SUPPORT INNOVATE INFLUENCE

2019–2020 Scientific Activities Report

HEMA-QUÉBEC

Dear Reader:

We are pleased and proud to present Héma-Québec's 2019–2020 Scientific Activities Report.

With this first edition, we wish to present a detailed picture of the structure, objectives, and achievements of our scientific teams over the past year.

Since 2017 and the integration of new fields of expertise, scientific activities have supported and advised the organization in many areas of activity, including hematology, microbiology, human tissues, stem cells, analytical, scientific, and medical support to our hospital clients, operations support, innovation through research, training of the next generation, surveillance, epidemiology, biological risk management, and commercialization of intellectual property. Our team also ensures that the eligibility criteria that donors must meet provide optimal protection to both donors and recipients. We are engaged in detecting blood-borne pathogens. Our team is also responsible for tracking reactions in donors, transfusion reactions in recipients and blood product recalls. We are responsible for producing and disseminating statistical reports regarding donors and transmissible disease markers. This team also conducts several studies and surveys among blood donors.

To fulfill our mission, we can count on mobilized and dedicated teams that contribute, each in their own vital way, to the success of the entire organization and its influence at the highest level. During 2019–2020, our scientific and medical team published 26 scientific articles in peer-reviewed journals, presented 25 posters at conferences, and delivered 12 oral presentations or talks as invited speakers. In addition, we assessed the prevalence of certain infections in our blood donors, in particular hepatitis E and babesiosis. These studies were necessary to assess the risk posed by these pathogens to the safety of our blood products. In our role as a healthcare network partner, these data also informed public health authorities about the burden of these emerging infections in the general population and thus helped decision making for the management of these risks. On the provincial level, we are responsible for organizing and participating in the Comité consultatif québécois en médecine transfusionnelle (CCQMT). The CCQMT is a permanent provincial forum for exchanging information and discussing scientific aspects related to transfusion practices and the use of blood products.

Throughout this report, we have chosen to show, through the prism of research activities, our contribution to Héma-Québec's operations and to Québec's healthcare system. We also present how we ensure the safety of donors and recipients, as well as the monitoring activities that enable us to remain at the cutting edge of our field of activity.

In the wake of the arrival of COVID-19 in Québec in March 2020, our operations and scientific activities underwent significant reorganization. This report does not detail our involvement in COVID-19-related projects, since these were mostly completed during the 2019–2020 fiscal year. The next scientific activity report will outline all the scientific areas in which we participated regarding this pandemic.

Marc Germain

Dr. Marc Germain
Vice President, Medical Affairs and Innovation

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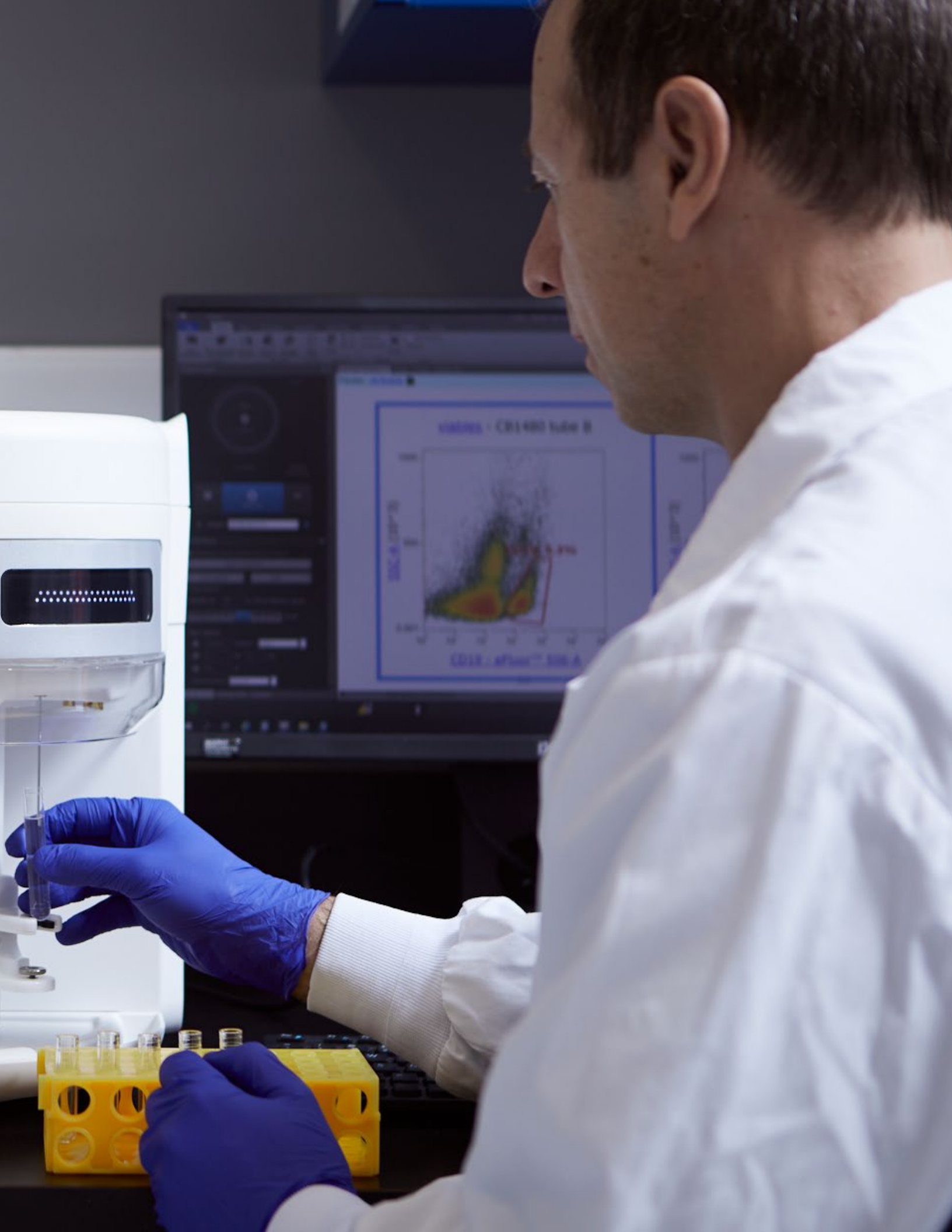
MANDATE

To integrate all research and development activities and provide support and advice to Héma-Québec operations to enable the organization to become a world model in innovation for all activities related to the medical field.



ORGANIZATIONAL STRUCT

Scientific activity revolves around eight divisions and one administrative unit:

Medical Affairs, Microbiology

Dr. Gilles Delage, vice president

Medical Affairs, Hematology

Dr André Lebrun, vice president

Human Tissues Operations

Étienne Fissette, director

Research Operations

François Drouin, director

URE

Transfusion Medicine

Dr. Nancy Robitaille, vice president

Innovation

Renée Bazin, director

Stem Cell Donor Registry and Reference and Stem cell Laboratories

Marie-Claire Chevrier, director

Nursing Services

Isabelle Rabusseau, director

Epidemiology, Surveillance and Biological Risk Management Unit

Antoine Lewin, head


ACTIVIT

IES

Most of the activities are largely reflected in the organizational structure. Several divisions contribute to the training of the next generation.

Support to partners in the healthcare network

Many divisions provide specialized services to the healthcare network. his is especially true of the Stem Cell Donor Registry and Reference and Stem cell Laboratories.

Reference and Stem Cell Laboratories

- conducts specialized red blood cell serology and immunology testing and genotyping in the field of transfusion medicine for donors and recipients of blood products.

