>significant Antibodies	2019	2020	2021
Anti-Lea	14	5	6
Anti-Leb	8	6	3
Anti-P1	3	1	2
Autoantibody	8	35	70
Antibody to HLA Antigens	9	1	11
Cold Agglutinin	11	3	4
Unidentified	2	5	3
Passive Anti-D	43	104	88
Antibody to low prevalence antigen	1	1	0
TOTAL: Clinically <u>In</u>significant Antibodies	99	161	187

Figure 2: Total Number of Antibodies Detected in Prenatal Samples

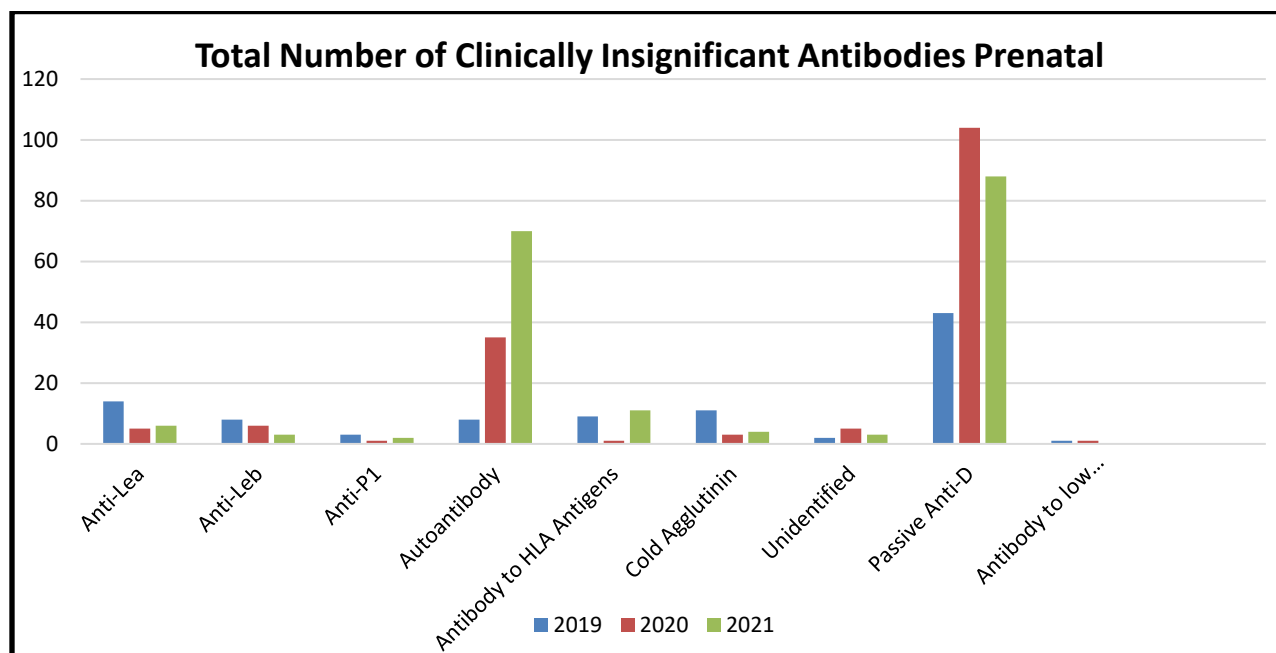
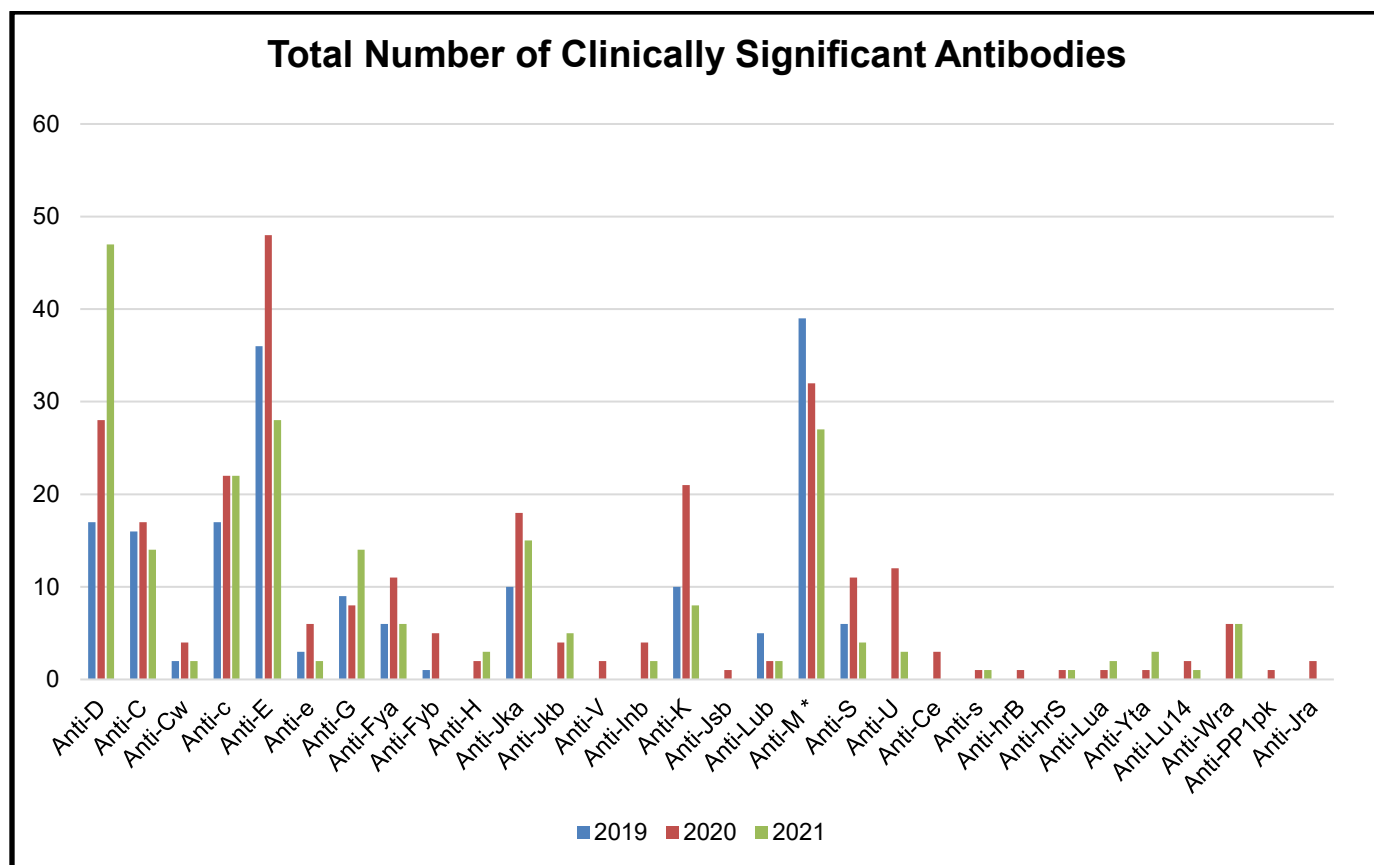


