Centre for Innovation Annual Progress Report

2019-2020

27 August 2020

Canadian Blood Services

BLOOD
PLASMA
STEM CELLS
ORGANS
& TISSUES

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Opening letter

Dear reader,

It is our pleasure to present the 2019-2020 Canadian Blood Services Centre for Innovation annual progress report.

This report details achievements that have been made by our network of scientists, medical experts, research partners, and collaborators. Now two years into a five-year funding cycle, 2019-2020 marked the start of new initiatives, such as a social science research program and an MSM Plasma Program. As you'll discover in this report, the work of the Centre for Innovation led to changes in donor selection criteria, improvements in the products supplied by Canadian Blood Services, the development of clinical practice guidance, and new discoveries — all to better meet patient needs.

On March 11, 2020, a few weeks before the close of the 2019-2020 fiscal year, the COVID-19 pandemic was declared. It has been the Centre for Innovation's honour to step up and work alongside many others across the organization to support its pandemic response plan and ensure Canada's Lifeline can keep flowing despite the diverse challenges. We were proud to witness the flexibility, adaptability and resiliency of the staff during these challenging times and are confident that these qualities will shine as we continue to adapt to this global crisis.

We are deeply grateful for the ongoing support we receive from our funders, Health Canada Strategic Policy Branch and the provincial and territorial ministries of health, and our partners and colleagues across the transfusion and transplantation communities. We continue to be inspired by the achievements of our network as we rise to the challenges before us and work together to support Canada's Lifeline in its vigilant stewardship of the Canadian blood system.

Sincerely,

Dr. Isra Levy

Vice President, Medical Affairs and Innovation

Canadian Blood Services

Dr. Chantale Pambrun

Director, Centre for Innovation

Canadian Blood Services

2019-2020: Centre for Innovation year in review

Discovering Research from the Centre for Innovation discovered that a plasma-derived drug currently used for two diseases may have the potential to treat others (page 17). Research uncovered important new links between viral infections and coagulation, suggesting potential new targets for anti-viral treatments (page 20).

Leading donor selection change The Centre for Innovation secured more research funding to inform alternative screening approaches for plasma donors. This new MSM (men who have sex with men) Plasma Program complements the MSM Research Program in generating evidence that could evolve the current donor eligibility policy (page 12). The Centre led a Knowledge Synthesis Forum to engage with MSM Research Program stakeholders (page 12). Findings from the MSM Research Program informed Health Canada's decision to approve a Canadian Blood Services' license amendment to reduce the donor deferral period for men who have sex with men from 12 months to 3 months (page 11).

Guiding clinical practice The Centre for Innovation supported a national study that found that fibrinogen concentrate is equivalent to cryoprecipitate in controlling post-operative bleeding. This finding could impact how cardiac patients are treated and inform Canadian Blood Services' formulary (page 18). The American Society of Hematology affirmed that two guidelines published by the International Collaboration for Transfusion Medicine Guidelines, supported by the Centre for Innovation, have value for hematologists (page 32).

Meeting every patient need Under Health Canada's Special Access Program, the Centre for Innovation produced and shipped a vital plasma medication to treat a patient with plasminogen deficiency, an extremely rare condition (page 27).

Advancing blood product formulary The Centre for Innovation developed a freeze-drying protocol for plasma and conducted a product characterization study which demonstrated that freeze-dried plasma is comparable to frozen plasma, suggesting it should yield similar clinical benefits. These are important steps towards adding freeze-dried plasma to Canadian Blood Services' formulary (page 25).

Responding Since early 2020, the Centre for Innovation has played a key role in Canadian Blood Service's response to the COVID-19 pandemic, informing the organization's evidence-based approach and facilitating several studies, including clinical trials to test the safety and efficacy of COVID-19 convalescent plasma in treating patients with this new virus (page 24).

Engaging and disseminating The Centre for Innovation supported 102 investigators through competitive research funding and products for research programs. The Centre's network published 123 peer-reviewed publications and 30 technical reports to support decision-making by Canadian Blood Services and stakeholders. The Centre's medical and scientific staff delivered over 300 presentations at local, national, and international conferences. The Centre engaged with over 2,800 attendees at knowledge exchange and educational events.

In this report, we highlight the activities and achievements of Canadian Blood Services' Centre for Innovation over the past fiscal year (1 April 2019 – 31 March 2020). We begin by introducing the Centre for Innovation and its members, then we provide stories and insights that highlight the Centre's research and development work to support a safe, effective and responsive system of blood, blood products, plasma and stem cells in Canada. The report concludes with training, education and engagement activities, as well as a governance section outlining the Centre for Innovation's outputs and outcomes.

The Centre for Innovation

Our Vision

To gain insights into the life-to-life continuum in order to inform and optimize Canada's biological lifeline to achieve a sustainable and progressive operation in a public healthcare system.

Our Focus

The Centre for Innovation supports Canadian Blood Services to continuously improve blood products and their utilization to **help every patient, match every need, and serve every Canadian.**

Safeguard **We support a safe, effective and responsive blood system.** We help ensure Canadian Blood Services' life-saving products are as safe and effective as possible through research, product and process development, and professional education, including the development of clinical guidelines and best practices. We support Canadian Blood Services in responding to emerging threats to safety, efficacy or supply.

Engage **We connect an interdisciplinary and collaborative network of experts.** We engage with our network of researchers, clinicians, and health-care professionals to ensure the knowledge generated by the Centre increases our collective understanding of the blood system, informs best practices and influences policies. We maintain strong connections nationally and internationally to ensure Canadian Blood Services stays at the forefront of developments for the benefit of all Canadians.

Improve **We innovate to prepare the Canadian blood system for tomorrow.** We continuously improve and transform the systems and processes that help Canadian Blood Services achieve its ultimate goal – improving the health of Canadians. We are always evolving our programs to address changing needs. We embrace constant change for a brighter future.

Our Team

We are a world-class team of discovery, development and social scientists, and medical experts, supported by a dedicated administrative team. We are housed within Canadian Blood Services' Medical Affairs and Innovation division. We are uniquely positioned at the interface between academic discovery and operational implementation to optimize our response to the needs of Canada's blood system.

Our Activities

We work along the entire "life-to-life" continuum, from donors to recipients, to serve **Canada's Lifeline**. We are organized around three main pillars.

Research Discovery research provides new insights into blood, blood products, plasma, and stem cells. Social science research supports donation and donor engagement.

Product and process development Applied development work improves both the blood and stem cell products we supply, and the technologies and processes used to produce them.

Knowledge mobilization and strategic alliances Research and training are supported through competitive funding programs and knowledge mobilization activities. Healthcare professionals are supported through education and clinical guideline development.

Our Network

We engage with a broad research and education network of multidisciplinary partners both within Canadian Blood Services and in academic institutions, industry and government. Our reach is national and international.

Members of the Centre for Innovation and our extended network, June 2019

We are proud to be part of **"the connection between the profound discoveries of science and the joyful restoration of health."**

Learn more about Canadian Blood Services' mission.

Appointments and awards

In 2019-2020, the Centre for Innovation welcomed new research appointments, and our staff and research and education network received national and international recognition.

Research appointments

In 2019-2020, the Centre for Innovation launched a social science research program and welcomed **Jennie Haw** as research associate (now scientist). She was joined in early 2020 by research associate **Kelly Holloway**. This new program focuses on donors and the donation process for all Canadian Blood Services product lines to inform and optimize organizational operations. It will seek partnership with social and behavioural scientists in Canada and around the world.

The following Canadian Blood Services Adjunct Scientists were appointed or reappointed:

Donald Arnold (McMaster University)
Robert Ben (University of Ottawa)
Nancy Heddle (McMaster University)
Dean Fergusson (Ottawa Hospital Research Institute)
Lani Lieberman (University Health Network)
Elisabeth Maurer-Spurej (University of British Columbia)
Alan Tinmouth (Ottawa Hospital Research Institute)

Dana Devine, Narges Hadjesfandiari and Michael F. Murphy from the AABB

Abstract and publication awards

Senior scientist, **Heyu Ni** received the University of Toronto division of hematology 2019 Keating Award, awarded to the #1 paper of the year for his publication entitled "GPIbα is required for platelet-mediated hepatic thrombopoietin generation."

Postdoctoral fellow, **Narges Hadjesfandiari** (pictured left), from chief scientist **Dana Devine**'s laboratory, won 2019 Outstanding Abstract Award for Trainees for her oral presentation at AABB 2019.

An article by senior research assistant **Roya Pasha** and co-authors from senior scientist **Nicolas Pineault**'s laboratory entitled "Overcoming the deceptively low viability of CD45+ cells in thawed cord blood unit segments" was short listed for the *Vox Sanguinis* Best Paper Prize 2019.

An abstract by postdoctoral fellow **Javed Manesia** and co-authors from **Nicolas Pineault**'s laboratory was selected for an Abstract Achievement Award at the 2019 American Society of Hematology conference.

Canadian Blood Services Transfusion Medicine fellow **Aditi Khandelwal** was the winner of the 2020 Canadian Blood Services Lay Science Writing Competition.

Several members of the Centre for Innovation network contributed to publications in transfusion medicine that were recognized as important by the NHS Blood and Transplant Systematic Review Initiative. In April 2019, two articles were highlighted in their top ten:

> Patient Blood Management: Recommendations From the 2018 Frankfurt Consensus Conference. *JAMA*. 2019 Mar 12;321(10):983-997.
>
> Fetal and neonatal alloimmune thrombocytopenia: Recommendations for evidence-based practice, an international approach. *Br J Haematol*. 2019. May;185(3):549-562.

Recognition and honours

In recognition of more than 40 years of major contributions to transfusion medicine and hematology, senior scientist **Donald Branch** (pictured below) was awarded the 2019 Tibor Greenwalt Memorial Award and Lectureship from AABB.

Branch was also awarded the 2019 Michigan Association of Blood Banks' Kay Beattie Lectureship at their annual meeting.

Senior scientist **Heyu Ni** received Unity Health Toronto's Keenan Legacy Award, given to a scientist who enhances the reputation of biomedical or translational research and whose actions help develop the next wave of scientists.

QUEST investigator **Yulia Lin** received the 2019 AABB President's Award in recognition of her master educator role in the field of transfusion medicine, particularly her role in Transfusion Camp.

Adjunct scientist **Lani Lieberman** was awarded the 2019 Blum Award for outstanding service at the Canadian Society for Transfusion Medicine annual conference.

Adjunct scientist and **MCTR** director, **Donald Arnold** was awarded a Mentorship and Supervision Excellence Award by McMaster University's Department of Health Research Methods, Evidence and Impact.

Donald Branch receiving the Tibor Greenwalt Memorial Award and Lectureship

2019-2020 spotlight: Acker's accolades

Jason Acker is a senior scientist at the Centre for Innovation and a professor in the department of laboratory medicine and pathology at the University of Alberta. Whether doing research to better understand blood products or finding new methods to preserve cells, he focuses on quality: the quality of blood products and what quality means for patients. His hope is that the technologies he is researching will one day change the way blood products are stored and assessed, ultimately improving their quality for the benefit of patients. With a slew of publications and awards, 2019-2020 was a big year for **Acker** and his team.

Doing "cool" science

Acker has a long-standing and enduring interest in the field of cryobiology. He has worked on the development of "ice recrystallization inhibitors," new molecules that can protect cells and tissues during freezing. Together with his colleague Robert Ben from University of Ottawa, **Acker** has investigated various "cryoprotectant" solutions.

An ACS Editor's Choice was awarded to **Acker** and collaborators for their manuscript: "Modulating intracellular ice growth with cell permeating small molecule ice recrystallization inhibitors" published in June 2019 in *Langmuir*.[1]

Assessing red blood cell quality

With collaborators in Toronto, the **Acker** laboratory is exploring new ways to assess red blood cell quality:

- Using state-of-the-art flow cytometry technology, **Acker**'s new technique offers good potential for studying the relationships between red blood cell morphology (shape) and blood storage lesions.[2]
- Developing an innovative photoacoustic method, **Acker** is measuring the oxygen saturation of red blood cells in their storage bags. This non-invasive quality test could be used to assess quality without compromising the sterility of the blood product.[3]

Mentoring the next generation

Acker was awarded the University of Alberta Graduate Students' Association 2019 Graduate Student Supervisor Award. Making this award even more special –he was nominated by his graduate student, Ruqayyah Almizraq (pictured right with Acker), something that **Acker** describes as particularly humbling.