More than **5,000 TESTS A YEAR** for the healthcare network

Division of Medical Affairs, Hematology

- provides expertise to transfusion physicians treating patients with special transfusion needs;
- is responsible for following up cases of non-infectious transfusion reactions.

Division of Medical Affairs, Microbiology

- is responsible for following up presumed cases of transfusion-acquired infections.

Operations support

From collection to storage, the various steps involved in preparing biological products of human origin require scientific and technical expertise, state-of-the-art equipment, and functional premises, all in a regulated environment. This responsibility falls on the Division of Operational Research.

Division of Operational Research

- consists of a team of researchers and research assistants dedicated to scientific and technical support in Héma-Québec's five activity sectors;
- has a strong presence in the technology assessment phases of the call for tenders' processes;
- provides support in investigations of technical or operational problems requiring scientific expertise;
- contributes to the continuous improvement of operations by conducting optimization studies of procedures and logistics.

Prior to being operational, all new technology or equipment is assessed by the Division of Research Operations teams.

Innovation

Héma-Québec also conducts innovative research, primarily within the Division of Innovation.

Division of Innovation

- conducts research into and development of new products that fall within one of Héma-Québec's five activity sectors;
- invests significant resources into the development and optimization of product qualification tests.

Héma-Québec also conducts research into cell therapies.

Training the next generation

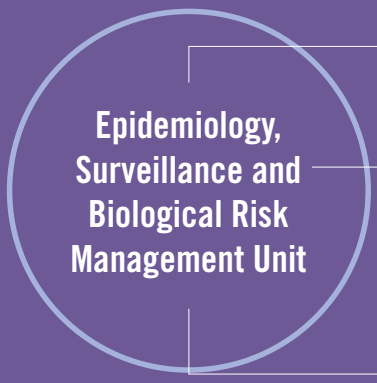
A key aspect is training the future generation specialized in transfusion medicine, cell and molecular biology, immunology, cell and tissue therapies, and microbiology. Many bodies contribute to achieving this objective.

- regularly welcomes transfusion medicine Fellows, i.e., resident physicians pursuing training in transfusion medicine in a program accredited by the Royal College of Physicians and Surgeons of Canada;
- also welcomes residents in hematology from four faculties of medicine in Québec as part of two- to three-day internships to initiate them to Héma-Québec's activities;
- facilitates the deployment of the University of Toronto's Transfusion Camp to the faculties of medicine at Université Laval, Université de Sherbrooke, and McGill University. Héma-Québec was responsible for the French translation of the Transfusion Camp's education material used to teach transfusion medicine to residents in medical and surgical specialties during the five days of lectures and seminars.

- guide their researchers in the co-leadership of students enrolled in master's and PHD programs at Université Laval;
- regularly welcome college and university interns, as well as students, into the research laboratories of the Quebec City facilities to enable them to benefit from practical experience in the workplace.

Epidemiology, surveillance and biological risk management

The activities of the Epidemiology, Surveillance and Biological Risk Management Unit are conducted by a four-person team. Its mandate is to develop an epidemiological hub centred on issues of donor population, transfusion risks and the use of products.



- performs strategic surveillance of Héma-Québec's fields of activity;
- provides risk management expertise for products prepared by Héma-Québec, as well as for blood drive staff, tissue collection, product preparation, and research and development in the laboratory;
- provides scientific and methodological support to the design, management, completion, analysis and publication of scientific studies and research protocols within Héma-Québec.

Commercializing intellectual property

All innovative activity generates potentially valuable intellectual property. Commercializing this intellectual property can occur in different ways, including new product development, patent protection, assignment or granting of a licence to a third party to operate an innovative technology.

Office of the Vice President, Medical Affairs and Innovation

- assesses the commercialization potential and management of intellectual property;
- manages the organization's patent portfolio;
- is responsible for the filing and follow-up of patent requests for inventions that show strong commercialization potential;
- participates in commercialization processes of intellectual property through partner research and the negotiation of co-development, assignment or licencing agreements of technologies developed internally.

GOVER

and contribution of scientific activities to the 2017–2020 strategic orientations


NANCE

Governance

The Office of the Vice President, Medical Affairs and Innovation is governed by many decision-making and advisory committees.

Medical Affairs and Innovation meetings – Transfusion Medicine

Merging the offices of the vice presidents of Medical Affairs and Research and Development in 2017 led to the employees of these two sectors meeting to better coordinate the organization's research needs with those of its hospital clients.

These meetings fall within Héma-Québec's vision to "become a strategic partner of Québec's healthcare system."

Monthly meetings:

- •encourage increased coordination between the research and transfusion medicine staff, especially through the participation of managers;
- offer researchers the opportunity to present a start-up or ongoing project, a topic presented as part of a scientific conference, or discuss any subject of interest.

Annual meeting:

- brings together almost all employees;
- enables divisions to present their annual report and perspectives for the coming year;
- ensures that the staff of the research laboratories are fully engaged in the preparation of the program and presents posters submitted to scientific conferences during a period dedicated to external outreach.

Medical Affairs and Innovation Project Governance Committee (GoPAMI)

Since 2018, Héma-Québec has had an internal structure aimed at reviewing, evaluating, approving, and monitoring all internal research projects: the Medical Affairs and Innovation Project Governance Committee (GoPAMI).

The GoPAMI:

- Is responsible for examining requests for research and development projects submitted by the project managers of the Office of the Vice President;
- Scrutinizes the alignment of the project with Héma-Québec's mission, mandates, strategic orientations, and priorities;
- Subsequently evaluates the scientific validity, feasibility and risk level of the research projects submitted;
- Evaluated more than 25 internal projects in 2019–2020.

Submitting a project to the GoPAMI is not a mere formality but rather a process that a researcher must undergo to obtain approval to start a new project.

Medical Affairs and Innovation Joint Action Committee

The Medical Affairs and Innovation Joint Action Committee, which consists of a group of experts within the Office of the Vice President:

- is made up of physicians, nurses, an epidemiologist, and a biostatistician;
- meets periodically to discuss issues of a medical nature, including those related to the health and safety of donors and the safety of the biological products delivered to hospitals.

This discussion platform develops and formalizes the notifications and recommendations of the Office of the Vice President intended for Héma-Québec's senior management, including the Executive Committee.

Executive Committee

Héma-Québec's Executive Committee, which is the decision-making body overseeing the management and follow-up of the organization's strategic orientations:

- is made up of the President and CEO, and the vice presidents;
- may consider issues that concern the activities of the Office of the Vice President, Medical Affairs and Innovation, especially those affecting the management of biological risks.

Safety Advisory Committee

The Safety Advisory Committee, made up of outside experts:

- advises Héma-Québec on safety issues concerning supplied products and donors;
- is consulted regarding the appropriateness of risk mitigation measures designed and recommended by the Medical Affairs and Innovation team.

Research Ethics Committee

The Research Ethics Committee, tasked with the examination and ethical approval of all research projects involving the participation of human subjects or the use of blood products of human origin:

- reports to the Board of Directors;
- is a decision-making body;
- plays a major role in the approval process of many research projects, given the central role of the Office of the Vice President, Medical Affairs and Innovation.

2017–2020 Strategic Plan orientations

Medical Affairs and Innovation works actively on many of the orientations, areas of intervention and specific objectives of Héma-Québec's 2017–2020 strategic plan. Following are two examples.

Strategic Orientation 2 "Keep up with the latest developments in human biological products and be proactive so that the healthcare network can benefit from this expertise":

- the Office of the Vice President is central to this orientation, which is deployed in two areas that include the implementation of a governance framework to analyze requests for new products and services, the recovery of sub-products and production rejects, and the integration of monitoring practices.