Figure 3: Frequency of Clinically Significant Antibodies

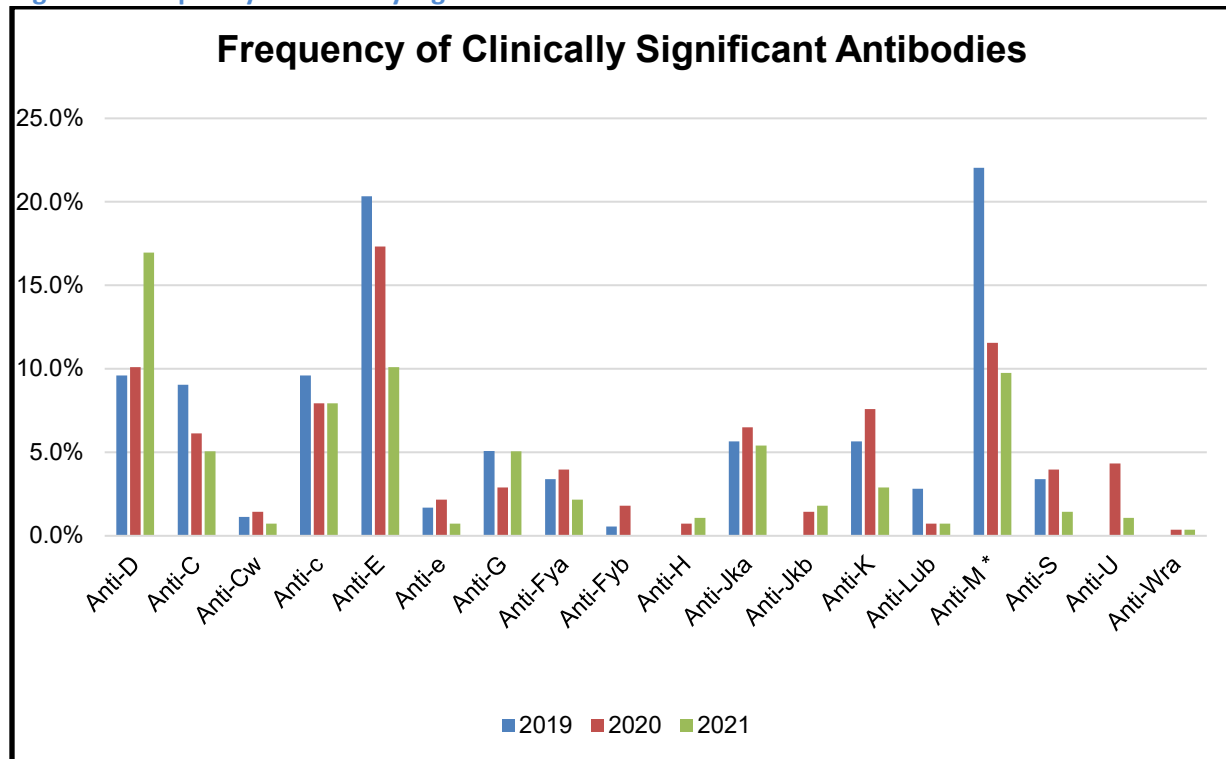


Table 6: Prenatal Combination Antibodies

Summary: In 2021 there were 46 antibody investigations for multiple antibodies with 36 different antibody combinations examined.

Multiple Antibody Combinations Identified	Number of Prenatal Multiple Antibody Investigation in (Current Year)
Anti-Jsb, Anti-E	1
Anti-s, Anti-D	1
Anti-c, Anti-Inb	1
Anti-Kpa, Anti-D	3
Anti-N, Anti-E	1
Anti-c, Anti-Jka	1
Anti-hrS, Autoantibody	1
Anti-C, Anti-E, anti-D	1
anti-M, Anti-c	2
Anti-C, Anti-Lea	1
Anti-Fyb, Anti-M	1
anti-M, anti-Jkb	2
Anti-S, Anti-c	1

Multiple Antibody Combinations Identified	Number of Prenatal Multiple Antibody Investigation in (Current Year)
Anti-G, Autoantibody	1
Anti-G, Anti-C	2
Anti-Leb, Anti-c	1
Anti-G, Anti-c	2
Anti-Jka, Anti-Lea	2
Anti-Jka, Anti-E	2
Anti-Jka, Anti-S, Autoantibody	1
Anti-c, Anti-Jra	1
Anti-Jkb, autoantibody	1
Anti-Lea, Anti-Leb	3
Anti-Wra, Anti-K, Anti-E	1
Anti-K, Autoantibody	1
Anti-S, Anti-Lea	1
Anti-S, Anti-D	1
Anti-C, Anti-M	1
Anti-K, Anti-Fyb, Anti-E	1
Anti-D, Anti-Cw	1
Anti-S, Anti-U	1
Anti-S, Anti-Lea	1
Anti-Jka, Anti-E	1
Anti-Jkb, Anti-K	1
Anti-E, Cold antibody	1
Anti-c, Anti-Lua	1