Acker also received the University of Alberta Faculty of Medicine and Dentistry 2020 Tier 1 Basic Science Award for Excellence in Mentoring which recognizes outstanding performance in mentoring research trainees.

Research funding and dissemination

Supporting innovative research requires funding, and **Acker** is thankful to the many organizations which have funded his laboratory. Current funding includes:

- $1.12M in direct investigator-driven, peer-reviewed grants, including Canadian Blood Services **Intramural Research Grant Program** and **Blood Efficiency Accelerator Award Program** funding, and a Women & Children's Health Research Institute – Community Research Integration Support Program grant.
- Over $3M in additional funding from research grants with collaborators, including through the Canadian Institutes of Health Research and the US National Institutes of Health.

In 2019-2020, the **Acker** laboratory

- had **15** publications published or accepted
- delivered **24** presentations
- conducted **3** media interviews
- supported **4** projects directly supporting Canadian Blood Services operational activities.

International recognition

Acker was recognized for his exemplary impact on the field of cryobiology with his induction as a Fellow of the Society for Cryobiology. Only 27 scientists have been granted this prestigious international award, and **Acker** is one of only four Canadians inducted in the society's 55-year history. At the Society's 2020 Annual General Meeting in San Diego, **Acker** was presented with the 2019 Basile J. Luyet medal recognizing his sustained scientific contributions to the field, his training of the next generation of cryobiologists and his distinguished service to the Society (pictured below).

Learn more in our R.E.D. blog post "Centre for Innovation scientist recognized for his contributions to the field of cryobiology."

> "It is an incredible honour to be inducted as a Fellow of the Society for Cryobiology. I have been fortunate enough to have had the opportunity to contribute in a meaningful way to a very 'cool' science that has led to improvements in how we store biological materials for use in transfusion medicine, transplantation, biotechnology, and conservation biology."
>
> *Jason Acker*

Research & development highlights

Safe

"All blood transfused in Canada is collected from volunteer donors. To ensure the safety of the blood products, donors are carefully screened against an extended list of eligibility criteria. In addition, the donated blood is tested to identify the donor's blood group and to detect blood group antibodies and transfusion-transmissible pathogens. Donor eligibility criteria and testing also benefit the donors by, for example, reducing potential blood donation-related health risks."

From Canadian Blood Services Clinical Guide to Transfusion Chapter 6: Donor Selection, Donor Testing and Pathogen Reduction[4, 5]

Safeguarding donors

Reducing donor faint reactions

The health and well-being of every donor who so generously contributes to Canada's Lifeline is hugely important. In March 2019, Canadian Blood Services implemented a donor wellness initiative, which aimed to improve the donation experience and reduce the likelihood of donors experiencing a vasovagal reaction (feeling faint or fainting). As part of this initiative, all blood donors were offered water and salty snacks before they donated and were encouraged to do muscle tension exercises during their donation. Data gathered by associate director of epidemiology and surveillance **Sheila O'Brien** and her group after implementation show that vasovagal reactions decreased from 18.8 to 16.2 per 10,000 whole blood donations and more severe post-donation reactions also trended downwards (see: 2019 Surveillance report).

Reassuring mothers or mothers-to-be

Iron deficiency is a global problem in women of child-bearing age and is associated with poorer outcomes in mothers and newborns. With partners in Montreal and Ottawa, medical director **Mindy Goldman** and **O'Brien** investigated whether there is an association between repeated blood donation in women of child-bearing age and poorer maternal or neonatal outcomes.[6] Comparing outcomes in women who were blood donors and those who were not revealed that repeated blood donation prior to pregnancy is not associated with worse outcomes for mothers or their babies, a reassuring finding for female donors, their children, and clinicians and policy makers.

Safeguarding recipients

Can bacteria adhere to blood sets?

In Canada, health-care providers change blood administration sets during transfusions every 4 hours based on the manufacturers' recommendations. This time limit is thought to minimize the risk that bacteria could adhere to the inner surfaces of the set's tubing and pose a safety risk to the recipient but there's a lack of supporting scientific evidence. In a pilot study, senior scientist **Sandra Ramirez-Arcos** found that during a mimicked 4-hour red blood cell transfusion,

bacterial adhesion is limited; however, by 24 hours, bacterial concentrations can reach clinically significant levels.[7] This work and future studies will help determine the safe interval for changing sets, while reducing costs and unnecessary plastic waste.

Mitigating false positive test results

Associate director of microbiology **Steven Drews** reported on a case series of five donors whose donations tested positive for West Nile Virus. All had recently received vaccination against Japanese Encephalitis virus and none had strong evidence for West Nile Virus infection. West Nile Virus and Japanese Encephalitis virus are members of the same family of viruses, and a review of laboratory results and the donors' epidemiologic risks suggested that the positive test results were due to assay cross-reactivity.[8] To avoid future false positives, a temporary blood donor deferral following Japanese Encephalitis vaccination will come into effect at Canadian Blood Services in Fall 2020.

Modelling to estimate risk

Modelling is an important tool to assess the impact of changes that may affect blood safety. For example, modelling HIV risk helped inform advances in donor eligibility criteria for men who have sex with men, a population who up until 2015 were indefinitely deferred from donating blood. However, once changes to these eligibility criteria were implemented in various countries, post-implementation data showed that the modelling studies used had predicted greater risk than was observed.

Did you know?

In 2019, the estimated residual risks of infectious diseases in donations to Canadian Blood Services are:

HIV: 1 in 12.9 million donations
HCV: 1 in 27.1 million donations
HBV: 1 in 1.38 million donations

Learn more in the 2019 Surveillance Report.

As part of an International Society for Blood Transfusion (ISBT) working group, **O'Brien** helped develop an optimized model for HIV risk.[9] The optimized model's predictions were confirmed by data collected after a change to a 12-month deferral for men who have sex with men in the UK and Canada.

The same international team, which includes members from Canada, France, the USA, the UK and Australia, used this model to estimate HIV residual risk if donor eligibility criteria were further changed to a 3-month deferral for men who have sex with men. Their modelling showed the additional risk under a 3-month deferral is extremely low.[10] This study, funded by the Centre's **MSM Research Program**, provided part of the data presented to Health Canada that informed a change to a 3-month deferral in Canada in June 2019. The team are currently using their model to estimate risks of plasma donation for fractionation by men who have sex with men without a time deferral.

2019-2020 Spotlight: Building the evidence to evolve a donor policy

Canadian Blood Services continues to work on advancing Canada's blood donor eligibility criteria for men who have sex with men. Here we showcase some of the Centre for Innovation key activities in this area for 2019-2020.

MSM Research Program

The **MSM Research Program** funds 15 research projects across Canada engaging 11 investigators and over 90 team members, collaborators and partners. Each project addresses one or more of the Program's priorities:

- to support development of alternative eligibility criteria for men who have sex with men;
- to assess the acceptability of alternative eligibility criteria to men who have sex with men and Canadians in general;
- risk modelling to determine how changes to donor eligibility might impact blood safety and sufficiency;
- to assess the operational feasibility of changes to donor eligibility.

While many projects will be completed in 2020 or 2021, the **MSM Research Program** has already generated data and an interim report has been published:

- 'One step closer': Acceptability of a programme of plasma donation for fractionation from men who have sex with men (Caruso et al., 2019;[11] article available free online)
- Changing the deferral for men who have sex with men - an improved model to estimate HIV residual risk (Davison et al., 2019)[9]
- Gay and bisexual men's views on reforming blood donation policy in Canada: A qualitative study (Grace et al., 2019;[12] article available free online)
- HIV residual risk in Canada under a three-month deferral for men who have sex with men (O'Brien et al., 2019)[10]
- MSM Research Program Knowledge Synthesis Interim report (available online at blood.ca)[13, 14]

Knowledge Synthesis Forum

In November 2019, a Knowledge Synthesis Forum for the **MSM Research Program** was held in Toronto bringing together researchers and stakeholders (pictures below). During this Program milestone event, research progress to-date was presented, findings were discussed, and gaps, emerging challenges and opportunities were identified.

Engagement at the Forum

Discussions at the Forum highlighted an appreciation of the volume of data generated so far, the dedication of the research teams and the stakeholders, and the commitment of Canadian blood operators. The need for better knowledge dissemination from blood operators regarding blood donor eligibility criteria and the evidence supporting the criteria was raised.

Based on needs identified at the Forum, an opportunity for funding for knowledge mobilization activities was made available to funded principal investigators. Ten projects received funding in March 2020 to develop resources and events which will disseminate research findings to the research and stakeholder communities.

MSM Plasma Program

Based on the needs identified through the **MSM Research Program**, the Centre for Innovation submitted a proposal to Health Canada to obtain research funding to establish evidence-based alternative screening and collection approaches for source plasma donors. In Fall 2019, Health Canada awarded $2.4M in new funding to support the MSM Plasma Program.

The **MSM Plasma Program** launched in February 2020 with a meeting in Ottawa. The 37 participants included representatives from across Héma-Québec and Canadian Blood Services. The purpose of the meeting was to build understanding and awareness of the Program across various groups within the blood operators, identify organizational interdependencies and develop an action plan.

In addition, through a rigorous peer-review process, the Program awarded funding to four research projects. Some of the projects supported by this Program are national in focus but regional studies are taking place in Calgary (project led by Justin Presseau from the Ottawa Hospital Research Institute), London (project led by William Fisher at Western University), Montreal (project led by Joanne Otis at Université du Québec à Montréal) and Halifax (project led by Jacqueline Gahagan at Dalhousie University). These projects will focus on feasibility and acceptability of new screening questions by potential donors from the gay, bisexual and other MSM (gbMSM) and trans community as well as by staff and current donors.

Safeguarding supply

Understanding donor behaviour

In a letter to *The Lancet Haematology*, chief scientist **Dana Devine** highlighted the need for research to better engage donors and ensure supply sufficiency of life-saving products.[15]

Many countries are seeing declining numbers of eligible people willing to donate as a form of societal engagement. To develop long-term sustainable policies that balance the need for donations with the health concerns of frequent donors, more research is needed, especially in social sciences.

In 2019-2020, the Centre for Innovation instituted a social science research program and welcomed scientist **Jennie Haw** and research associate **Kelly Holloway**. Their donation research will support the organization by informing approaches to donor engagement, with a particular focus for now on source plasma donors and donor diversity and inclusion.

A Biomedical Excellence for Safer Transfusion (BEST) Collaborative study involving **Goldman** and **O'Brien** examined the donation records of over 700,000 first-time Canadian Blood Services whole blood donors to understand their likelihood of returning for another donation. The results show that the largest group of first-time donors—younger donors—have less clear patterns of return than middle-aged and older first-time donors.[16]

Response to a pandemic

The spread of the SARS-CoV-2 virus and the disease it causes, COVID-19, meant that by the end of 2019-2020 planning was underway to address risks to blood, blood products, plasma and stem cells in Canada. Top concerns related to the infectious risks to donors and staff, risks to the adequacy of the blood supply if donation levels and collection capabilities were to drop, and transfusion-transmission risks associated with this new pathogen. The Centre for Innovation refocused its priorities to contribute to Canadian Blood Services' pandemic response plan. The surveillance team reviewed emerging evidence about the virus and its routes of transmission to ensure the continued safety of the blood supply.

Learn about Canadian Blood Services' early response to the pandemic in a Canadian Blood Services' story highlighting "how data science helped the organization prepare and respond" and in our 2020 top 5 R.E.D. blog post which explains "why you won't get COVID-19 from a blood transfusion".

The Centre for Innovation also redirected resources and expertise to support new projects related to convalescent plasma (see page 24).

Effective

Red blood cell transfusions

Donated red blood cells support patients with a wide variety of disorders and are a vital part of their care. But not all red blood cell units are the same. When and why do these variations arise? Are units as unique as the people who donate them? How do the various processes to produce a unit from whole blood impact quality? These are some of the questions being addressed by the Centre for Innovation.

Does sex matter?