Strategic Orientation 3 "Manage risks in an integrated manner at all levels of the organization in accordance with best practices":

- medical Affairs and Innovation also contributes to an alignment of risk management related to pathogens and toxins within a research framework, and of specific risks in the field of medical affairs to the risk management structure of the organization.

SUPPO

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OUR OPERATIONS

Evaluating the performance of new technologies for our future operations

Calls for tenders

Evaluating operational implications and product quality

As part of the call for tenders (CT) process in effect at Héma-Québec, the Office of the Vice President, Medical Affairs and Innovation frequently helps assess the operational implications and quality of the manufactured products affecting each of the new devices or equipment that may be integrated into operations. This activity is vital to the CT process to ensure compatibility, continuity of operations and product quality.

Evaluating the performance of products and devices

By way of example, new whole blood collection devices were assessed to replace those currently in service. Following the transfer of technology between the supplier and Héma-Québec, numerous tests were carried out to verify that the preparation of blood components (red blood cells, platelets, and plasma) with the new devices attained the expected level of satisfaction.

Each year, many performance evaluations are conducted on products and devices that are subject to calls for tenders.

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Sampling of platelet concentrates: SampLok® Sampling Kit from ITL BioMedical

Today, bacterial contamination of labile blood products still represents the greatest risk of infection through blood transfusion.

Platelet concentrates (PC) are more susceptible to the proliferation of bacteria

A basic difference between contamination by viruses and bacteria is that the latter can continue to replicate in PCs during their lifetime. Under normal storage conditions between 22 and 24°C, even small quantities of bacteria can multiply and reach clinically dangerous levels during their storage period. PCs are more susceptible to the proliferation of many bacteria and represent the category of blood products at greatest risk.

Reducing the risk of bacterial contamination of PCs

To reduce the risk of bacterial contamination, PCs must systematically undergo a culture screening test. A technological bench test was launched to evaluate devices specially designed by ITL BioMedical for the collection of PC samples to seed the BacT/ALERT® environments used for bacterial analysis at Héma-Québec. ITL BioMedical and Héma-Québec collaborated on evaluating the performance of SampLok® Sampling Kit (SSK) platelet samples. The main objective of the project was to study the growth dynamics of the bacteria, known to contaminate PCs, in a SampLok® sampling device up to the moment of seeding in a culture medium for bacterial detection in an automated microbial detection system, such as the BacT/ALERT®.

Consequences of storage on bacterial viability

Since PC samples can be collected at sites other than where the bacterial analysis is performed strictly speaking, prolonged storage of PCs in the sampling kit will be tested as part of this study to verify the impact on bacterial viability. Testing has already begun and should make it possible to verify that the PC samples preserve their biological properties without affecting the sensitivity of the bacterial analyses, thus ensuring the safety of our PCs. By reducing the risk of bacterial contamination and, thus, of post-transfusion complications, these performance evaluations ensure the safety and quality of the blood products.

Residual leukocyte count in labile blood products: performance evaluation of NanoEnTek's ADAM-rWBC2 technology

Method of analyzing residual leukocytes

The labile blood products distributed by Héma-Québec are subject to rigorous control tests aimed at ensuring quality and safety. Determining post-treatment residual leukocytes is among the tests performed on packed red blood cells and platelet concentrates to ensure that they are low in number, guaranteeing better transfusion tolerance.

Currently, the determination of residual leukocytes is done using a recognized method of analysis based on flow cytometry, despite its complexity and increased need for a highly qualified labour force.

Possible alternative

The main objective of this project is to evaluate the performance of NanoEnTek's ADAM-rWBC2, an innovative, inexpensive, and efficient technology for quality control applications.

Simply stated, NanoEnTek has developed the ADAM-rWBC2 technology, an automated solution to quantify residual leukocytes in blood products. The small device uses a dedicated kit in the form of a microscope slide that identifies cells of interest through fluorescent markers.

Comparing the parameters of two methods of analysis

The main aim of this project evaluation will be to compare the parameters of the ADAM-rWBC2 analytical method with those of the method currently used at Héma-Québec to determine residual leukocytes. More specifically, the accuracy, repeatability, reproducibility, linearity, detection, and quantification limits, as well as the quantification of methods, will be compared. In addition, the sampling rates related to the productivity level of the two methods will be compared and used to judge the efficacy and financial impact of the two technologies. Results of this project are expected by the end of 2020.

Measuring plasma hemoglobin: the HemoCue® system

Measuring the amount of hemoglobin in blood plasma

One of the indicators of the quality of our blood products and their proper storage is measuring the amount of hemoglobin in blood plasma. This reflects a process of destruction of red blood cells, or hemolysis, that has a direct impact on the potential therapeutic efficacy and safety of the red blood cells administered. Given that it represents a critical stage in the process for determining the rate of hemolysis, the method used to measure plasma hemoglobin (Hbp) must be reliable, reproductible and accurate.

Envisaging and analyzing a new system

The Quality Control Laboratory (QCL) currently uses the HemoCue PLHP (Plasma/Low Hb Photometer) measuring device designed to determine low amounts of hemoglobin present in biological samples. New systems are arriving regularly on the market and require analysis, compared to the systems already used to assess performance. The system put forward by Terumo BCT was thus evaluated in comparison with the HemoCue system.

Choosing to maintain the method already in place

Because the Hbp measurements obtained using Terumo BCT's Harboe method appear to be inferior to those of the HemoCue PLHP, it was suggested that the current method to determine free hemoglobin be maintained. The HemoCue PLHP presents a greater level of reliability than the Harboe method, is simpler to use and eliminates cross-contamination by employing a single-use sampler. In addition, the HemoCue PLHP device offers the advantage of being pre-calibrated based on the reference method suggested by the International Council for Standardization in Haematology (ICSH). This project makes it possible to evaluate the quantity of hemoglobin in blood plasma throughout the storage period, thereby ensuring the quality of the products delivered to hospitals.

Developing innovative methods

A proof-of-concept project of temperature control systems founded on Internet of Things technology for the control and monitoring of the transportation conditions of blood products.

The main objective of this project is to develop innovative temperature control systems adapted to the transportation of blood donations and blood products to Héma-Québec. Part of the proof-of-concept project is to assess the possibility of developing a smart transportation box founded on Internet of Things (IoT) technology to acquire and transmit data in real time. The deployment of these technological tools will allow access to tangible logistics information to improve the state of knowledge of transportation conditions, the behaviour of temperature control systems in operational situations, and the real temperature conditions of blood components.

Convincing results

Proof-of-concept tests show that the use of IoT technology allow for the transmission and accessibility of temperature and position data in real time or historic mode. Many scenarios of the positioning of the transceiver module on transport vehicles have been envisaged to obtain robust communication without interference, either with tags or satellites (GPS).

Evaluating the use of drones for the transportation of blood products

Under the McGill University Health Centre (MUHC) and the Montreal General Hospital (MGH) initiative, Héma-Québec participated in a research project aimed at evaluating the feasibility of using drone for the transportation of labile blood products (packed red blood cells (PBC), platelet concentrates (PC), and frozen plasma (FP)). The tests were focused on developing a packaging method that would maintain the internal temperature of each type of blood product within its respective acceptable range during the drone flights. In addition, the timeframes of the delivery of blood products (PBC, PC and FP) transported by land and air over identical distances were also compared, since they represented a major issue in terms of measurements.

Positive first phase of the project

This first phase of the project showed that the time to transport blood products by drones to hospitals was more consistent compared with land transportation, the latter being subject to the variability of road conditions (for example, traffic, accidents, closed-off areas), which are more sensitive to disruptions in emergency situations.