Table 7: Perinatal Patient Antibody Titres

Antibody	Critical Level	Non-Critical Level	Non-Critical to Critical
Anti-D	2	4	1
Anti-C	0	1	0
Anti-c	0	1	0
Anti-E	0	2	0
Anti-M	0	1	0
anti-C, anti-G	0	3	1
anti-D, anti-G	1	0	0
anti-Jka	0	2	0
Anti-Jkb	0	1	0
anti-S	0	1	0

Table 8: Number of Investigations for Antibodies Detected in Patient Reference Samples

Common Clinically Significant Antibodies in Patient Reference Samples	2021
Anti-D	77
Anti-C	56
Anti-c	43
Anti-E	118
Anti-e	9
Anti-f	2
Anti-G	15
Anti-K	45
Anti-M	46
Anti-S	33
Anti-s	5
Anti-Fya	36
Anti-Fyb	2
Anti-Jka	48
Anti-Jkb	19
Anti-U	2
TOTAL:	556

Clinically <u>In</u>significant Antibodies	2021
Anti-A1	9
Anti-Lea	15
Anti-Leb	5
Anti-McCa	2
Anti-N	3
Anti-P1	5
Anti-Rg	1
Autoantibody	351
Antibody to HLA Antigens	33
Anti-Xga	1
Cold Agglutinin	37
Unidentified	5
TOTAL: Clinically <u>In</u>significant Antibodies	427

Figure 4: Total Number of Clinically Significant Antibodies Detected in Patient Reference Samples

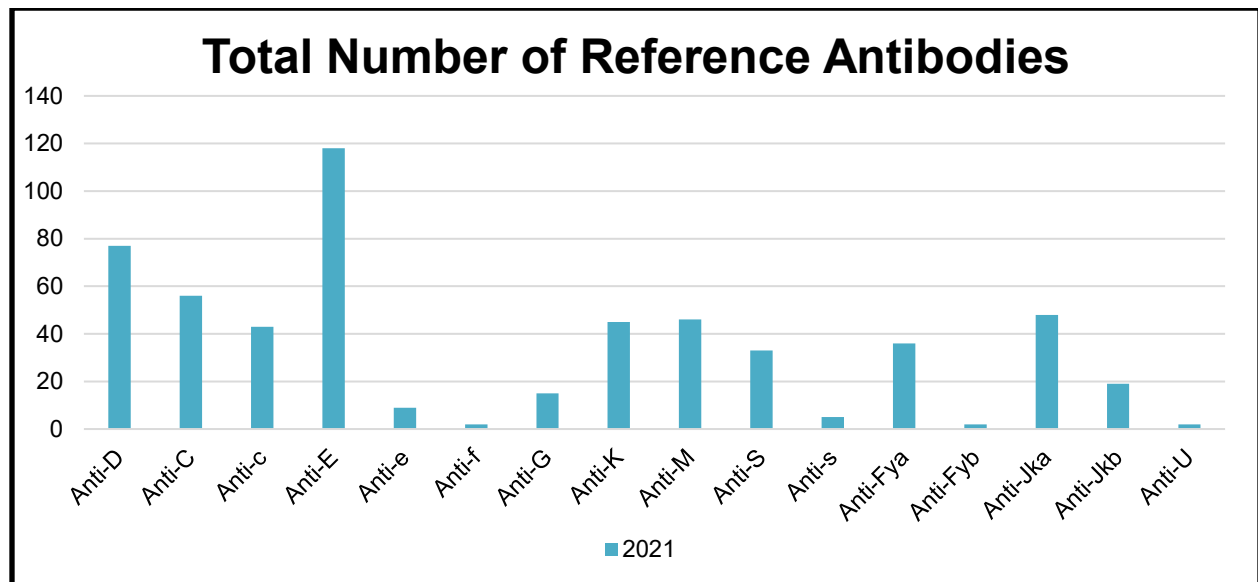


Figure 5: Frequency of Clinically Significant Antibodies in Patient Reference Samples (2021)