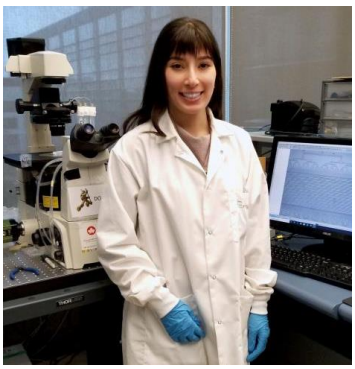
A study led by medical officer **Michelle Zeller** suggests that the sex of the patient and the donor may be a factor worth considering when selecting blood for transfusion.[17] Her team critically upraised the evidence from studies that compared outcomes in patients who received sex-matched or sex-mismatched red blood cell transfusions. Their analysis suggests that sex-mismatched red blood cell transfusions may be associated with a higher risk of death. **Zeller** notes that the findings need to be interpreted with caution because the quality of the evidence is very low. "Although our study looked at the outcomes of over 85,000 patients, we found only observational studies, which have a higher risk of bias," she says. "But the findings suggest sex-mismatching in red blood cell transfusion is potentially important and needs to be more rigorously examined."

Senior scientist **Acker**, who was also involved in the above study, published a review of the biological mechanisms that might underlie these findings, suggesting three physiological mechanisms (oxygen delivery, coagulation and the formation of microvesicles) that may play a role.[18]

Learn more in our Research Unit[19, 20] "Sex-mismatched red blood cell transfusions and mortality".

Searching for "super-storers" donors

A unique device developed in a research laboratory at the Centre for Blood Research can sort stored red blood cells based on their "squeezability," which reflects how well red blood cells can squeeze their way through circulation after a transfusion. The work was conducted by Canadian Blood Services **Graduate Student Fellowship Award** recipient, **Emel Islamzada** (pictured below), under the supervision of Hongshen Ma, and in collaboration with senior scientist **Mark Scott**. Their study shows the potential of deformability-based sorting to identify "super-storers", donors who have extra hardy red blood cells that store particularly well, and whose donations could be matched to recipients who



would most benefit, for example, chronic transfusion recipients.[21]

Learn more in our R.E.D. blog post "A novel microfluidic device to aid in the search for red blood cell "super-storers."

Understanding manufacturing impacts

A BEST Collaborative study, involving senior scientist **Acker**, surveyed blood manufacturers worldwide to understand details of their processes to collect, manufacture and conduct quality control testing on red blood cells.[22] This survey lays the groundwork for future studies to understand the impact of manufacturing variations on red blood cell quality.

With collaborators at Héma-Québec, **Ramirez-Arcos** investigated the impact of manufacturing variables on bacterial growth in red blood cells—a rare but serious clinical concern. By examining three different manufacturing methods and resuspension of red blood cells in four different additive solutions, the team found that manufacturing variables, rather than additive solution or the sex of the donor, affects bacterial growth in the red blood cell product.[23]

Work from the **Acker** laboratory showed that small vesicles derived from platelets remaining in red blood cell units are associated with inflammatory activity.[24] The study by Canadian Blood Services' **Postdoctoral Fellowship** recipient **Ruqayyah Almizraq**, showed that washing red blood cells, a process applied to improve the safety of these products for at-risk populations, removed platelet microvesicles and may improve transfusion outcomes.

Mapping stressed red blood cells

In collaboration with researchers at the University of Colorado, associate director **William Sheffield** investigated the metabolism of red blood cells after exposure to environmental stressors, such as lack of nutrients or extreme temperature changes.[25] "Metabolomics" analysis, which builds a comprehensive picture of the metabolic changes in the cells, revealed an array of different alterations in response to different stressors. The results will inform studies that could target the pathways identified as contributors to the red blood cells' responses to stress and help develop biochemical approaches to mitigate these responses during storage.

Optimizing pathogen inactivation

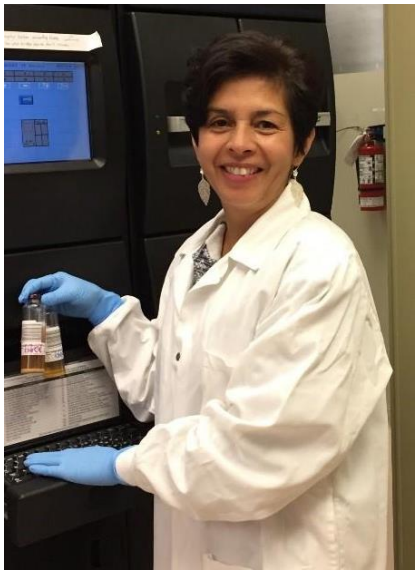
Pathogen inactivation is a safety technology that is licensed in various jurisdictions for use with plasma and platelet blood components. Whether it is effective on other blood components remains unclear. A team from **Devine**'s laboratory devised an experimental approach to test the hypothesis that deoxygenation (reducing the levels of oxygen) of whole blood or red blood cell concentrates might limit the negative impact of pathogen inactivation.[26] The results suggest that reducing oxygen levels in whole blood before pathogen inactivation might limit the negative impact on red blood cell quality. How this impacts the effectiveness of pathogen inactivation remains to be assessed.

Plasma and IVIg use

Plasma is the protein-rich liquid in blood. Donated plasma is used for transfusion or fractionated into plasma-derived products. The list of illnesses that can be treated by plasma-derived products is growing, and so too is the need for plasma. How can we best use plasma-derived medications to meet patient needs? How can we safeguard product supply? These are some of the questions being addressed by the Centre for Innovation.

Reducing plasma waste

Work by **Ramirez-Arcos** (pictured below), **Sheffield** and colleagues from Héma-Québec and the UK supported the inclusion of plasma under the Canadian Standards Association's "60-minute" rule. The standard guides the length of time that units can be out of storage at a controlled temperature before they must be discarded. The study provided evidence to show that quality and safety are not compromised and plasma units that have been out of storage for 60 minutes or less can be safety returned to storage. Under the previous standard, plasma had to be discarded after 30 minutes, so this change should reduce waste of plasma.



Testing new treatments

IVIg and subcutaneously-delivered Ig (SCIg) are effective treatments for many autoimmune and inflammatory conditions. However, they have limited availability and are expensive plasma-derived products so developing alternative treatments would be beneficial. Senior scientist **Donald Branch** and collaborators at CSL Behring previously investigated an engineered molecule—a recombinant human IgG1 Fc hexamer—and demonstrated that it is more effective than IVIg in treating a variety of autoimmune diseases in mice. In 2019-2020, **Branch** and colleagues tested this in a mouse model of chronic rheumatoid arthritis (RA). They found that it was effective at about a 10-fold lower dose than IVIg or SCIg, suggesting it may be a powerful treatment for the prevention and treatment of severe chronic RA.[27] Further studies on this and other immunoglobulin-based treatments for RA are warranted.

IVIg generally has few side-effects. However, high-dose IVIg can cause a serious reaction called red blood cell hemolysis in patients with blood groups A, B or AB. Isoagglutinin-reduced IVIg is a new product with lower anti-A and anti-B antibody titres that was introduced to reduce side effects. Using *in vitro* assays and mouse models, **Branch**

demonstrated that isoagglutinin-reduced IVIg should work as effectively as standard IVIg while causing less IVIg-associated hemolysis, suggesting it may be a safer product.[28]

Novel uses for plasma-derived drugs

A plasma-derived treatment now used to fight two diseases might have the potential to help patients with other conditions. Anti-D is a medication made from human plasma and supplied by Canadian Blood Services to treat the autoimmune disease immune thrombocytopenia (ITP) and to prevent hemolytic disease of the fetus and newborn (HDFN). Using mouse models, senior scientist **Alan Lazarus** (pictured below) discovered that a red blood cell antibody similar to anti-D works in three models of inflammatory arthritis, as well as one model of transfusion-related acute lung injury (TRALI).[29] TRALI is very rare, but it's one of the leading causes of transfusion-related deaths, and there is no good treatment.

Learn more in our Research Unit[30, 31] "Fighting inflammation with inflammation."

> "The knowledge that anti-D could be used to treat TRALI as well as autoimmune diseases other than ITP is good news for patients. This may have broad therapeutic potential. If it's demonstrated to work in humans, this approach may also provide an alternative to immune suppression, which is how doctors typically approach autoimmune disorders, but not a good option for everyone."
>
> *Alan Lazarus*

Funded by a **Canadian Blood Services-CIHR grant**, Laura Sly from the University of British Columbia is working to expand treatment options for inflammatory bowel disease. Her study shows a new mechanism of action of IVIg that suggests IVIg or IVIg-treated macrophages could be a useful treatment for people with intestinal inflammation, and particularly those with refractory inflammatory bowel disease.[32]

The role of prothrombin in PCC

Prothrombin complex concentrates (PCC) are protein drugs derived from plasma. PCCs are used to reverse warfarin anticoagulation but may also be useful to control more general bleeding. To better understand this product, **Sheffield** used a mouse model to identify the main factor responsible for the procoagulant or clotting activity of PCCs.[33] The study found that prothrombin is the most important procoagulant component of PCCs, a finding that could direct therapeutic approaches to limiting bleeding in trauma.

2019-2020 spotlight

The University of Toronto **QUEST** Program is a research collaborative supported by the Centre for Innovation's **Transfusion Medicine Research Program Support Award**.

The QUEST team

Under the leadership of professor Jeannie Callum, **QUEST** is setting and changing transfusion practice. The **QUEST** team brings together transfusion medicine scientists, physician-investigators, clinicians, research personnel and graduate students.

The **QUEST** program focuses on three research themes, with the aim of improving transfusion care in Canada: transfusion utilization, transfusion education and transfusion safety. The program's seamless integration with other transfusion research programs, particularly the **McMaster Centre for Transfusion Research** (**MCTR**) (also funded through the Centre for Innovation) and the Ontario Ministry of Health (the Ontario Regional Blood Coordinating Network), and the Centre for Innovation Research Program keeps Canada at the cutting edge of transfusion innovation and scientific discovery.

Transfusion utilization

The **QUEST**'s START study implemented a multifaceted intervention at 13 hospitals across Canada to ensure red blood cell transfusions are only transfused when required by international consensus guidelines. Completed in 2019, the study's findings show that appropriateness of transfusions significantly increased following the intervention and the proportion of single unit transfusions significantly increased. The study's intervention significantly decreased the total number of red blood cells transfused, with an estimated annual savings of 5,500 units equivalent to $4 million in healthcare costs at the 13 sites. START results have been submitted for presentation at the 2020 AABB meeting and will be published shortly.

QUEST is investigating the use of intravenous iron in surgical patients, pregnant patients and patients with heart failure as a blood sparing technique. This information will inform patient blood management best practices. The team also partnered with hospitals and **MCTR** to examine the use of plasma. Data extracted from five centres across Ontario will be analysed to better understand how plasma use can be optimized.

A clinical trial called FIBRES has resulted in a potentially safer treatment for cardiac patients who have an undersupply of the blood clotting protein fibrinogen.[34] The **QUEST** team compared two fibrinogen replacement products and showed that fibrinogen concentrate, which is pathogen-reduced and easier to administer, was non-inferior to cryoprecipitate—the most commonly used fibrinogen replacement product in Canadian hospitals. By showing that fibrinogen concentrate is as effective as cryoprecipitate, this study has changed the standard of care across Canada as more hospitals switch from using cryoprecipitate to fibrinogen concentrate.

Learn more in our Research Unit[35, 36] "Reducing bleeding after cardiac surgery: fibrinogen concentrate vs cryoprecipitate" and our R.E.D. blog post "Fibrinogen replacement products: how do they stack up against each other?."

Transfusions safety

In 2019, the TAD-POL (Transfusion-Associated Dyspnea: Prospective Observation and Laboratory Assessment) study was launched to better understand why patients sometimes experience difficulty breathing in reaction to transfusion. TAD-POL is a multicentre study across all the **QUEST** hospital sites. Patients undergo a standardized set of clinical and laboratory tests, including NT-pro-BNP, histamine, cytokine profiling, leukoagglutinin assays and microparticle quantification.

Other studies with a focus on patient safety include an ongoing prospective study to understand the frequency and severity of hemolysis from IVIg transfusion. In addition, basic science studies are underway to understand why some patients aggressively destroy transfused red blood cells. The team is also analysing errors reported to the Transfusion Error Surveillance System (the Canadian system that monitors the blood transfusion process for errors involving patients who receive blood components or blood products) to identify potential areas for improvement.

QUEST also completed a trial of pre-transfusion diuretics to reduce the risk of heart failure after transfusion (the most common cause of death from transfusion) and is working on additional studies on the use of diuretics to improve blood safety.

Transfusion education

QUEST continues to lead Transfusion Camp, a widely successful education program that was recognized with the AABB President's Award in 2019. To better understand the factors affecting the decision to transfuse blood and perceived challenges, **QUEST** completed a qualitative study with trainees and faculties in key specialties across Canada. Evidence from this study will be used to refine the Transfusion Camp curriculum.