Evaluating the functionality of hematopoietic cells

Teams are working on developing a test to evaluate the functional state of the hematopoietic stem cells (HSC) contained in cord blood units banked at Héma-Québec and intended for transplantation. Patients most likely to benefit from these usually suffer from malignant hemopathies or other hematological disorders.

Conclusive benefits of the test developed by Héma-Québec

The reference method currently used by all cord blood banks in the world is the CFU method, a recognized method whose results align with engraftment but which presents the disadvantage of taking up to 14 days before producing a result, delaying the release of the product. The method developed internally (which appeared in a publication earlier this year) generates results in less than 24 hours and presents excellent correlation with CFU analysis results.

Test in the final optimization phase

Testing is currently in the final optimization phase with a view to its transfer to the Public Cord Blood Bank operations. At the same time, the presentation of the test at international conventions and meetings of experts has generated great interest, leading to the launch of a multicentre study aimed at testing and standardizing the method in cell therapy centres in Canada, the United States, Europe, and Asia. Many cell therapy centres have also indicated the need for a similar test that could be applied to HSC patients. Optimization of the test continues to make it accessible for evaluation of the therapeutic potential of this type of cell.

Impact of wait time before banking cord blood units on the functionality of HSC

Evaluating the impact of delays between the collection of cord blood and its banking

In relation to the previously described project, this one uses the functional test resulting from our research to evaluate the impact of the delay between the collection of cord blood and its banking (freezing). The markers used up to now are count measurement and cell viability (viability of total cells or HSC). It is now known that viability is not a very predictive marker of the functional quality of a product. Therefore, we are evaluating the potential of the HSC present in umbilical cord blood using a functional test, which will enable us to document the impact of wait time prior to banking (currently 30 hours on average) on the quality of our products and possibly recommend changes to current procedures to optimize the therapeutic potential of our products.

Developing a functional test to evaluate the potential of mother's milk to prevent necrotizing enterocolitis in newborns

In recent years, Héma-Québec has established a Mother's Milk Bank to treat premature babies. Mother's milk helps reduce the risk of necrotizing enterocolitis, a serious disease that affects babies' intestinal tissues. The factors contained in mother's milk that produce this protective effect are not well known.

To better characterize this product, we initiated a project in which a cellular model (primary intestinal cells) is used to test the efficacy of various lots of mother's milk to counter inflammation experimentally induced to mimic the disease. In a subsequent phase, the factors that contribute to this beneficial effect will be identified using techniques to separate the various components of mother's milk and of the functional test developed. Identifying these factors will enable us to better understand the mechanism of protection provided by mother's milk and may lead to defining new quality markers for this product.

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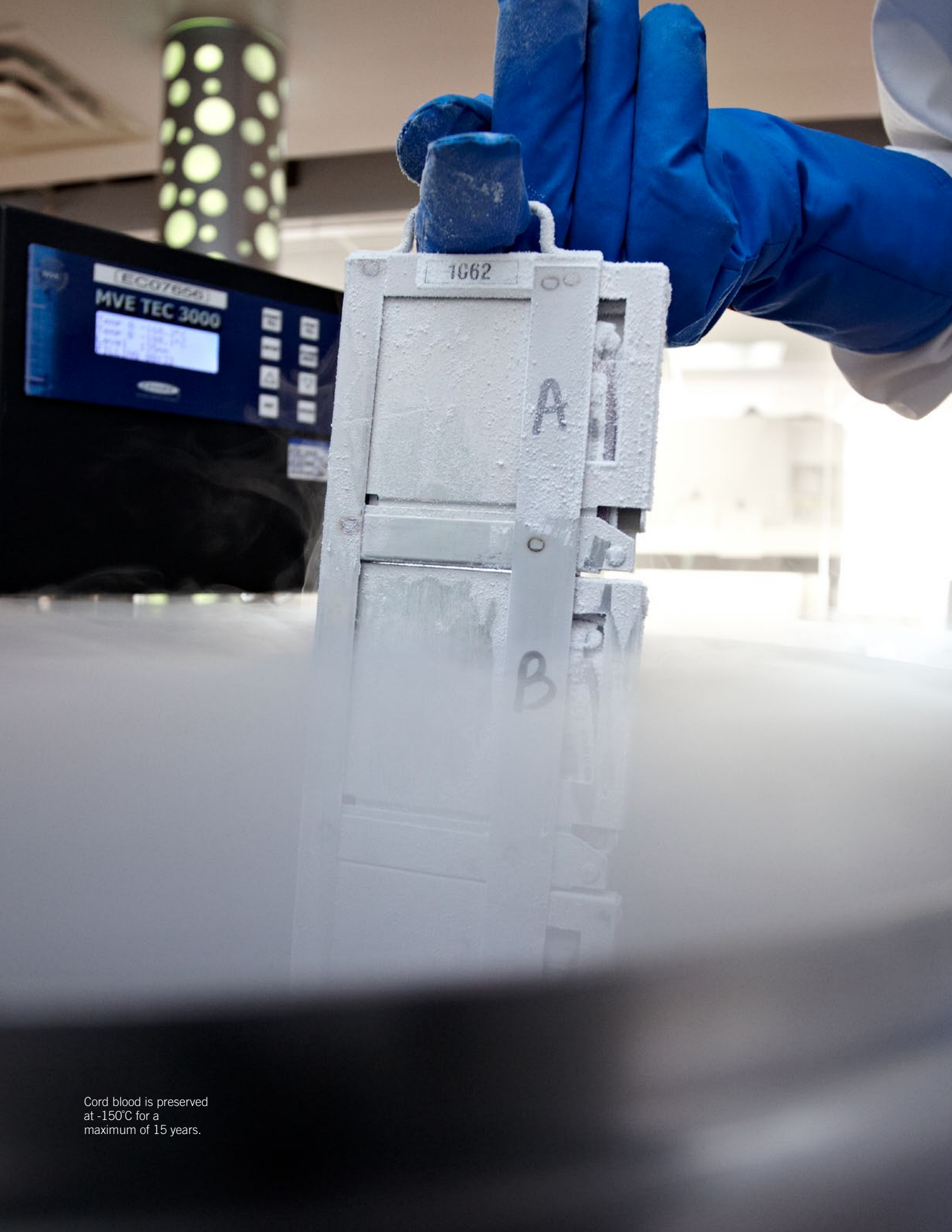
Optimizing and improving our procedures

Developing a method for cleaning and sterilizing musculoskeletal tissues

Currently, musculoskeletal tissues intended for transplantation are decontaminated by irradiation. For several years now, clients are abandoning irradiated tendons based on the scientifically controversial notion that irradiation, even in low doses, has a deleterious effect on the biomechanical characteristics of tendons. Our method of processing musculoskeletal tissues has not been reviewed for many years, and new technologies have appeared on the scene in the interval.

Our teams are working to develop a cleaning method using supercritical CO2 and a combination of chosen additives to



Cord blood is preserved at -150°C for a maximum of 15 years.

reduce the bacterial count, amount of lipids and proteins on tendons and spongy bone cubes. Developing a complementary sterilization method will make it possible to ensure that bacteria are eliminated. The biomechanical, structural, and functional properties of the tendons and bones cleaned and sterilized using supercritical CO2 (+ additives) will be compared to irradiated (the current method) or non-irradiated products.

The ongoing development efforts have made it possible to achieve the required level of sterilization (reduction of the bacterial count to less than $1:10^6$) for all tested tibial tendons. No bacterial growth was observed after incubation of the treated tendons during seven days in a nutrient medium. Tests are continuing to optimize these operations while ensuring maximum preservation of the integrity of the tissues.