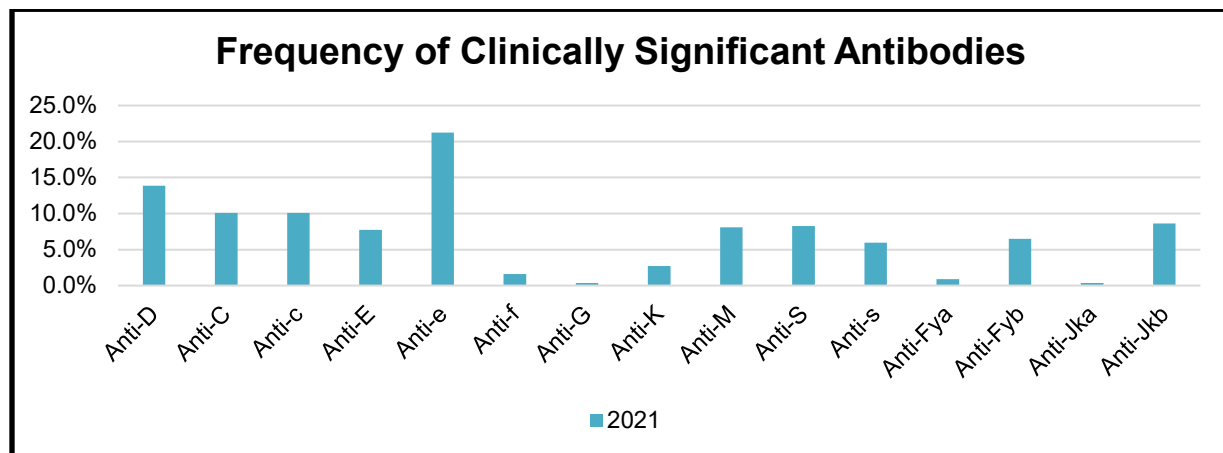


Table 9: Number of Investigations for Antibodies to Low Prevalence Antigens

Antibody	Number Identified
Anti-Cw	2
Anti-Dia	3
Anti-Jsa	3
Anti-Lua	4
Anti-VS	1
Anti-Kpa	2
Anti-Mia	7
Anti-V	3
Anti-Dantu	1
Anti-He	1
Anti-Mia	6
Anti-Cob	3
Anti-Wra	5
Antibodies to low prevalence antigen	41

Table 10: Number of investigations for Antibodies to High Prevalence Antigens

Antibody	Number Identified
Anti-Ch	1
Anti-H	4
Anti-hrB	1
Anti-Jk3	2
Anti-Fy3	1
Anti-Kna	2
Anti-Kpb	2
Anti-hrS	2
Anti-Coa	3
Anti-LW	3
anti-Ge2	4
Anti-Dib	2
Anti-Inb	1
Anti-Lub	3
Anti-PP1Pk	1
Anti-U	2
Anti-Joa	2
Anti-Jsb	2
Anti-Yta	3
Anti-Csa	1
Anti-Hr	1
Anti-JMH	2
Antibodies to high prevalence antigen	25