With funding from the Centre for Innovation's **BloodTechNet program**, **QUEST** developed interactive eLearning modules to assist hematology trainees in learning immunohematology. The modules available at LearnSerology.ca highlight the basics of blood groups and laboratory testing techniques and include interactive cases to guide trainees through investigations. Testing of the modules has been completed with hematology trainees at the University of Toronto using a validated test that was published as part of the project.[37] For trainees that used the modules, there was a trend towards improvement in overall serology knowledge and in their ability to complete antibody panels.

Learn more! Consult the **QUEST**'s website at transfusionquest.ca.

> "Transfusions, even when performed under optimal conditions, can have adverse consequences for patients."
>
> *Jeannie Callum*

Understanding diseases to find more effective treatments

Blood and blood products are used to treat patients with a variety of diseases, and the Centre for Innovation works to understand disease processes with the aim of developing improved or more effective treatments

Immune thrombocytopenia

Immune thrombocytopenia (ITP) is a disease in which platelets are inappropriately cleared from the circulation. Antigens on the platelet surface are recognized by autoantibodies (from the patient's own immune system), which flag the platelets for destruction, leading to low platelet counts and an increased risk of bleeding. The mechanisms underlying ITP can vary patient to patient, depending on which platelet antigens (glycoproteins [GPs] on the platelet surface) and autoantibodies are involved. Understanding these mechanisms is important to guide effective and appropriate treatment. For example, ITP patients with autoantibodies against the platelet antigen GPIb-IX may be less responsive to IVIg and other first-line therapies.

Senior scientist **Heyu Ni** together with Canadian Blood Services' **Postdoctoral Fellowship** recipient **Miguel Neves** have been working to develop novel detection strategies for platelet antigens and anti-platelet antibodies present in ITP patients. This rapid test approach has been filed for patents as it may help clinicians choose the appropriate treatment and conserve IVIg.

Lazarus contributed to a systematic study with collaborators from Germany to assess the prevalence and functional importance of autoantibodies against another platelet antigen called GPV.[38] They found that platelet-bound auto anti-GPV was present in the majority of in which platelet-bound autoantibodies were detected. These findings establish GPV as a potential target in ITP.

The **Lazarus** laboratory, in collaboration with the **Branch** laboratory, also helped shed light on how platelets are cleared from the circulation in ITP mediated by autoantibodies against GPIIbIIIa.[39] Their results suggest that treatments that block receptors called Fc gamma receptors may be particularly useful in patients who are refractory to other treatments such as IVIg or steroids.

Heparin-induced thrombocytopenia

The **McMaster Centre for Transfusion Research (MCTR)**, which is supported by the Centre for Innovation's Transfusion Medicine Research Program Support Award, is a leader in research on the clinical management of thrombocytopenia and other

> **Did you know?**
>
> The McMaster ITP Registry now contains data on close to 1,000 patients with thrombocytopenia. This dataset has informed projects on the use of IVIg and IVIg alternatives and provides patient material for translational studies on disease mechanisms.

bleeding disorders. In 2019-2020, they published several studies related to the diagnosis and treatment of heparin-induced thrombocytopenia, which is the development of a low platelet count after administration of the anticoagulant heparin.[40-43]

Viral infections and coagulation

Senior scientist **Ed Pryzdial** focuses on understanding how infection with a virus influences bleeding and clotting. His work has uncovered evidence that several viruses build complexes of proteins involved in blood clotting on their surfaces. The viruses "borrow" these proteins from the host, disrupting the body's usual mechanisms that regulate the balance between bleeding and clotting, and helping the virus create a local environment that promotes blood clotting to increase viral infection.[44] The research revealed the involvement of other proteins in this process, providing direction for future work to find targets to prevent viral infection.

The "model" virus used by **Pryzdial**, HSV-1, is an enveloped virus, just like SARS-CoV-2. There is now overwhelming evidence that coagulation disorders are involved in COVID-19. The mechanisms uncovered by **Pryzdial** could help decipher how SARS-CoV-2 interacts with the blood clotting system in COVID-19 patients, which may inform patient management. **Pryzdial**'s research also shows that a virus' link with its host's coagulation system might aid the virus' ability to infect. This knowledge can inform the development of new treatments that simultaneously curtail COVID-19 symptoms and virus generation, a hopeful possibility as the world battles the pandemic.

Learn more in our R.E.D. blog post "Tipping the balance: research finds new links between viral infections and coagulation."

Hemophilia

Hemophilia, an inherited blood disorder that affects mostly men, impairs a person's ability to clot blood. Although it can't be cured, hemophilia can be treated by injecting a patient with clotting factor concentrates to help restore clotting factors to normal levels. But treatment is expensive and may not be available to all patients, especially in lower-income countries. A study by an international team that included researchers from **MCTR** suggests more men have hemophilia worldwide than previously thought and highlights the need for improved hemophilia care.[45] The study's lead author, Alfonso Iorio notes the dramatic link between a country's economic status and life expectancy for patients with hemophilia. Their study shows there are still large gaps to fill in improving hemophilia care.

Learn more in our Research Unit "Estimating hemophilia prevalence and life expectancy" and R.E.D. blog post "Hemophilia's global impact is greater than previously thought."

Stem cells therapies

Blood stem cells can be found in the bone marrow, circulating (peripheral) blood or umbilical cord blood. Stem cell transplants can treat over 80 diseases and disorders, including blood cell cancers such as leukemia. The Centre for Innovation supports Canadian Blood Services to optimize processes for the collection and storage of stem cells and conducts research to understand how to make stem cell transplants more effective.

Optimizing the selection of cord blood

Research by senior scientist **Nicolas Pineault** and Canadian Blood Services operations sought to improve pre-transplant quality tests of cord blood units to better inform decisions about whether a cord blood unit is suitable for transplantation.[46] The new method developed by the team could increase the number of units that can be released for transplantation by reducing the number that are discarded due to failed quality tests.

Learn more in our Research Unit[47, 48] "Improving quality testing of stem cells for patients" and R.E.D. blog post "Improving a quality test for cord blood samples."

Better freezing to improve engraftment

Pineault is also investigating the normal process of ice recrystallization, the uncontrolled growth of ice, during cord blood cryopreservation.[49] This process can cause cell loss during freezing and thawing, which could affect the function of the cells in a transplant. **Pineault** and his group found that adding an ice recrystallization inhibitor (IRI) during freezing had several beneficial effects. After transplantation of the cord blood in a mouse model, those units treated with IRI showed indications of improved engraftment as indicated by the higher levels of platelets in circulation and higher human bone marrow chimerism. This is highly relevant given that platelet engraftment is significantly delayed following cord blood transplantation in patients.

2020 Top 5 R.E.D. blog post: I'm fascinated by the power of stem cells: Q&A with Dr. Nicolas Pineault

Private cord blood banks

In 2019-2020, the University of Alberta's Timothy Caulfield was awarded funding through the Centre for Innovation **James Kreppner Award**.

> "The entire Health Law Institute team is thrilled about this award, and we truly appreciate the opportunity to dig into the complex issues associated with donation, blood products and policy development."
>
> *Timothy Caulfield*

Caulfield's project analyzes the marketing practices of private cord blood banks, assesses their claims, and considers how regulatory tools can help ensure services are marketed in a scientifically informed and

evidence-based manner. Private banks market cord blood banking services for future medical use, which may include unproven treatments or treatments that do not yet or will never exist. These practices raise ethical and legal concerns about what can and should be marketed. In 2019-2020, Caulfield published an analysis of 400 articles from 2007–2017 about cord blood in Canadian and American news sources.[50] The majority detailed umbilical cord blood use that aligns with clinical evidence, but some portrayed speculative or experimental therapies as efficacious. Caulfield's findings so far show the need for continual monitoring of media portrayals and that inaccurate or hyped information needs to be countered with accurate information to help inform and educate the public.

Learn more in our R.E.D. blog post "University of Alberta's Timothy Caulfield receives James Kreppner Award."

Cord blood for regenerative therapy

Funded by the **Kenneth J. Fyke Award**, medical director for stem cells **David Allan** investigated the responsible use of umbilical cord blood in regenerative therapy. The discovery that cord blood contains more than just blood stem cells has spawned interest in its use for indications other than blood cancers, bone marrow failure and other disorders for which it has been proven effective. Cord blood's potential to be used as a novel regenerative therapy is promising, with early clinical trials on its use in a range of disorders, from traumatic brain injury to dementia. **Allan**'s research assessed whether these novel uses are proven therapies. He concludes that none of the new indications studied to date for cord blood can be regarded as proven, based on guidelines from the International Society for Cellular Therapy. Controlled clinical trials are needed to evaluate these uses, and provide clear data to help cord blood banks, healthcare providers and patients assess their potential.[51]

Organs and Tissues

The Centre for Innovation, in consultation with Canadian Blood Services' Organ and Tissue Donation and Transplantation group, supports research in organ and tissue donation and transplantation primarily through two competitive funding programs: the James Kreppner Award and the Kenneth J. Fyke Award.

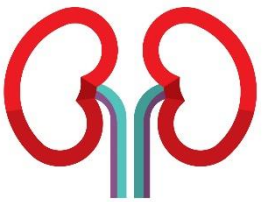
Donation after cardiocirculatory death

With funding from the **Kenneth J. Fyke** Award, Ian Bell from Western University is leading a mixed methods study to understand attitudes and opinions regarding cardiac donation after cardiocirculatory death (DCDD). DCDD could help decrease transplant wait times for patients with end-stage heart disease. Bell's study will explore the attitudes and opinions of health-care providers on heart DCDD and describe opportunities and challenges in ensuring the heart DCDD programs in Canada are consistent with Canadian values as a first step towards large-scale implementation of programs nationwide. They will also explore the attitudes of members of the public toward DCDD.

Of skin, sperm and blood

Supported by the **James Kreppner Award**, Alana Cattapan from the University of Waterloo has been researching how blood and tissues are governed across Canada, and how these policies have evolved. Her research investigates legal, ethical and social issues related to the commercialization of human tissues and will provide comparative data upon which recommendations to reform and harmonize legislation across Canada can be built.

More information and key findings from this project can be found on the project team website: "Of skin, sperm and blood"



Responsive

The Centre for Innovation helps Canadian Blood Services respond to ever-changing needs by providing a solid footing for making evidence-based decisions. In early 2020, when the COVID-19 pandemic was declared, the need to respond rapidly and effectively was never more pressing.

New products

Responding to a pandemic

As a pan-Canadian health-care organization with the expertise and infrastructure to collect and manufacture plasma, Canadian Blood Services is well positioned to step up to the front lines of the fight to find a safe and effective treatment for COVID-19.

> "Canadian Blood Services will be responsible for collecting convalescent plasma to treat patients. We will process the plasma for transfusion and ship it frozen to the clinical trial sites participating in the studies. We think this treatment will be an interim measure until other treatments and vaccines are developed for COVID-19."
>
> *Dana Devine*

As 2019-2020 ended, **Devine** began to engage with our extensive network of researchers and medical professionals in Canada and internationally to develop clinical trials protocols for evaluating the safety and efficacy of COVID-19 convalescent plasma. These clinical trials were stood up rapidly in response to the pandemic, thanks in part to the close and long-standing relationships with **MCTR** and **QUEST** teams. We look forward to sharing the results as they come through in later 2020 and 2021.

Learn more. Visit our Professional Education website here.

A new take on whole blood

What's old is new again. Recent research has shown that whole blood may be the best fluid to replace what's being lost in actively bleeding (trauma) patients. However, for the past 50 or so years, whole blood for transfusion has not been readily available in Canada or many other countries. The Centre for Innovation's product and process development group, led by associate director **Ken McTaggart**, is working to (re)-introduce this product to the Canadian Blood Services formulary.[52]

Learn more in our 2020 top 5 R.E.D. blog post "From whole blood to blood components…and back again!"

Although it's not a new approach, there are many questions that need to be answered to successfully re-introduce whole blood. In 2019-2020, the Centre for Innovation evaluated a whole blood product called "leukoreduced, cold-stored whole blood." This product is stored in the refrigerator and has been reduced of white blood cells using an Imuflex filter (TerumoBCT), the only commercial platelet sparing whole blood filter on the market and licenced by Health Canada.