Developing and evaluating a blast freezer method to prepare plasma

Héma-Québec has the exclusive mandate to distribute stable products. These are primarily proteins from plasma used to treat patients with hemophilia, autoimmune or inflammatory diseases, circulatory disorders, and other diseases. The manufacture of stable products depends essentially on the supply of plasma destined for fractionation. The plasma collected is sent to fractionation plants to extract many components, including immunoglobulins, coagulation factors and albumin. It is well recognized that the recovery yield of some of these components is directly tied to the freezer settings of the plasma bags (time, temperature, freezing kinetics, among others). An evaluation of the performance and benefits of blast freezer technology in the preparation of plasma was launched by our teams. This type of freezer may represent a promising alternative to conventional devices, in addition to simplifying the high maintenance needs. Blast freezer technology is highly energy efficient, would enable quicker freezing of plasma bags, greatly simplify the plasma preparation process, and potentially increase productivity.

To ensure rapid freezing of the plasma collected, Plasmavie Donor Lounges are currently equipped with Thermo Fisher Scientific's Blast Freezer systems. The operating principle of these devices rests on convection cooling (i.e., temperature exchanges produced in the gaseous state). One of the benefits of the system is uniform freezing kinetics inside the chamber. However, convection adapts less well to quick freezing or when major temperature variations result from the frequent opening of the chamber. A high frequency rate of freezing cycles, combined with use of the device in non-optimal conditions, adds major mechanical stress on the system, mainly the compressors. Finally, Blast Freezer systems must remain in continuous operation to maintain the chamber at the target temperature. The energy footprint of Blast Freezers when in operation becomes important, in addition to the need for adapted facilities to ensure the efficient dissipation of the large amount of heat generated by each device in use.

Preliminary results obtained show that blast freezing is potentially quicker and better adapted to freezing plasma, as well as being more economical.

Thirty-minute rule: plasma thawed at room temperature

Bags of plasma destined for transfusion are preserved at a temperature at or under -20°C for a maximum of 12 months. In the hospital, prior to transfusion, plasma units are thawed in a water bath and can then be stored at 1 to 6°C for a maximum of five days. The Canadian Standards Association stipulates that packed red blood cells can remain at room temperature for 60 minutes without affecting their quality or safety. Although no similar study has been conducted specifically on thawed plasma products, transfusion centres often apply this "60-minute" rule to these products.

As part of the collaboration between Héma-Québec, Canadian Blood Services (CBS) and the United Kingdom's National Health Service Blood and Transplant (NHSBT), this study set out to determine if repeated exposure to room temperature for 30 or 60 minutes, or a single exposure for five hours, could affect the quality of thawed plasma and/or promote bacterial growth.

The results obtained revealed that, five days after thawing, thawed plasma exposed twice to room temperature during storage between 1 and 6°C could remain at room temperature for a period of five hours prior to transfusion without negatively affecting the quality of the plasma or threatening the health of the recipient. Changes to clauses 10.10.5 and 11.4.7 of standard CSA-Z920-15 to include units of thawed plasma should not have any impact on the safety and quality of a blood product.

Platelet aggregates: more uniform classification of thrombopheresis aggregates

Apheresis platelet concentrates (APC) are used in surgery, hematology, oncology, and neonatology. The presence of aggregates in APC is a phenomenon known by blood bank operators worldwide. The causes of the appearance of these aggregates seems to be multifactorial. The management of APC that show an aggregation phenomenon represent a significant operational issue.

The management of apheresis platelet concentrates that show an aggregation phenomenon represent a significant operational issue.

In the context in which no standardized or systemic procedure was applied to identify aggregates in APC upon receipt of products in the blood component preparation (BCP) laboratory, our teams were tasked with developing a classification method for aggregates present in APC. A point system designed by the blood products treatment centre in Belgium, which had demonstrated its efficiency, served as a model. By using this classification method, it is not necessary to apply zero tolerance to the presence of aggregates, given that APC are filtered at the time of transfusion.

Despite aggregates remaining in APC, applying this method has shown a decrease in the loss of platelet products and increased the efficiency of BCP staff.

Analyzing and improving the production process of cadaver skin manufactured in the human tissue bank

Skin from deceased donors can be used to treat patients, such as severe burn victims. The human tissue bank provides this type of product. The tightening of industry standards issued by the American Association of Tissue Banks (AATB) has resulted in the need to review certain procedures for preparing human tissues to ensure their compliance with these new standards. Whenever changes are required, there must be assurance that the new procedure complies with the standard while being applicable in production mode. The aim of this large-scale project is to list the improvements to be made to the production procedure for cadaver skin to make it compliant with the new standards in effect (AATB, ISO13485; ACNOR, Health Canada). The main steps upon which the evaluation of this preparation is based are: 1) the effect of antibiotics on the growth of undesirable microorganisms stored at 4°C; 2) the bacteriostatic effect of the disinfection of the donor with chlorhexidine on the results of the sterility tests; and 3) the bacteriostatic effect of the antibiotic treatment of skin tissue on the results of the sterility tests.

In summary, the bactericidal quality of antibiotics is relatively low in the case of storage at 4°C. However, sterilization of skin tissues is not necessary since they are used as a dressing on patients heavily treated with antibiotics, and allografts are usually rejected after about two weeks. During this study, there was no bacterial growth shown but rather a maintenance or decrease in the population of undesirable microorganisms.

Evaluating the disinfection process of ocular tissues

Bacterial contamination is always an issue that has direct repercussions on our tissue stocks, and potentially for recipients. Our teams work to help reduce rejects linked to ocular tissue (OT) contamination without compromising the safety of recipients. The current process for collecting and preparing OT involves bacterial detection following disinfection of the eye but prior to storage in an antibiotic solution. Some unacceptable microbes cause rejection of the graft, regardless of the potential disinfection of the OT during the antibiotic bath. It is possible, therefore, that some tissues are rejected inappropriately, especially if the antibiotic bath has effectively eliminated the contamination. In 2018, 124 corneas were rejected because of the presence of unacceptable microorganisms, which represents 7.6% of the annual production. The aim of this project is to evaluate the true efficacy of the antibiotic bath on various bacterial strains to eventually change our current practices and thus reduce our OT rejection rate. The first phase of this project has now been completed with the development of an effective method for detecting microorganisms by eliminating the bacteriostatic effects of the antibiotic contained in the bath solution, thereby ensuring the reliability of a negative culture result obtained on the tissue after the decontamination step.

In the second phase of this project, the bacterial effect of antibiotics (gentamicin and streptomycin) contained in the cornea preservation solution (Optisol-GS) will be examined under normal temperature storage conditions. During the preservation period, the corneas will be cold stored at (4°C), except for a brief prior of reheating (from 0 to 4 hours at 35°C) needed for the examination to evaluate the integrity of the corneal endothelium under a microscope. These conditions will be reproduced to evaluate the efficacy of the bactericidal effect of the preservation solution.

Sealing stored bags of lyophilized musculoskeletal tissues

For various reasons, some patients require surgery to replace a loss of bone tissue. Lyophilized bones are often used for this purpose. These bones resulting from our tissue preparation process must be maintained in a low humidity environment (≤ 6%) to safeguard them from contamination that could occur following final irradiation. Our teams have been mobilized to check the integrity of the external seals on the bags used to store spongy bones. According to the manufacturer's specifications, the model of bag used was replaced with a new product that offered a better seal against humidity. However, stability tests revealed that the humidity level of the stored tissues in the new bags increased more rapidly over time than those stored in the original bag.

Various tests were conducted to verify the integrity and tightness of the seals. In the end, results suggest that the new bags with the recommended seal provided better protection against humidity than the previous model. Additional tests were done to check the protection against the penetration of bacteria.