Table 11: Number of Patient Investigation for a Combination Antibodies

Multiple Antibodies Detected	2021	Multiple Antibodies Detected	2021
Anti-C, Anti-S	1	Anti-D, Anti-E	5
Anti-Sda, Warm Autoantibody, Cold Agglutinin	1	Anti-D, Anti-C, Anti-E, Anti-S, Anti-K, Anti-Fya	1
Anti-Wra, Antibody to HLA related antigen	1	Anti-D, Anti-C	10
Anti-E, Anti-c, Anti-Jka	2	Anti-E, Anti-Cob	1
Anti-E, Anti-VS, Anti-Jka, Anti-V, Anti-Jsa, Autoantibody	1	Anti-c, Anti-Jka	1
Anti-E, Autoantibody	15	Anti-S, Autoantibody	3
Anti-E, Anti-S, Anti-K	1	Anti-C, Anti-S, Anti-K	1
Anti-K, Autoantibody	8	Anti-E, Anti-M, Anti-Jka	1
Anti-E, Anti-S, Anti-Jka, Autoantibody	1	Anti-c, Anti-S, Autoantibody	2
Anti-C, Anti-K, Anti-Jkb, Anti-Jsa, Autoantibody	1	Anti-N, Warm Autoantibody	1
Anti-E, Anti-M	1	Anti-D, Anti-Ge2	1
Anti-M, Anti-Fya, Antibody To HLA related antigen	1	Anti-Leb, Anti-Jka	1
Anti-E, anti-c, Anti-Jka	1	Anti-E, Anti-Wra, Antibody to HLA related antigen	1
Anti-E, Anti-Lua, Anti-Jka	1	Anti-E, Anti-Cw	1
Anti-E, Anti-Lua, Antibody to HLA related antigen	1	Anti-C, Autoantibody	3
Anti-C, Anti-E, Anti-Kpa, Anti-Wra, Autoantibody	1	Anti-Jka, Autoantibody	5
Anti-C, Anti-Fya, Anti-Jkb	1	Anti-E, anti-s, Anti-Jka	1
Anti-Lua, Autoantibody	1	Anti-C, Anti-S, Anti-Kpa, Autoantibody	1
Anti-C, Anti-E, Anti-S, Anti-Fya, Anti-Jkb	1	Anti-Fya, Antibody to HLA related antigen	1
Anti-Cw, Anti-Fya	2	Anti-E, anti-c	4
Anti-K, Anti-Fya, Anti-Jka, Antibody to HLA related antigen	1	Anti-C, Anti-e, Anti-Jka, Autoantibody	1
Anti-E, Anti-K	1	Anti-c, Anti-S, Autoantibody	1
Anti-C, Anti-E, Anti-Lea, Anti-Fya, Anti-Jkb	1	Anti-D, Anti-C, Anti-P1	1

Multiple Antibodies Detected	2021	Multiple Antibodies Detected	2021
Anti-E, Anti-V	1	Anti-K, Anti-Ch	1
Anti-C, Anti-e, Autoantibody	2	Anti-Fya, Anti-Jka, Autoantibody	3
Anti-E, Anti-K, Autoantibody	1	Anti-E, Anti-Fya, Anti-Wra	1
Anti-E, Anti-K, Anti-Fya	2	Anti-C, Anti-e,	2
Anti-c, Autoantibody	1	Anti-c, Anti-S, Anti-Fyb, Anti-Mia	1
Anti-He, Anti-Wra, Autoantibody	1	Anti-D, Anti-G	3
Anti-E, Anti-c, Anti-M, Cold Agglutinin	1	Anti-Fya, Autoantibody	1
Anti-E, Anti-c, Anti-M, Autoantibody	2	Anti-s, Anti-Fya, Anti-Jkb, Autoantibody	1
Anti-E, Cold Agglutinin	1	Anti-E, Anti-S, Anti-K, Anti-Fya-, Anti-Jkb, Anti-Cob	1
Anti-D, Anti-Lua, Autoantibody	1	Anti-E, Anti-S, Anti-K, Autoantibody	1
Anti-E, Anti-S, Anti-K	1	Anti-Lea, Anti-Fya, Cold Agglutinin	1
Anti-E, Anti-c, Anti-S	2	Anti-E, Anti-c, Anti-Fya	1
Anti-E, Anti-Kpa	1	Anti-E, anti-c, Anti-Jkb	1
Anti-S, Anti-Ch	1	Anti-M, Anti-Fya, Antibody to an HLA related antigen	1
Anti-f, Anti-Fya	1	Anti-E, Anti-c, Autoantibody	1
Anti-C, Anti-Cw, Anti-Leb	1	Anti-N, Anti-S, Anti-Fya	1
Anti-E, Anti-Lua	2	Anti-C, Anti-G	2
Anti-M, Anti-Jkb	1	Anti-D, Anti-C, Anti-G	1

Summary: In 2021 there were 141 antibody investigations for multiple antibodies with 80 different antibody combinations examined.