Different production parameters for leukoreduced, cold-stored whole blood and their impact on the *in vitro* quality of the product were tested by various groups including the Centre for Innovation's **blood4research development facility** in Vancouver, the **Sheffield** laboratory and the **Devine** laboratory. The results show that the process is straightforward and robust and a pre-submission meeting with Health Canada was held in 2019. Work to transfer the process to Canadian Blood Services' operations for validation and implementation is now in process.

Freeze-dried plasma

In another case of what's old is new again, the Centre for Innovation has been investigating freeze-dried plasma – a product first introduced during World War II. Usually, plasma is stored as a frozen liquid in a large bag. While this presents only minor challenges in a modern, urban hospital with a reliable source of power, what happens in other environments? Consider the front lines of a military operation, or the site of a natural disaster such as an earthquake or wildfire? Unfortunately, these are the situations in which plasma for trauma patients is often needed as a life-saving treatment. Freeze-drying removes the water from the plasma, transforming it into a stable, easily transported product that does not need to be stored frozen.

Did you know?

Canadian Blood Services provides blood components and plasma protein products to support the Canadian Armed Forces (CAF). Canadian Blood Services' Product Innovation Operational Committee, chaired by Centre for Innovation director, **Chantale Pambrun**, also oversees a portfolio of potential new products, some of which are being developed in collaboration with the CAF.

For examples, the Centre is working to produce and characterize a freeze-dried plasma product produced from donated plasma as part of a study with the CAF. The CAF are also interested in a whole blood transfusion product to treat trauma patients.

In 2019-20, a freeze-drying unit was installed in the Centre for Innovation's development laboratories in Ottawa and work was initiated by senior manager **Craig Jenkins** to make and test freeze-dried plasma from frozen plasma. A product characterization study conducted at several sites across the Centre for Innovation, including the **blood4research facility**, and the **Sheffield** and **Devine** laboratories, as well as several external labs, provided promising data, which were presented to Health Canada in early 2020. The *in vitro* characteristics of the freeze-dried product were comparable to the frozen plasma from which it was made, suggesting that freeze-dried plasma should yield similar clinical benefits to frozen plasma.[53] This hypothesis will be tested in a

clinical trial for which the Centre for Innovation will provide the freeze-dried plasma.

Pathogen-reduced platelets

By providing broad spectrum inactivation of pathogens, pathogen inactivation methods add an additional layer of safety to blood products. To support Canadian Blood Services' goal to provide a pathogen-reduced platelet product, the Centre for Innovation has conducted development work using the Cerus Intercept system, the only licensed pathogen reduction system in Canada, and platelets in additive solution[54] which will support a submission to Health Canada to license this product.

Bacterial growth in cold-stored platelets

Platelets for transfusion are usually stored at room temperature. However, storing platelets in the cold improves their hemostatic (i.e. clotting) ability, and there is growing interest in using cold-stored platelets to treat actively-bleeding patients. **Ramirez-Arcos** is leading a multicentre and international study to assess bacterial growth in cold-stored platelets.[55] This study is an initiative of the ISBT, Transfusion Transmitted Infectious Diseases Working Party-Bacterial Subgroup.

New processes

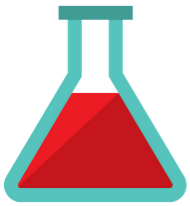
A new approach to quality control testing

The Centre for Innovation is leading the development of non-destructive quality control (QC) testing. Why? Current processes require that the entire blood product destined for QC testing be removed from the inventory and stored until expiry, precluding their transfusion to patients. This is the fate of a small percentage of donated blood. Non-destructive QC testing is an alternative approach — using small aliquots drawn from units at production for QC testing — which could improve product availability and reduce production costs while maintaining control of product quality for optimum patient outcomes.

The product and process development group's **McTaggart**, and research associate (now senior scientist) **Peter Schubert** completed the development work for non-destructive QC testing of both platelets and red blood cells,[56, 57] while research engineer **John Blake** led a modelling study that showed removal of small aliquots for non-destructive QC testing did not adversely impact the volume and therapeutic dose of red blood cell units.[58] A business case is in process and once completed, Health Canada approval for non-destructive QC testing will be sought. It is hoped that this new QC approach can be applied broadly, so when new products are developed the effectiveness of non-destructive QC testing for these products will be assessed.

Research & education network

102 **investigators supported**



49 with financial support
44 with research and/or data products
9 with both

2019-2020 spotlight: Breaking down barriers for a child with a rare condition

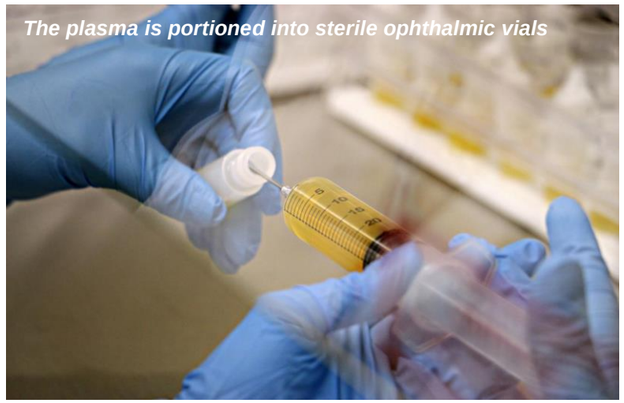
It started when a physician contacted one of our medical directors, **Kathryn Webert**, asking how to get a very specific medication. The physician had a patient, a small child, with a very rare condition—plasminogen deficiency—that was causing the child's eyes to fill with woody growths. **Webert** immediately started an internal discussion about how Canadian Blood Services could help.

"Plasminogen is a precursor to plasmin, which breaks down clots. Plasmin in tears usually keeps the eyes free of clot-like woody growths," says associate director of research, **William Sheffield**. "It's such a rare disorder—literally one in a million—there's not a ton of literature."

These woody growths can be surgically removed, but to stop them from growing back, the child needed special eye drops made from human plasma containing plasminogen.

"What do we do when there's a child in Canada with a rare disorder, and only we can help? We work together and find a way," says senior manager of product and process development, **Craig Jenkins**. It was up to his team to figure out how Canadian Blood Services could to do it.

Craig Jenkins removes a unit of plasma from a freezer



The plasma is portioned into sterile ophthalmic vials

"The first question was, can we get this product from elsewhere in the world? When those avenues were exhausted, we knew we had to figure something out within our own regulatory environment, working through Health Canada," **Jenkins** says.

To start, **Jenkins** received two plasma units destined for research to see what he could do with them.

"We didn't have an eye drop vial to put this stuff in, or any automated method for filling a vial, or a process for shipping it. These were all things we had to figure out before we could proceed," he says.

Sheffield's laboratory was responsible for quantifying the amount of plasminogen in the plasma, to make sure it was in the normal range to help the child. While **Jenkins** and his colleagues found special ophthalmic vials. To prepare the eye drops, they manually transfer the plasma into these vials. They pack the vials in dry ice and ship them to the local blood bank. The bank gives the vials to the family, who administer them to the child. By all accounts, the eye drops are working, and the child is doing well.

What we do matters

Through Health Canada's Special Access Program, Canadian Blood Services got approval to produce and ship 680 vials of these plasma eye drops.

"This project embodies what we hope we're doing every day. It's obvious this patient needed one medicine only we could provide," says **Sheffield**.

Jenkins relates that both as parents and as Canadian Blood Services employees, it's something he and **Sheffield** felt a personal responsibility to do.

Infinite connections

This couldn't have happened without the infinite connections we are proud to be part of—in this case, from patient to primary care physician; from that physician to one of our medical directors; from her to our researchers and product and process developers; from them to the blood bank; and from the blood bank back to the patient. These are the infinite connections between two lives: that of the donor and the patient.

Tamiko Stewart holds a vial of plasma

2020 Top 5 R.E.D. blog post "Only we can help: breaking down barriers for a child with a rare condition."

Training, education and engagement highlights

Building for the future

Developing the next generation

Over the last year, the Centre's 11 staff scientists and the 24 external principal investigators funded via the Centre's competitive research programs supervised more than 90 students at the undergraduate to postgraduate level. In addition, through the Centre's competitive **Postdoctoral Fellowship** and **Graduate Fellowship Programs**, Canadian Blood Services provides salary support to promising young investigators. Six postdoctoral and 13 graduate fellows were supported this year.

Through its continuing collaboration with the Centre for Blood Research (CBR) in Vancouver, the Centre for Innovation provided support for one summer student through the **CBR-School of Biomedical Engineering Summer Studentship Program** and for four graduate students through the **CBR Graduate Student Award Program**. Altogether this cohort of young scientists represents the next generation of blood scientists.

In 2019-2020, several trainees completed their training, including five who completed their Master's or PhD theses. Our alumni continue to apply their training for the benefit of the blood system. Of note, Syed Qadri, former Canadian Blood Services Postdoctoral Fellowship recipient in the **Sheffield** laboratory, was appointed assistant professor at Ontario Tech University and is leading his own transfusion research program. Jessica Poisson, former Canadian Blood Services Graduate Fellowship recipient in Robert Ben's laboratory (University of Ottawa), obtained a scientific evaluator position at Health Canada. Maria Loza, former Postdoctoral Fellowship recipient in the **Ramirez-Arcos** laboratory, is now at the Canadian Institutes of Health Research in the Program Design and Delivery Branch. Genevieve Marcoux, former Graduate Fellowship recipient in Éric Boilard's laboratory (Université Laval), is now a postdoctoral fellow at Lund University supporting transfusion research.

Making connections

The Centre for Innovation Knowledge Mobilization and Strategic Alliances team, in collaboration with **CBR**, organized its second workshop for research trainees at Canadian Blood Services' Calgary Donor Centre in May 2019. Twenty-two participants toured the donor centre, learned about blood donor selection criteria and collection processes, and participated in a workshop on scientific blogging. Eleven trainees were supported with travel bursaries to attend the workshop and our annual Research Day.

Learn more in our R.E.D. blog post written by workshop attendees (pictured below) "Research trainees on why eligibility, donor care, and science blogging matter to them".

> "I was inspired by the donors who enable us to save lives and conduct research."
>
> *Trainee feedback about the workshop*

Wenhui Li, Carly Olafson and Anusha Sajja from the Acker laboratory attending the trainee workshop

Education for medical professionals

Elianna Saidenberg Transfusion Medicine Traineeship Award

In 2020, Canadian Blood Services renamed its Transfusion Medicine Traineeship Award as the Elianna Saidenberg Transfusion Medicine Traineeship Award in honour of Dr. Saidenberg, a hematologist, patient rights advocate, mentor, and teacher. This award provides funding for physicians accepted to the Royal College of Physicians and Surgeons of Canada Area of Focused Competence diploma program in transfusion medicine. This year, of the seven transfusion medicine trainees enrolled in this course, two were supported by the Canadian Blood Services award.

Transfusion Camp

Transfusion Camp is a high-quality education program for non-hematology specialty-based medical postgraduates. Established in 2012 by **QUEST** at the University of Toronto, Transfusion Camp's national and international reach has grown with the administrative support of the Centre for Innovation Knowledge Mobilization and Strategic Alliances team. Transfusion Camp involves multiple partners: transfusion experts, residency training program administrators, and academic partners who facilitate the program's local delivery.

In a 2019 study published in the journal *Transfusion*, we showed that Transfusion Camp increased knowledge, fostered positive attitude towards transfusion medicine and enabled a self-reported positive impact on transfusion practice in postgraduate trainees.[59]

Program highlights for the July 1 2018 – June 30 2019 academic year:

- 215 trainees, representing 12 medical specialties from 10 Canadian universities and one university in the UK participated in Transfusion Camp.
- 15 hours of didactic lectures were delivered by 17 transfusion experts and supplemented by 13 hours of team-based learning seminars delivered by 25 faculty members from across Canada.
- In feedback surveys, the majority of trainees reported applying their Transfusion Camp learning to their clinical practice.

Transfusion Camp continues to expand its reach. New universities continue to join and the number of participating medical

programs within universities is also increasing:

- June 2019: L'Université de Sherbrooke, Université Laval and University of Alberta joined.
- 2019-2020: Development of resources in French for Transfusion Camp.

In September 2019, Transfusion Camp was adapted to develop the Nurse Practitioner Transfusion Camp Pilot in collaboration with Andrew Shih, Doug Morrison, and the BC Provincial Blood Coordinating Office. There were 23 participants in the pilot program and results were published in *Transfusion*.[60] Work is now underway to expand the Nurse Practitioner Transfusion Camp nationally.