Preparing blind tests to identify bacteria

Since March 2018, the Quality Control Laboratory (QCL) in Québec city has been using the automated VITEK® 2 Compact (bioMérieux) platform to draw up a list of contaminants found in biological products of human origin, such as blood, milk, and tissues. Some pathogens are rare, while others are more prevalent. Those pathogens frequently observed are easily

identified by the VITEK technology. To maintain the expertise of their staff in identifying less common bacterial strains, the QCL asked our researchers to provide it with clinical strains that had characteristics that were different from those often encountered. Since May 2019, blind bacterial identification tests have been prepared monthly from the accessible bacteria bank. In addition to contributing to the maintenance of the staff's expertise in identifying less common strains, this project has helped establish the difficulties inherent in the use of cards to identify certain bacteria that are more difficult to detect with the VITEK technology. There are currently some 50 strains available for the project.Caractérisation des granulocytes destinés à la transfusion.

Characterizing granulocytes destined for transfusion

Granulocytes are transfused into patients with profound neutropenia who suffer refractive infections to standard treatments. The true efficacy of this therapy of last resort is not the subject of consensus in the medical community because of ambivalent results in the rare clinical studies conducted to date. Few studies have focused on the characterization of these cells, including their ability to perform antimicrobial functions. The aim of this project is to characterize the function and viability of the granulocytes destined for transfusion and prepared according to the three different methods used around the world. Firstly, granulocytes will be collected by apheresis in healthy donors stimulated beforehand with prednisone. This is the method currently in use. Secondly, granulocytes will also be collected by apheresis but this time in donors stimulated with G-CSF, a molecule used to cause the release of precursors of granulocytes from the bone marrow into the bloodstream. This is the method most frequently used in the world. Finally, granulocytes will be collected from the leukoplatelet layer of a regular blood donation. This method is used in Great Britain and will also soon be the method chosen by France for the preparation of granulocytes destined for transfusion.

Preserving human tissues.


SERVIN

G THE HEALTHCARE SYSTEM

Proposing biological products of exception

Producing plasminogen concentrate drops

Some people have rare or orphan diseases for which no specific effective treatment exists. Experimental treatments may be developed to meet demand. Since 2013, research and development has produced eyedrops composed of plasminogene concentrate from fresh frozen plasma (FFP) to treat a young boy with ligneous conjunctivitis. Without this treatment, the young boy might have completely lost his sight. Thanks to this biological product of exception, the worst outcome was avoided.

Producing genotyping material

Before performing a transfusion in hospital, compatibility between blood products and recipients must be assessed. This can represent a high degree of difficulty because of rare blood groups, pathologies, or other reasons. Analyzing genes and variations in the sequence of the nucleic acids that form a given gene (genotyping) is one way of ultimately assessing the compatibility of blood products from donors with the blood of recipients. In accordance with its mission, Héma-Québec's Reference Laboratory performs certain complex genotyping analyses for hospital blood banks. For example, by genotyping donors Héma-Québec can identify new donors of rare blood and facilitate the search for compatible donors for patients who have developed antibodies to certain antigens or rare combinations of phenotypes. The material needed by the Reference Laboratory to conduct manual genotyping of blood groups is produced by Héma-Québec's teams. This consists in the production of a sufficient quality and quantity of strips of reaction mixes and primer mixes. Between 75 and 200 strips of each of these six reaction mixes, and the same number of bands of primer mixes for genotyping some 20 Rh blood groups are produced annually.

Innovating

Developing a new formulation of bone for the Human Tissue Bank

Québec hospitals can be supplied with bone products from our Public Human Tissue (HT) Bank. However, one product used extensively in orthopedic surgery, demineralized bone putty, is not part of our bank's current offering. We have begun developing this product, called DBM putty (Demineralized Bone Matrix Putty), based on existing protocols, as well as experimenting with various innovative alternatives to preserve a maximum of functional activity while enabling the manufacture of a putty that is resistant to body temperature. To follow the activity of the various DBM putty recipes being studied, tests are evaluating a quantity of factors responsible for bone formation after implantation (osteoinduction factors) and their functionality (trials of DBM putty implantation in vitro and in an animal model).

Processing hematopoietic stem cells (HSC) from umbilical cord blood to improve engraftment

Patients suffering from malignant hemopathies or certain hematological disorders may be offered a treatment that consists of grafting hematopoietic stem cells. Cord blood is a recognized alternative for grafts for HSC adults, but it presents the disadvantage of containing a lower number of HSC, which limits its use in pediatric patients. This project is evaluating an approach to conditioning HSC using platelet lysate that would enable these cells to migrate more effectively toward the bone marrow following a graft and encourage their retention at this site. During the current year, we completed a demonstration of the efficacy of our approach to engraftment in an animal model. The initial work was done on purified HSC from umbilical cord blood, which is less practical for clinical use. We then launched a second component of the study, now aimed at processing the graft product (reduced cord blood) instead of purified HSC. This will make it possible to complete a process of several hours immediately before performing the graft without needing to manipulate the cell content of the product to be grafted.

DARA interference: Developing methods to counter the interference of a therapeutic antibody (daratumumab) on serological testing

Blood donations destined for transfusion are tested to check that they are compatible with the recipients' blood. The Reference Laboratory is often called upon to work on complex cases of this type of evaluation, which are difficult for hospitals to resolve. One of the difficulties encountered recently was the presence of a therapeutic antibody (anti-CD38) found in the blood of patients treated with anti-CD38. This antibody interferes with tests to detect the presence of antibodies directed against antigens of blood groups in these patients. These tests are vital to identify compatible blood for transfusion. Unfortunately, the anti-CD38 therapeutic antibody recognizes a structure present on all red blood cells, rendering the results of the tests impossible to interpret. We are currently developing a method that will eliminate the interference of anti-CD38 using membranes extracted from cells expressing this antigen to absorb the therapeutic antibodies. This approach could also be used to counter the interference of new therapeutic antibodies, such as anti-CD47, that also recognize a structure on all the blood cells, thereby making analysis impossible..

Implementing a test to evaluate the clinical relevance of antibodies found in samples of patients (MMA test)

The aim of this project is to improve the compatibility between the blood of donors and that of recipients. Repeated transfusions

of blood products whose donor-recipient compatibility is not 100% because of the high number of clinically important antigens expressed on the surface of red blood cells can provoke alloimmunization in the recipient. Recipients may develop numerous antibodies directed against antigens of various blood groups, putting them at risk of hemolytic reactions during subsequent transfusions. As part of this research project, we implemented a method to predict if an antibody presents the potential of inducing an adverse transfusion reaction and help select better units of red blood cells to transfuse. In the second phase, we will aim to make this method faster and objective by applying flow cytometry principles.

Determining the expression density of RhD antigen type 42 on red blood cells

Whether in the context of transfusions or pregnant women for whom the red blood cells of the fetus can come into contact with maternal blood, production of antibodies capable of destroying red blood cells can occur. Not all determining factors of this type of reaction are known. Cross-immunity between individuals of the same species, or alloimmunization, can represent a health risk (for example, haemolytic disease in the fetus or newborn following fetal-maternal alloimmunization). Several years ago, a demonstration was done of the absence of the risk of alloimmunization in patients whose red blood cells expressed a certain type of RhD antigen, i.e., weak RhD type 1, 2 or 3, leading to recommendations for the prevention of haemolytic disease in the newborn. As a result, pregnant women expressing weak RhD type 1, 2 or 3 are now considered as expressing normal RhD when transfusions are required and do not receive anti-D immunoglobulin (WinRho) to prevent haemolytic disease in the newborn. Weak RhD types 1, 2 or 3 are the most common in the world's population, except in Québec. Weak RhD type 42 is the most common found in the Québec population but is almost completely absent elsewhere in the world. Our focus, therefore, is on determining if weak RhD type 42 presents a transfusion risk or not, and a risk for haemolytic disease in the newborn. A retrospective study of a database of RhD type 42 recipients who received Rh+ blood products is under way. To better characterize the alloimmunization potential of RhD type 42, a comparison of the expression density of the RhD antigen on weak RhD type 42 red blood cells with the red blood cells of types 1,2 and 3 by flow cytometry is under way. This project could establish the absence of any alloimmunization risk in persons with weak RhD type 42, like those with type 1, 2 or 3. The study is being carried out with the collaboration of Dr. Pierre-Aurèle Morin, a hematologist at CHU de Sherbrooke.