Table 12: Antibody Complex Procedures Performed

Procedures	Number of Prenatal Samples	Number of Referral Samples
Autoadsorption	14	40
Alloadsorption	31	94
Elution	76	581
Direct Coombs	720	2567

REFERRAL SAMPLES

1.2. Red Cell Genotyping

The BioArray BeadChip™ test system has been installed and validated in the Diagnostic Services Laboratory in Edmonton for RHD genotype testing used for the identification of RHD variants. The Edmonton CBS laboratory is accredited by the College of Physicians and Surgeons of Alberta (CPSA). Any patient samples requiring extended red cell genotype testing other than for D variant are referred to the National Immunohematology Reference Laboratory (NIRL) in Brampton. NIRL performs extended genotype testing using the Progenika ID Core XT™ assay. If genotype test results are required urgently, testing results can be provided within 24 hours of the sample receipt.

Table 13: Genotype procedures referred by Canadian Blood Services

Number of Ontario Genotype Procedures 2021	
Procedures	Number
RHD Genotype Procedures	331
Non-RHD Genotyping	1737

1.3. Red Cell Serological Reference Testing

The National Immunohematology Reference Laboratory (NIRL) in Brampton is a highly specialized laboratory that focuses its attention on the identification and resolution of exceedingly complex red cell transfusion-related problems. The laboratory is accredited by Accreditation Canada Diagnostics.

QUALITY INDICATORS

The laboratories monitor many quality indicators and the two which are most relevant to this document are turnaround times and rejected specimens which are presented below.

1.4. Turnaround Times

To ensure timely reporting of patient test results, Canadian Blood Services monitors turnaround time (TAT) from when the specimen is received at Canadian Blood Services in Brampton to the time when the results are available. Since monitoring of this quality indicator began in 2008, the percentage of specimens has consistently exceeded the predefined TAT threshold of 75% of samples to be tested and reported within 5 days of receipt. In 2021, 87% of the samples received were tested and reported within 5 days of receipt. Samples whose testing exceed the expected TAT are usually those where complex clinically significant antibodies are detected or where a referral to the National Immunohematology Reference Laboratory for additional investigation or genotype testing is required.

1.5. Rejected Specimens

The laboratory reserves the right to refuse improperly labelled specimens. Consistent practices for specimen rejection are employed across CBS. The laboratory takes measures to maintain specimen integrity during the process of following up on the receipt of an improperly identified specimen. The high number of specimens received by the laboratory makes it impossible to positively identify specimens that are not clearly labelled in accordance with standard specimen identification criteria. The specimen rejection rate in 2021 was 1.1% which is decreased from the 1.4% in 2020.

1.6. Proficiency Testing

- **College of American Pathologists Survey Participation**

This summary is based on all the College of American Pathologists (CAP) survey reports from the Brampton Diagnostic Services site. This summary includes all the blood group serology processes.

Table 13: CAP Proficiency Testing Results

Brampton Diagnostic Site (Red Cell)	2019 CAP Proficiency Results	2020 CAP Proficiency Results	2021 CAP Proficiency Results
ABO/Rh Type	100%	100%	100%
Antibody Titre	100%	100%	100%
Antibody Identification	100%	100%	100%
Antibody Identification Eluate	100%	100%	100%
Direct Coombs C3	100%	100%	100%
Direct Coombs IgG	100%	100%	100%
Unexpected Antibody Detected	100%	100%	100%

Table 14: IQMH Proficiency Testing Results

Brampton: TMED	Kit #	Date Results Received	Results
Brampton	TMED-2103-Advanced	2021-03-09	100%
Brampton	TMED-2106-Advanced	2021-07-01	100%
Brampton	TMED-2109-Advanced	2021-09-14	100%

DIAGNOSTIC SERVICES UPDATE 2021

Updates pertain to all Diagnostic Services sites within Canadian Blood Services: Vancouver, Edmonton, Winnipeg, and Brampton