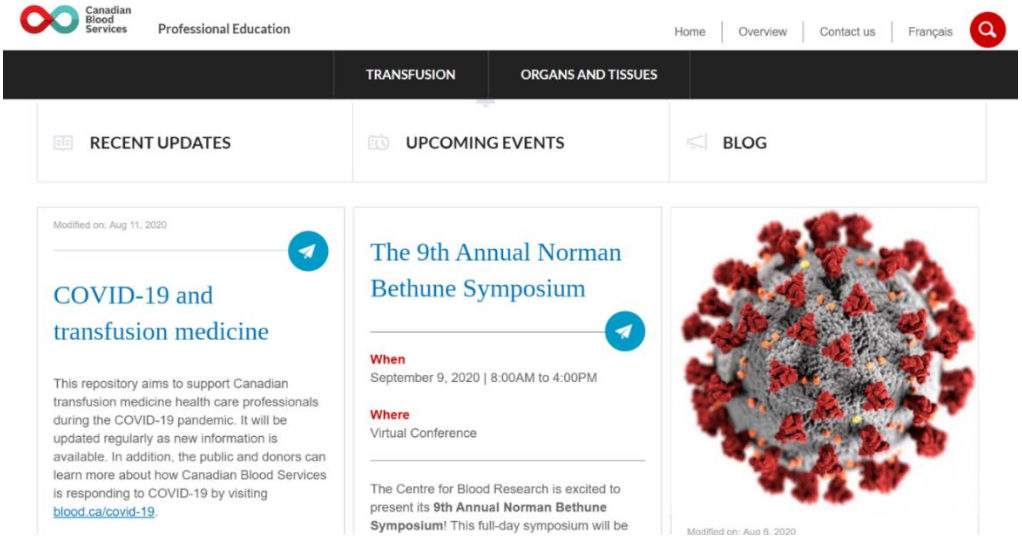
Professional Education website

Canadian Blood Services' Professional Education website (profedu.ca) is a resource hub for health-care professionals working in transfusion medicine and in organ and tissue donation and transplantation. The Centre's Knowledge Mobilization and Strategic Alliances team leads the development of transfusion related content by working with experts from our network to develop clinical guidelines, best practices and other educational resources.

In 2019-2020, the website recorded over 444,000 sessions (a 77% increase from the previous year), engaging almost 390,000 users, primarily from Canada (38%).

The 18 chapters of the Clinical Guide to Transfusion, available in both English and French, remain the most popular resources. The following chapters and publications were updated or added to the website this year:

- Chapter 6, Donor selection, donor testing and pathogen reduction[4, 5]
- Chapter 7, Fractionated blood products and associated pathogen safety[61, 62]
- Nine serological best practices
- Platelet clinical best practices
- 2018 Surveillance Report of transmissible blood-borne infection
- Striking the balance: protecting data privacy in research
- A Guide to Reporting Adverse Transfusion Events



385 Learning opportunities & knowledge exchanges

2800+ stakeholders reached

88% of stakeholders report they acquired knowledge and skills

700,000+ pageviews on our websites

Guideline development

The Centre for Innovation Knowledge Mobilization and Strategic Alliances team hosts the Secretariat for the International Collaboration for Transfusion Medicine Guidelines (ICTMG), a group established to advance the field of transfusion medicine through the development of clinical guidelines. With the leadership of medical director and ICTMG Chair **Nadine Shehata**, the Secretariat supports the work of six ICTMG committees and several Guideline Development Groups. ICTMG publications and resources are available at ictmg.org.

Highlights from this year include:

- ICTMG continued guideline development for: Use of albumin including a systematic review on albumin use in cardiac surgery; platelet transfusion including a systematic review on the quality of evidence-based guidance; hemolytic disease of the newborn; and fetal and neonatal alloimmune thrombocytopenia (FNAIT).
- The American Society of Hematology affirmed that ICTMG's guidelines on hemoglobinopathies and on FNAIT have value for hematologists.
- The British Society for Haematology published a position paper on ICTMG's hemoglobinopathies guideline.
- A partnership was formally recognized with ISBT to facilitate collaborative activities.

Supporting innovative ideas

The Centre for Innovation leads the **BloodTechNet program**, an initiative that supports the development of educational tools and resources for health professionals in transfusion, cellular therapy and transplantation. Two projects were completed during the year:

How to use satellite fridges

Led by Clare O'Reilly, BC Children's and Women's Hospitals.

The team supported a practice change in the use of satellite fridges by creating educational resources for clinical and allied staff.

Stem cell transplantation multimedia toolkit

Led by Warren Fingrut, University of British Columbia.

The team developed three online tools to educate health-care professional students about stem cell donation.

Learn more by visiting the **BloodTechNet Program** page on profedu.ca.

A supported and engaged network

Funding research

The Centre for Innovation Knowledge Mobilization and Strategic Alliances team develops and administers competitive Research Funding Programs to address key strategic research priorities while engaging the right individuals so that their expertise is brought to bear on important issues. In 2019–2020, 56 research projects received funding through nine programs, including 14 new projects (Appendix I).

Notably in 2019-2020, the **Intramural Research Grant Program (IRGP)** was expanded and funded three extra projects, for a total of six new projects. The **IRGP** is the Centre's flagship program, supporting research that will advance knowledge around specific research priorities.

Learn more by visiting our Research Funding Programs descriptions at blood.ca.

Engaging researchers

The Centre for Innovation employs 11 scientists, and their dedicated research teams, each of whom are cross appointed with academic institutions across Canada. The Centre also engages with 25 medical experts and epidemiologists, seven adjunct scientists, and more than 35 investigators who receive funding through our various competitive research funding programs.

Facilitating interactions between members of this research network has been a key priority to foster collaboration and promote innovation. In 2019-20 the Centre hosted several events.

Nine **webinars** for our scientists, medical experts and adjunct scientists to discuss "work-in-progress."

Our annual **Research Day** in Calgary, Alberta which saw the participation of 53 individuals from our extended research network. Research Day 2019 looked to the future with talks on "Blood Products of the Future" and sessions on new technologies and advances in the areas of donor and clinical research. A session on "Scientists of the Future" provided an opportunity for research trainees to give two-minute talks about their research.

> "I always think it is a great event—where I learn about and discuss potential projects and questions with scientists and come away with renewed enthusiasm."
>
> *Research Day 2019 participant*

In 2019-2020, the Centre for Innovation instituted **ReCon (Research Consultation) working groups**. Four working groups (platelets, plasma, red blood cells, stem cells) composed of Centre's scientists were established to encourage connection, scientific consultation and discussion. Each ReCon meeting includes guests from Canadian Blood Services operations or medical to enrich the discussions. Seven ReCon working group meetings were held during the year and, based on the success of these initial meetings, the initiative will be extended.

Sharing knowledge

CSTM 2019

The annual Canadian Blood Services/Héma-Québec/Canadian Society for Transfusion Medicine (CSTM) conference is a highlight in the Canadian transfusion medicine calendar. The Centre for Innovation supports this meeting with both funding and organizing resources, and members of our network participate in the event. At the 2019 conference in Calgary, Canadian Blood Services' staff gave 16 presentations during oral sessions or workshops. Together with 39 poster presentations, Canadian Blood Services' participation in the conference program was high as always.

Centre for Blood Research symposia

Through a formal partnership, the Centre for Innovation supported two CBR annual symposia. The highly regarded Norman Bethune (April 2019) and Earl W. Davie (November 2019) symposia held in Vancouver featured expert presentations from Canadian and international experts, as well as patients, and are broadcast to facilitate remote attendance. They provide excellent learning and networking experiences for trainees, patients, and established researchers alike.

Did you know?

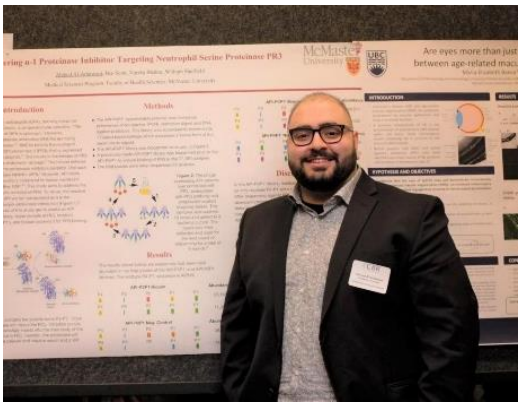
The Centre for Blood Research at the University of British Columbia hosts three Centre for Innovation scientists and affiliated staff, postdoctoral fellows and students. The Centre for Innovation is proud to partner with the Centre for Blood Research to deliver training and education events including two annual symposia.

***The Earl W. Davie Symposium 2019**. (L-R): Dr. Ross MacGillivray, a founder of the CBR and a former student of Dr. Davie's, with Dr. Davie, Jim Davie (Dr. Davie's son), and Dr. Dominic Chung, also a former student of Dr. Davie. (Photo courtesy of the CBR).*

New travel bursary established

To facilitate attendance of Canadian Blood Services trainees at CBR symposia, the Centre for Innovation established a new travel bursary.

This year, master's student **Ahmed Al-Arnawoot** (**Sheffield** Laboratory, McMaster University, pictured below) was the bursary recipient and attended the 2019 Norman Bethune Symposium. He presented a poster and talk describing new approaches to find therapies for auto-immune vasculitis.



> "It is great that there's an opportunity for Canadian Blood Services' trainees to travel to Vancouver and present their work. Presenting here has been a great experience; there are lots of opportunities for dialogue with many high-profile investigators in my field."
>
> *Ahmed Al-Arnawoot*

Education Symposium

Over 1,000 participants attended the 14th Annual Transfusion Medicine Education Symposium held in April 2019 at the Thunder Bay Regional Health Sciences Centre. Sponsored by the Centre for Innovation in partnership with the Ontario Regional Blood Coordinating Network, the symposium's focus was on platelets. The event was primarily experienced through webcast and drew an audience that included medical laboratory technicians, nurses and physicians, from 114 sites and 7 provinces.

Engagement and outreach

In 2019-2020, together with Canadian Blood Services' Public Affairs division, the Knowledge Mobilization and Strategic Alliances team refreshed the Centre' science communication strategy. Our overarching goal is to establish Canadian Blood Services as the Canadian knowledge leader for research, innovation and education in blood, plasma, and stem cells.

A cornerstone of our communication strategy remains our monthly Research & Education Round Up e-newsletter. In 2019–2020, the number of subscribers rose to more than 1,800 representing an increase in audience of 40%, while maintaining a higher than industry average opening rate. The newsletter keeps our community engaged by providing relevant and timely information about our latest publications, funding competitions and upcoming events.

Another important component of our science communication strategy is Canadian Blood Services' Research.Education.Discovery. (R.E.D.) blog which primarily showcases the work of the Centre for Innovation. In 2019–2020, 41 R.E.D. blog posts focusing on Centre for Innovation stories were published. The R.E.D Blog has seen immense growth attracting more than 68,000 views and almost 50,000 unique visitors last year, a 63% and 85% increase, respectively, from the previous year.

Once again, we teamed-up with Science Borealis and the CBR to run a Lay Science Writing Competition. This competition, themed "a story worth telling", gave our trainees an opportunity to showcase their research on the R.E.D blog while developing their communication skills. Congratulations to Transfusion Medicine Fellow **Aditi Khandelwal** (pictured below) whose heartfelt entry won the competition. Learn more in our R.E.D. blog post "Lay Science Writing Competition winner"

Governance

Embedded within Canadian Blood Services Medical Affairs and Innovation division, the Centre for Innovation benefits from our organization's sound governance. The administration of the Centre for Innovation is supported by dedicated staff and Canadian Blood Services' financial, legal, and information technology groups.

Research oversight

The Safety, Research & Ethics Committee (SREC) oversees research, scientific and innovation activities, including the Research Ethics Board (REB), among other responsibilities. To keep them connected to the work of the Centre for Innovation, **Pambrun**, Centre for Innovation director, attends SREC meetings regularly as a guest while in 2019-2020 each of the Centre's associate directors presented to this committee. **Sheffield**, associate director of research, presented on discovery research and IVIg, **McTaggart**, associate director of product and process development, presented on new products, and **Sophie Chargé**, associate director of knowledge mobilization and strategic alliances, presented on knowledge dissemination and professional education.