Studying the prevalence of the weak RhD type 42 blood group in the Québec population

As mentioned in the project description above, weak RhD type 42 is widespread in the Québec population. The goal of this project is to conduct a population study using the CARTaGENE bank, a biobank at CHU Sainte-Justine that can supply DNA samples that are representative of the entire Québec population. We obtained 1,000 samples from this biobank to conduct the project. Red blood cell (RBC) genotyping techniques developed in our laboratories are being used to analyze these 1,000 samples. We will thus be able to determine which administrative regions of the province have the highest prevalence of this type of RhD and perhaps identify the founder effect.

Developing a method to produce antiviral T lymphocytes using B lymphocytes as antigen-presenting cells

Infections caused by bacteria or viruses often occur following cell or organ transplantation. The usual therapeutic arsenal requires employing pharmaceutical molecules. A new treatment method consists of using immune cells to destroy the viruses. We are using technology developed by our researchers to extract and multiply B lymphocytes extracted from leukoreduction chambers (devices recovered following platelet donations by thrombapheresis) to teach T lymphocytes (also recovered from leukoreduction chambers) to recognize and kill the viruses often responsible for post-transplantation infections. This project could lead to the therapeutic use of produced cells in the foreseeable future. The work is being led by a postdoctoral researcher funded through the MITACS program (MITACS is a non-profit national research and training organization dedicated to promoting collaborations between Canadian universities, private industry, and government, and to encourage two-way international research collaboration between Canadian universities and research partners abroad), jointly with Dr. Jean-Sébastien Delisle (a hematologist-researcher at Hôpital Maisonneuve-Rosemont) and Héma-Québec.

Genome editing of hematopoietic stem cells (HSC) and in vitro production of mature red blood cells

Blood is a valuable resource whose supply depends solely on donations. It is an essential product since no other substitute exists today. For several years, innovations in molecular and cellular biology have pointed to the possibility of manufacturing red blood cells in the laboratory. In the case of platelets, this has almost become a reality. The genome editing expertise (CRISPR/Cas9) of some of our university collaborators has allowed us to envisage the production of mature red blood cells from HSC, and by ex vivo culture, that have modifications introduced into the genome beforehand. Applications extend ultimately from the modification of blood groups for the production of serology reagents to the production of red blood cells for transfusion purposes.

This work is part of a research project led in collaboration with Université Laval.

Developing new RBC genotyping tests: 3rd generation sequencing

Genetic analysis technology is evolving rapidly. By complementing or replacing serology tests, this technology makes it possible to identify the antigen characteristics of the red blood cells of donors or recipients. As such, it plays a part in assessing the compatibility between donors and recipients in a transfusion situation. A new method of DNA sequencing has just been introduced: 3rd-generation sequencing or nanopore sequencing. Within the framework of this project led by a postdoctoral researcher (funded by MITACS), we are evaluating the possibility of using this technology to predict antigens of blood groups, especially those that cause problems with currently available methods (for example, RhD, RhCE and MNS antigens).

Recovering sub-products and production rejects

Leukoreduction system chambers (LRS)

Our operations generate biological by-products that can be used for medical or clinical research. These can include cells or proteins of interest, such as antibodies, used extensively in a clinical setting to treat patients, and in the medical diagnostics field. Leukoreduction system chambers (LRS) recovered at the end of platelet donations are an invaluable source of cells that could be used for research at Héma-Québec or in projects carried out in collaboration with outside researchers. For example, we are collaborating with researchers from the National Research Council of Canada (NRC) on a project aimed at showing the feasibility of using B lymphocytes recovered from LRS chambers to stimulate secretion of the product of these cells, i.e., antibodies, as a diagnostic tool to detect pathogens, or a therapeutic tool to treat diseases.

To achieve this, Héma-Québec needed to be able to supply special LRS chambers, which was accomplished with the collaboration of some of our GLOBULE centres.

Characterizing soluble factors contained in the plasma of umbilical cord blood

The banking of cord blood units destined for transplantation involves separating the various components of blood to eliminate most of the plasma and red blood cells. To recover these production rejects, we are studying the content of the soluble factors contained in the plasma of cord blood. These factors could be beneficial for the use of plasma as eye drops or as an ex vivo culturing supplement in the production of cells/tissues for therapeutic use in humans. In the latter case, there is keen interest in replacing products of bovine origin (bovine serum) in the development of therapeutic cell and tissue products.

Offering services of exception

RBC genotyping tests and the transfer of tests to the Reference and Stem Cell Laboratory

Genotyping blood groups has now become indispensable when units of blood from donors cannot be characterized by serology or for red blood cell testing of patients when commercial antiserum antibodies are not available.

For many years now, we have been mandated to develop RBC genotyping tests and provide scientific support in the field. These tests help better characterize the profile of donors and recipients to ensure better compatibility when the time for transfusion arrives.

Blood is a valuable resource whose supply depends solely on donations. It is an essential product since no other substitute exists today. For several years, innovations in molecular and cellular biology have pointed to the possibility of manufacturing red blood cells in the laboratory.

Despite implementing an automated genotyping platform in the Reference and Stem Cell Laboratory (RSCL), many new tests had to be developed by our researchers to compensate for the tests not covered by the commercial platform. For example, we developed tests to identify weak RhD type 1, 2, 3. Following their development, these tests were transferred to the RSCL operations, which is responsible for conducting the tests. However, more than 20 other tests have been developed (for example, Knops, CEAG, He, KCAM) and are being routinely used without being transferred as of yet to the RSCL.

In considering the transfer of these tests to the RSCL, studies show that the protocols for genotyping done by Héma-Québec's Office of the Vice President, Research and Development are equivalent to those already in place within the RSCL regulatory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framework. A feasibility study conducted on four tests revealed a result that complies with all the assessed parameters, thereby confirming that the tests can be transferred for validation by the RSCL team. The technological transfer of these tests will expand the portfolio of genotyping tests already done. In the meantime, we continue to provide a service to meet genotyping requests of blood donors and recipients.

Screening for IgA deficiency

The transfusion of blood products is never innocuous since adverse reactions can occur. Therefore, it is important to know the determining factors behind these reactions. Selective IgA deficiency is the most common form of immunodeficiency and is found in approximately 1 out of 600 Caucasians. In most cases, this deficiency is not accompanied by any specific symptom and is considered an anomaly without a real pathology of the immune system. However, products containing IgA administered to patients with IgA deficiency have been suspected as the causal agent of severe transfusion reactions. While these reactions are extremely rare, it is important to keep in mind that a person with IgA deficiency who has developed anti-IgA antibodies may experience adverse effects when blood products containing IgA are transfused. A few years ago, we developed a highly effective screening test for IgA deficiency in all donors of blood products, which led to the creation of a registry of donors with IgA deficiency. This registry is used to maintain an inventory of IgA-deficient plasma for transfusion, for each blood group in the ABO system. The number of active donors enrolled in the registry reduces the screening of new blood donors and, if necessary, we help the group effort by conducting the final phase of testing.