ALL	<p>NEO Iris Analyzer implemented April to June 2021. Eight NEO Instruments in Diagnostic Services were replaced with the next generation NEO IRIS instrument. NEO Iris performs ABO/RH and antibody testing.</p> <ul style="list-style-type: none"> Edmonton- 2 NEO Iris' implemented May 2021 Vancouver- 2 NEO Iris' implemented April and May 2021 Winnipeg- 3 NEO Iris' implemented May and June 2021, with a fourth to be installed at CBS St.B satellite site in 2022"
Edmonton	Edmonton DS obtained the CPSA 4-year accreditation on 20021-02-25.
Edmonton	Transfer of HEA and RHCE genotype testing to Brampton, 2021-10-01
Vancouver	Awarded CAP Accreditation Dec 2021.
Vancouver	CPSBC – DAP ISO 15189 Audit. ISO 15189 accreditation pending final acceptance.
Winnipeg	Preparation for implementation of the Canadian Blood Services satellite Lab at St Boniface Hospital in March 2022. The Lab will act as a contingency site for services delivered by Winnipeg Diagnostic Services.
Winnipeg	Implementation of equipment in NPRL – Multisizer 3 (cell counter) and thermocyclers
Winnipeg	Management of supplies, inventory and testing to ensure provision of services are not impacted during supply chain issues experienced in a pandemic.

Winnipeg	eTraceLine environments (perinatal and Crossmatch) were merged to allow better efficiency and ease of use for the labs noe that staff are cross trained.
Winnipeg	Project to implement HistoTrac and replace the access database currently used as the LIS began in Winnipeg in 2021. Projected implementation is December 2022.
Presentations / Abstracts / Publications Listing	
<i>Lhevinne Ciurcovich, Lynnette Beaudin, Arianne Fuelles, Balkar Gill, Ilona Resz, Debra Lane, Judith Hannon, Gwen Clarke, Melanie Bodnar.</i> Comparison of Manual SIAT vs Automated Solid Phase Methodology for Perinatal Antibody Titration. Poster, CSTM 2021	
<i>Lhevinne Ciurcovich¹, Sarah Manfredi², Sarah Buchko², Darlene Mueller², Michelle Wong², Mohammad Bahmanyar², Matthew Yan¹, Gwen Clarke¹.</i> Anti-I_na Implicated in Hemolytic Disease of the Fetus and Newborn in an Indigenous Woman. Poster, CSTM 2021 1: Canadian Blood Services, BC and Yukon Centre 2: Fraser Health Authority, British Columbia	
<i>Lhevinne Ciurcovich, Gwen Clarke, Matthew Yan.</i> A Case of ABO Chimerism in a Perinatal Patient. Poster, CSTM 2021	
<i>Lhevinne Ciurcovich.</i> Cell-Free Fetal DNA Testing: Advantages, Challenges and Limitations. Presentation: Virtual Conference, 22nd Annual Education Day on Blood Transfusion Issues, 2021-09-24.	
<i>Lhevinne Ciurcovich.</i> Immunohematology Case Studies. Presentation: Immucor ImmuTECH Education Day (Virtual) 2021-05-05.	
<i>Lynnette Beaudin, Dr. Lani Lieberman MD, FRCP,</i> Fetal and neonatal alloimmune thrombocytopenia (FNAIT): Diagnosis, Investigation and Treatment. Presentation: U of T Monthly Transfusion Rounds (Virtual) 2021-02-25	
<i>Bodnar M, Hannaford K, Montemayor-Garcia C, Hannon J.</i> Blindspots in Immucor BioArray RHD Molecular BeadChip Test: A Review of Cases at Canadian Blood Services Referred Out for RHD Gene Sequencing. Poster/Abstract, CSTM 2021	

*Floch A, Vege S, Berardi P, **Hannon J**, Ochoa-Garay G, Lomas-Francis C, et al. A change in RHD is associated with aberrant transcription and very weak D phenotype. Transfusion 2021*

*Flegel WA, Bodnar M, Clarke G, **Hannon J**, Lieberman L., 'What constitutes the most cautious approach for a pregnant person with weak D type 4.0?' Letter to the Editor, CMAJ June 2021*