Research ethics

The Centre for Innovation Knowledge Mobilization and Strategic Alliances team hosts the Secretariat for the REB. This multidisciplinary board, chaired by Professor Michael McDonald (pictured right), and composed of legal experts, community members, and researchers reviews all research studies involving human participants conducted by or on behalf of Canadian Blood Services.

2019-2020 saw the implementation or continuation of several process improvements for the Research Ethics Program to improve workflow capabilities. Several REB members' terms came to an end and new members were appointed:

- Bob McRae (community member)
- David Ward (community member)
- Mark Bigham (researcher member).

> **Did you know?**
>
> The REB is an arm's length committee whose decisions not to approve research protocols cannot be reversed by the Canadian Blood Services Executive Management Team or the Board of Directors.

Learn more in our R.E.D. blog post "The ethics of doing good research".

One of the many ways in which Canadian Blood Services facilitates research is by providing internal and external researchers with access to biologic materials, data sets, and to Canadian Blood Services donors, volunteers, and staff. In 2019–2020, a total of 39 new studies were reviewed and approved, including by the REB to ensure compliance with research ethics.

Over 7,000 blood research products were distributed by the Centre's Blood4Research facility. The majority supported Centre for Innovation-led product improvement projects, but the work of 25 Canadian researchers were also supported with over 2,000 research products. Five Canadian researchers were supported with cord blood research products.

Research administration

The Centre for Innovation is partially funded through a contribution agreement with Health Canada (Strategic Policy Branch). Now in its second year of the current agreement, the Centre for Innovation leveraged its expertise and governance framework to secure funding and implement the newly funded MSM Plasma Program.

There has been continued attention to good governance practices in the administration of the Centre for Innovation competitive funding programs. This year, a focus was placed on improvements to the post-award administration of funding, to improve the management of awarded funds while ensuring sound financial practices are followed, as well as to comply with our Health Canada contribution agreement and other funding partners.

Program outputs and outcomes

The Centre for Innovation's performance measurement framework was developed together with Health Canada (Strategic Policy Branch) to meet the reporting requirements of the contribution agreement. This performance measurement framework ensures that the Centre for Innovation demonstrates its contributions to the Canadian health system and the health of Canadians and collects data that will be used in the continued evaluation of the program.

The next page catalogues our performance for 2019-2020, listing select program outputs and outcomes. The table also includes 2018-2019 data, the first year of the current contribution agreement. The Centre for Innovation continues to deliver on key performance metrics, indicating that our program is impactful and contributes to a safe, effective, and responsive system for blood and blood products in Canada.

Our impact: Blood safety improvements

In 2019-2020, the work of the Centre for Innovation contributed to new or updated measures to improve blood safety

- Updating of the top/bottom pack type for the production of platelets via the buffy coat method
- Establishing a method to prepare red cell aliquots for pediatric and neonatal patients
- Implementing a procedure for a slow freeze method for whole blood plasma
- Updating of component sterility testing processes
- Changing the deferral period for blood donors who are men who have sex with men
- Changing the Canadian Standards Association's standard for returning plasma to storage

Select Centre for Innovation program outputs and outcomes

	Intended Outputs & Outcomes	Indicators	Target	2018-2019	2019-2020
Outputs	Grants and awards	Number of grants and awards provided (Appendix I)	140	189	**197**
	Learning opportunities	Number of presentations and events	375	434	**385**
	Supported network	Number of distinct Canadian investigators supported	N/A	124	**102**
Immediate Outcomes	Canadian researchers advance knowledge on blood safety	Number of knowledge products published (Appendix II)	200	246	**189**
	Stakeholders access information on blood safety	Number of stakeholders attending events	5,000-7,500	3,763	**2,869**
		Page views of significant program websites	N/A	346,555	**711,980**
	Stakeholders are equipped with the knowledge, skills, and supports required to enhance blood safety	Percentage of event attendees reporting knowledge gain	>85%	89%	**88%**
		Number of Highly Qualified Personnel completing training	5-20	14	**8**
Intermediate Outcomes	Key research stakeholders in the transfusion and transplantation community use program research findings to inform blood safety research	Percentage of staff researchers with H-index ≥ Canadian science standard of 10.6 (Appendix II)	90%	100%	**100%**
	Key stakeholders make improvements in blood safety	Number of new or updated blood safety measures informed by the program	5-12	9	**11**
Ultimate Outcome	Canadians have access to appropriate and effective health services	Percentage of stakeholders reporting that Canadian Blood Services plays an essential role in achieving patient outcomes	90%	99%	**98%**

Note: Blood safety in the context of the program refers to a safe, effective, and responsive system for blood and blood products.

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Appendix I: Grants and Awards

Number of Centre for Innovation supported projects by program

Research Programs	**56**
Canadian Blood Services/CIHR partnership operating grants	6
Canadian Blood Services/CIHR partnership new investigator awards	1
Intramural research grants	15
MSM research grants	14
James Kreppner awards	3
Kenneth J. Fyke awards	1
Blood efficiency accelerator awards	13
Small project funding	1
Transfusion medicine program support awards	2
National Training Programs	**22**
Postdoctoral fellowships	6
Graduate fellowships	13
CIHR health system impact fellowship	1
Transfusion medicine traineeship awards	2
Research Laboratory Support Program	**11**
Development Research Programs	**76**
Deepening the understanding of our products and the processes used to manufacture them	15
Developing new or next generation products	16
Improving current generation products and the processes used to manufacture them	18
Improving and/or enabling the Product and Process Development Group	6
On demand unit investigation	11
Other	10

Education Programs	**7**
BloodTechNet awards	5
Education research grant	1
Centre for Blood Research program support collaboration	1
Clinical Guideline Development Program	**5**
Externally Funded Grants and Awards	**20**
Total number of projects	**197**

Titles of projects supported by program

Research Programs
Canadian Blood Services/CIHR Partnership National Operating Grant Program
Purpose: Transfusion science
Expanding treatment options for inflammatory bowel disease: a novel mechanism of antibody-based immunotherapy
Fetal and neonatal alloimmune thrombocytopenia: novel mechanisms and therapeutic approaches
Novel mechanisms of platelet aggregation: Roles of non-classical beta-3 integrin ligands and fibronectin in thrombosis and hemostasis
Purpose: Blood supply risk
Examining the relationship between repeated blood donations in female donors on maternal/neonatal outcomes: a cohort study
Purpose: Blood utilization and conservation
Polymer-based manufacturing tolerogenic miRNA-based therapeutics
Purpose: Transfusion-related acute lung injury
Transfusion-Related Acute Lung Injury and delayed TRALI: a prospective study in critically ill children
Canadian Blood Services/CIHR Partnership New Investigator Program
Code sepsis: defining and translating optimal resuscitation and care for children with septic shock
Intramural Research Grant Program
A multifaceted intervention to optimize red blood cell transfusion practice in two provinces
Anti-GPIb mediated thrombocytopenia: implications for IVIG and other therapies (new)
Development of a small molecule cocktail for the expansion of cord blood stem cells
Evaluating the role of donor characteristics and blood component manufacturing on the quality of red cell concentrates
Fc receptors and IVIg in ITP (new)
Human monoclonal CD44 antibodies as potential IVIg replacements
Influence of eryptosis and storage on transfused red cell recovery in sepsis

IN-TRUST: Using a transfusion database to explore the immune-modulatory impacts of blood transfusion and the clinical impacts of blood processing changes (new)
Modulating of biofilm formation, virulence, and antimicrobial resistance by Staphylococcus aureus during platelet storage (new)
Monovalent Fc receptor blockade using novel fusion proteins: The road towards an IVIg replacement
Optimization of monoclonal anti-erythrocyte antibodies for improved immunoprophylaxis in a murine model
Plasma transfusion or plasma protein product infusion in a murine model of trauma (new)
Plasma versus plasma protein concentrate transfusion for coagulopathic control
Small molecule drug development of phagocytosis inhibitors (new)
TAD-POL (Transfusion-Associated-Dyspnea: Prospective observation and laboratory assessment)
MSM Research Grant Program
A longitudinal analysis of behavioural and biological risk among men who have sex with men in metro Vancouver
ACB and MSM - it's not an oxymoron: A research project that explores the importance of ACB people in MSM blood donation research
Allowing MSM to donate in the context of pathogen reduction of blood components: mathematical modeling of the risk of HIV, HBV and HCV transmission through transfusion
Assessing alternative Canadian Blood Services blood donor deferral screening policies for men who have sex with men
Assessing unintentional creation of bias against MSM as a function of exposure to blood donor screening questionnaire and assessing sexual behaviour risk factors of those successfully passing blood donor screening
Attitudes, behaviours, and acceptability related to current and future blood donation policy: A qualitative study of gay, bisexual, and other men who have sex with men in Vancouver, Toronto, and Montreal
Estimating the probability of HIV risk in MSM donor policies through biobehavioural and mathematical modelling studies
Évaluation de l’acceptabilité et de la faisabilité d’un programme de dons de plasma destiné au fractionnement, pour les hommes ayant des relations sexuelles avec d’autres hommes de la communauté gaie montréalaise
Feasibility of implementing source plasma donation with alternative eligibility criteria for men who have sex with men
Mathematical modeling - comparing HIV risk between MSM donation strategies

Operational impact of individual risk assessment options
Safety, Acceptance, Fairness & Equality (SAFE project): Acceptable risk and donor selection
Sex Now 2018: A national survey on blood donation and undiagnosed blood borne infections
Understanding general population impact and opportunities from changes to blood donation deferral screening and criteria for men who have sex with men
James Kreppner Award Program
Canadian cord blood banking: Legal and policy responses (new)
The role of stakeholder trust in OTDT policy change: public and professional attitudes to ante-mortem interventions in organ donation
Of skin, sperm, and blood: A comparative analysis of exemptions in Canadian human tissue legislation
Kenneth J. Fyke Award Program
Canadians' attitudes and opinions regarding cardiac donation after cardiocirculatory death: A mixed-methods study (new)
Blood Efficiency Accelerator Award Program
A machine learning based framework to analyze blood product transactional data for reducing discards (new)
A program to minimize preventable and inappropriate blood product transfusions in liver surgery
A study to understand C1 Esterase Inhibitor distribution and patterns of use in Canada (new)
Are cervical cancer brachytherapy outcomes associated with pre-brachytherapy hemoglobin values and transfusion practice? An observational study comparing two academic centres (new)
Assessment of the quality of granulocyte concentrates to optimise their use in transfusion therapy
Blood product demand forecast modeling using clinical predictors
Blood utilization epidemiological profile to evaluate appropriate use (BLUE)
Demonstration of genetic blood group transition in patients undergoing ABO-mismatched hematopoietic stem cell transplantation by peripheral blood quantitative polymerase chain reaction targeting the ABO locus (new)
Evaluating unintentional warming of glycerolized red cell concentrates (new)
Management of iron deficiency anemia in the pediatric emergency department: Pilot study of red blood cell transfusion IV iron therapy
Measurement of heavy metals in donor blood in Canada (new)
Optimizing rejuvenation to improve the product quality of pathogen-inactivation and γ-irradiated red cell

concentrates
Rapid verification variant D phenotype by genotyping in a regional laboratory
Small Projects Funding Program
National evaluation of platelet transport bags to reduce wastage
Transfusion Medicine Program Support Award
McMaster Centre for Transfusion Research
University of Toronto QUEST Research Program

National Training Programs

Postdoctoral Fellowship Program
Development of a small molecule-based stem and progenitor expansion protocol to accelerate engraftment after cord blood transplantation
The mechanism of action of monoclonal antibody blends in the potential replacement of anti-D in hemolytic disease of the fetus and newborn
Novel detection strategies for new platelet ligands and anti-platelet antibodies
Donor characteristics and the quality of red cell concentrates
Development of a drug to replace IVIg, and antibody-dependent cellular cytotoxicity as cause for unexplained hemolysis post-transfusion (new)
Reducing IVIG usage by developing novel prophylaxis therapies against FNAIT (new)
Graduate Fellowship Program
A novel clot-dissolving agent derived from clotting factor Va (new)
Deformability based cell sorting enabling quality control of stored red blood cells (new)
Evaluation and improvement of cold stored platelets
Investigating a new class of small molecule ice recrystallization inhibitors for red blood cell cryopreservation
Investigating the mechanism of anti-CD44 antibody amelioration of IVIg-treatable disease
Monoclonal antibodies with anti-D activity in amelioration of murine ITP (new)
New solution for cord blood unit preservation (new)

Novel cell-surface engineering methods to increase immune-tolerance of allogenic cell transplantation
Platelet desialylation: Novel mechanisms of platelet clearance and immune tolerance
Recombinant Fc multimers to replace IVIG
Small molecule ice recrystallization inhibitors as cryo-additives for red blood cell cryopreservation
Study of the mechanisms implicated in platelets microparticle internalization by blood cells
Synthesis of carbohydrate derivatives for the improvement of red blood cell storage
CIHR Health System Impact Fellowship Program
Process evaluation of the Canadian Blood Services' cord blood bank: managerial and donor perspectives
Transfusion Medicine Traineeship Award
AFC diploma in transfusion medicine
AFC diploma in transfusion medicine

Research Laboratory Support Program

Blood product manufacturing and storage research laboratory
Immune biology research laboratory
Immune modulation research laboratory
Infectious diseases and immunopathology research laboratory
Infectious diseases and plasma protein research laboratory
Microbiology development research laboratory
Operational research engineering laboratory
Plasma and plasma protein research laboratory
Platelet biology and quality research laboratory
Platelet physiology and immunology research laboratory
Stem cell development research laboratory

Product and Process Development Program

Deepening the understanding of our products and the processes used to manufacture them
30-minute rule plasma
BEST Cryoprecipitate study (new)
Cord blood and registry composition analysis
Interruption of platelet agitation on product quality assessment for CSA (in collaboration with Héma-Québec) (new)
Measuring specific gravity of blood components
Platelet yield in B1 units held after centrifugation and before extraction (new)
Pooled platelet product production (dose) simulator
Post-thaw hematopoietic stem cell product quality attributes cord blood unit to segment correlation
Quality management program product characterization re-baselining post new production equipment installation (new)
Quantification of residual red blood cells in platelets (new)
Understanding high hemolyzers (new)
Understanding impact of time to test on product quality attributes for frozen plasma products
Understanding of, and feasibility of predicting changes in, product quality attributes (e.g. hemolysis and free iron release) during red cell storage in various anticoagulant and additive solution combinations (e.g. CPD-SAGM, CP2D-AS3)
Understanding the impact of donor and manufacturing process on platelet activation (new)
Understanding the impact of pre-processing delay on the potency of cord blood units
Developing new or next generation products
Blood bag (collection) request for proposal circa 2018/19
Cerus Intercept pathogen reduced platelets in platelet additive solution evaluation (new)
COVID-19 convalescent plasma (new)
COVID-19 neutralizing antibody assay validation (new)
Evaluation of products with x-ray versus irradiation (new)
Freeze dried plasma production technology development project in collaboration with Terumo
Fresh frozen plasma eye drop aliquots (new)
Growth of BIOBALLs in platelet concentrates (new)

Leukoreduced (platelet sparing) cold stored whole blood produced using Terumo IMUFLEX whole-blood filter saving platelets collection set
Long shelf life cold stored platelets in plasma and platelet additive solution (including non-destructive quality control testing) exploratory
Modelling demand and outdate impact of introducing 5-day expiry pathogen-reduced platelet concentrates in North Eastern Ontario and Nunavut (new)
Optimizing rejuvenation to improve the product quality of pathogen-inactivated and γ-irradiated red cell concentrates (new)
Platelet pooling bag request for proposal
Platelets in SSP+ platelet additive solution assessment study - Product quality perspective (including non-destructive quality control testing verification)
Small platelet units - COVID-19 contingency (new)
SSP+ platelet additive solution (apheresis platelets) assessment study – product quality perspective
Improving current generation products and the processes used to manufacture them
Bacterial growth in cold stored platelets (new)
Comparison of Hemocue and Sysmex Hemolysis (new)
Cryopreservation and characterization of donor lymphocyte infusion products
Extending freezing time for frozen plasma
Improved growth of anaerobic bacteria in platelets (new)
Increased source plasma volume
Modeling and simulation of the introduction of ferritin testing and its impact on donations
Modeling red cell unit doses after introduction of non-destructive testing (new)
Modelling red cell unit age at distribution after introduction of non-destructive quality control testing delayed bacterial sampling (new)
Non-destructive quality control testing for platelet products
Non-destructive quality control testing for red cell products
Non-destructive quality control testing for red cell products supplementary studies in support of the parent Product and Process Development red cell non-destructive quality control testing project
Non-destructive quality control testing red blood cell study – safety perspective in support of the parent Product and Process Development red cell non-destructive quality control testing project
Pool spin changes for Fresenius and Maco collection sets (new)

Post-implementation changes and work flow improvement to in-house sterility testing in the Centre for Innovation Microbiology Laboratory
Post-implementation revisions to cord blood sterility testing program (new)
Sealer request for proposal (new)
Trima software upgrade and process mapping (new)
Improving and/or enabling the Product and Process Development group
Acquisition and installation of Stago compact coagulation analyzer at netCAD (new)
Database design and development
Effect of sample left in a coupler (new)
Increase the netCAD Donor Base
Product and Process Development test method validation project: standardization and qualification of test assays in Centre for Innovation labs supporting Product and Process Development group projects
Transitioning in-house sterility testing to testing group
On Demand Unit Investigation
Blood box tamper indicating device lap shear and 180° peel strength testing
Brampton red cell hemolysis (new)
Brampton red cell hemolysis investigation (new)
Does an upside-down red cell filter cause reduced white blood cells or hemolysis failure in a red cell unit? (new)
Freon leak in red cell refrigerator (new)
Negative BacT bottles with precipitate (new)
Oak red cell units placed in freezer (new)
Oak red cell units with fibrin and clots (new)
Platelet and red cell testing from Cold B1s made at a production site
Red cell unit investigation from Pembroke (new)
Units collected with expired packs on QER 43-17-109203

Other
Blood transfusion sets
British Columbia Centre for Disease Control COVID-19 antibody assay blood draws (new)
Circular of Information overhaul (new)
Evaluating incidence of bacterial contamination in platelet concentrates in Colombia (new)
Extended shelf life platelets - post implementation optimization modelling
Hub and spoke platelet re-distribution simulator
Modeling and simulation education & training
Modulation of bacterial growth during platelet storage (new)
New Brunswick logistics modelling (redux)
Understanding physiological response to donation (aka Astroskin) study (new)

Education Programs

BloodTechNet Award Program
Applying educational tools of knowledge translation to reduce the inappropriate use of plasma in Ontario: A collaboration between Canadian Blood Services and Ontario hospitals
Better blood transfusion - Phase two
Development of internet modules for serology curriculum delivery
Stem cell transplantation multimedia toolkit
Virtual transfusions competency assessment (new)
Education Research Grant
An evaluation of learner perspectives and outcomes following completion of the transfusion medicine area of focused competence
Centre for Blood Research program support collaboration

Clinical Guideline Development Program

Fetal and Neonatal Alloimmune Thrombocytopenia (FNAIT)

Hemoglobinopathies
Hemolytic disease of the fetus and newborn
Use of albumin
Use of platelets

Externally Funded Grants and Awards

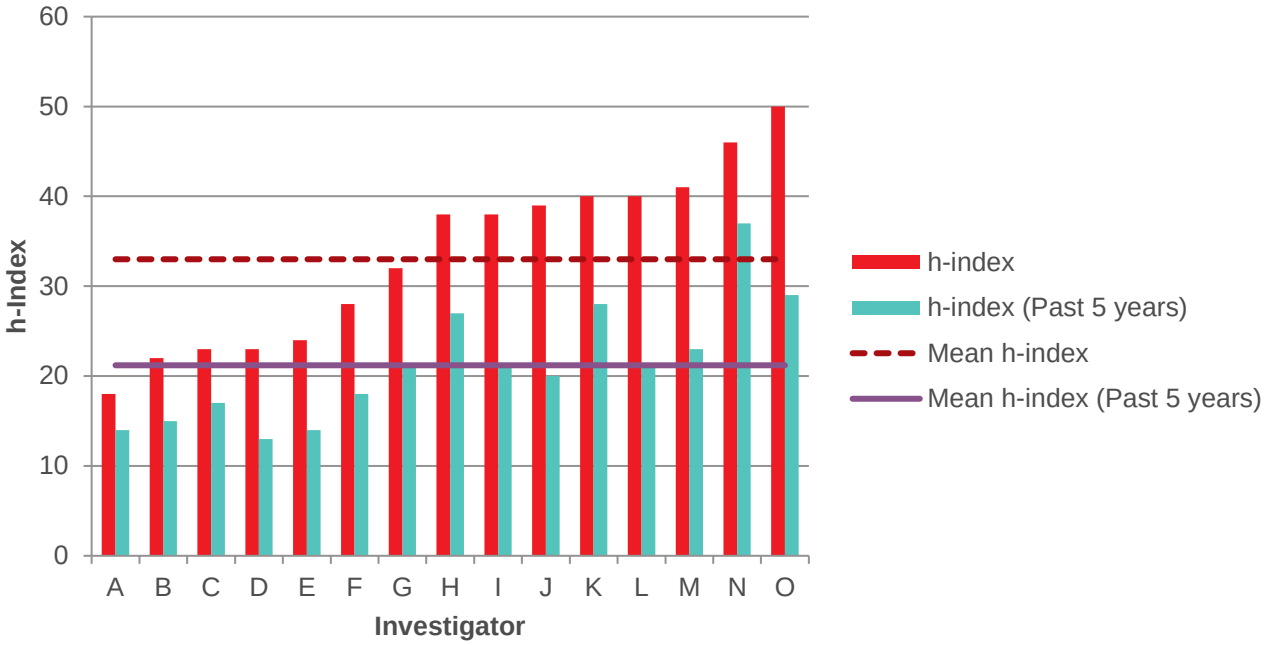
A novel approach to treating hemorrhage with mesoporous bioactive glasses
Aneurysmal subarachnoid hemorrhage - Red blood cell transfusion and outcome (SAHaRA): A randomized controlled trial
Apolipoprotein A-IV and platelet function: Novel links with thrombosis, inflammation, and atherosclerosis (new)
Deep supercooling of red blood cells: Towards practical long term storage (new)
Deformability based cell sorting enabling quality control of stored red blood cells
Do packed red blood cells prepared by different manufacturing processes modulate inflammasome activation? (new)
Efficacy of isoaggluttinin-depleted IVIg to ameliorate immune thrombocytopenia purpura and rheumatoid arthritis in mouse models
Hemostasis modulation by viruses (new)
Inhibiting ice recrystallization – A strategy to enable cellular therapies
Investigation of CryoProtectPure-STEM as a new DMSO-free cryoprotectant for stem cells (new)
Novel strategies to combat thrombogenic activated factor XI (new)
Polymer-grafted allogeneic leukocytes and systemic immune modulation
Scalable production, delivery and assessment of human pseudoislets for research and clinical applications
Splenic macrophage Fc receptors in autoimmune hemolytic anemia and immune thrombocytopenia pathophysiology and patient outcomes
The PSI domain of β3 integrin: A novel mechanism and target for anti-thrombotic therapy
Thrombosis and thrombocytopenia: Novel mechanisms and treatments.
Translating novel factor Xa function to treat thrombosis
Using operational research methods to improve decision making in Canada’s blood supply chain
Using small molecule ice recrystallization inhibitors to mitigate ice formation in complex tissue models of liver preservation

Appendix II: Knowledge products and their impact

Summary of peer-reviewed and non-peer-reviewed publications

Peer-reviewed publications	**123**
Journal Articles	92
Review Articles	15
Clinical Guidelines	0
Comment/Letters/Editorials	4
Books/Book Sections	8
Canadian Blood Services Circular of Information	4
Non-peer-reviewed publications	**68**
Canadian Blood Services Website Publications	36
Technical Reports	30
Other External Website Publications	2
Total number of publications	**191**

Summary of h-index factor analysis



1 Notes: i) H-index factors measured using Google Scholar on April 15, 2020. ii) Mean H-index calculated used H-index factors from the 15 core investigators. Core investigators include (Jason Acker, John Blake, Donald Branch, Dana Devine, Steven Drews, Mindy Goldman, Alan Lazarus, Heyu Ni, Sheila O'Brien, Nicolas Pineault, Ed Pryzdial, Sandra Ramirez-Arcos, Mark Scott, William Sheffield, and Kathryn Webert). iii) H-index is a single bibliometric indicator that is a measure of both the productivity and impact of published work. H-index is an indicator of research users being aware of and valuing published research evidence. Average H-index for Canadian university professors in the biological sciences is 10.6.

Publications' Details

Journal Articles

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