In conjunction with identifying IgA-deficient donors, our research teams have also developed a quantitative IgA test that confirms suspected deficiencies when clinical tests are performed using less sensitive methods than the one developed internally. Each year, we receive some 20 requests for an IgA deficiency test from Québec hospitals.

Fetal RhD screening

RhD is the most clinically significant RBC antigen after ABO system antigens. Transfusing RhD+ red blood cells into an RhD- individual frequently causes alloimmunization against the RhD antigen. This antigen is also involved in haemolytic disease in the newborn, a perinatal complication that can occur when an RhD- pregnant woman is carrying an RhD+ fetus. The transfer of a few RhD+ red blood cells from the fetal bloodstream into the maternal bloodstream is sufficient to cause maternal alloimmunization against the RhD. The maternal anti-RhD antigens can easily cross the placental barrier and destroy the red blood cells of the fetus, endangering its life. For several years now, an effective, minimally invasive, and safe preventative treatment has been administered systematically to RhD- phenotype pregnant women. This treatment consists of administering hyperimmune globulins directed against the RhD antigen. The idea behind this treatment is to eliminate the few fetal RhD+ red blood cells potentially present in the maternal bloodstream by attaching them to anti-RhD antibodies, thereby bringing about their elimination by the organism. The mother's immune system is not exposed to the RhD antigen and does not develop any alloimmune reaction that could be potentially harmful to the fetus. Up to 40% of the fetuses of RhD- mothers are also RhD- phenotype. In these cases, administering anti-RhD immunoglobulins is useless and incurs significant costs, as well as exposing the mothers to an anti-RhD immunoglobulin treatment that, in rare cases, can cause serious side effects.

The transfusion of blood products is never innocuous since adverse reactions can occur. Therefore, it is important to know the determining factors behind these reactions.

Over the past decade, refining DNA amplification techniques has made it possible to determine the RhD genotype of the fetus by using a sample of the mother's blood collected at the 10th week of pregnancy. Determining the RhD genotype of the fetus helps deduce its phenotype for this antigen. This test could prevent the useless administration of many anti-RhD immunoglobulin doses. The availability of this screening led Héma-Québec to think about offering this service to the Québec health care system. As part of this thought process, a multidisciplinary team prepared a business plan in which the scientific, technical, financial, and legal issues were analyzed in detail. Héma-Québec's proposal is currently being reviewed by the Institut national d'excellence en santé et services sociaux (INESSS).

Automated K phenotyping

The Kell blood group system consists of 35 antigens, including the K (Kell) antigen that has great immunogenic potential and is responsible for haemolytic disease in newborns, which can be severe. Published in 2020, the CSA Z902 standard recommends that women of child-bearing age be transfused with K-negative packed RBC to avoid alloimmunization. Héma-Québec decided to perform this test on an automated platform. Our teams participated in assessing the costs of this new approach. The number of donors targeted by this program was assessed over a one-year period with a mathematical probability model evaluated using a Monte Carlo simulation. These simulations made it possible to estimate the average cost associated with Kell tests, as well as the anticipated costs where some parameters changed independently.

HLA characteristics of First Nations

The Stem Cell Donor Registry must reflect the genetic diversity of the population. To meet this challenge, a project was initiated in 2015 to gain greater knowledge of the HLA characteristics of First Nations, as well as to promote enrolment in the registry. Many partners, including the First Nations of Quebec and Labrador Health and Social Services Commission, are collaborating to raise awareness and underscore the importance of representing cultural communities so that patients awaiting a transplant have a chance at a cure. To date, agreements have been reached with representatives of the Huron-Wendat, the Mohawk of Kahnawake, the Innu of Unamen Shipu, and the Algonquin of Kebaowek and Lac-Simon. Various awareness activities have resulted in the recruitment of 324 study participants, and 56 persons between the ages of 18 and 35 have also enrolled in the Stem Cell Donor Registry. Following completion of recruitment efforts among the Mohawk and Huron-Wendat, analysis of the demographic variables and frequency of HLA markers was launched.

Rosalie, a cord blood transfusion recipient, has First Nations ancestry.


ENSURING THE
SAFE

TY

OF DONORS AND RECIPIENTS

Donors safety

Salty snacks and water — vasovagal reactions

While blood donation is considered safe, there are inherent risks to donors. Characterized by a general feeling of discomfort and weakness accompanied by anxiety, dizziness, and nausea due to uncompensated blood loss, vasovagal reactions (VVR) are the most frequent side effects in donors. Various strategies exist to counter these reactions, including drinking water before donating blood along with consuming salt to preserve the liquid in the organism. In October 2015, Héma-Québec established a new provincial donor hemovigilance system, which documented VVR. In June 2017, a provincial intervention program requiring donors to drink water and eat salty snacks before giving blood was put in place to limit VVR. Two years into this intervention program, Héma-Québec measured the effect its program had on the provincial VVR rate through comparisons with VVR prior to implementing the program. An immediate reduction of 15.2% in the overall rate of VVR was observed following introduction of the program. Additional analyses revealed immediate reductions in the rates of VVR: 17.4% in men, 15.1% in women, 19.6% in whole blood donors, and 11.1% in young donors.

The program of eating a salty snack and drinking water at blood collection sites has led to a significant and immediate reduction of the incidence of VVR. In addition to contributing to the safety of donors, this action has improved the donation experience and increased the likelihood that donors will return to give blood.

Iron supplement pilot project among whole blood donors

Our medical and scientific teams are taking part in a pilot project to provide multivitamins containing 18 mg of elemental iron at blood drives. The aim of the project is to assess the feasibility of offering multivitamins at blood drives and to measure the effect of the program on the following parameters: blood drive operations, exclusion rate of donors due to ferritin < 12 mcg/L, rate of return of donors, donors' ferritin levels and compliance with taking supplements. Mobile blood drives in Alma and Rivière-du-Loup were chosen for the pilot project.

Protein dosage in plasma donors

Blood plasma consists mostly of proteins that play an important physiological role in maintaining osmolarity, the balance of biological fluids in the internal environment. Repeated collections and/or large volumes of plasma collected could result in a temporary reduction in the amount of total protein in the plasma of some donors. Current apheresis practices do not seem to cause a problem in this regard.

Héma-Québec submitted a request to Health Canada to stop the medical assessment of plasma donors and the related questionnaire. As a follow-up, our teams monitored plasma donors who were excluded following the medical assessment to ensure that their protein levels were normal.

Where this was the case, our approach would allow for optimization of our collection procedures while maintaining a high level of safety for our plasma donors.

Volume limit of plasma collected

As a continuation of the project presented above, our medical and scientific teams examined the possibility of increasing the volume limit of fractionation plasma to be collected from a plasma donor on a yearly basis. The total levels of protein and gamma globulins in frequent plasma donors was tracked over time. While the number of frequent donors was limited, no downward trend was observed over time, and average values, as well as standard deviation markers, remained above the safety benchmarks for plasma collection.

Our medical and scientific teams explored the possibility of increasing the volume limit of fractionation plasma to be collected from a plasma donor on a yearly basis.

These initial indicators point to the possibility of pursuing this approach to increase the volume of plasma collected annually from some frequent donors.

Optimal platelets

In 2017, Health Canada approved certification of the optimal platelet procedure request and asked Héma-Québec to produce a post-implementation follow-up report over a three-year period. Since the new procedure was implemented, donations have been collected before the results of the platelet count are known. The average platelet count of the last three platelet donations is used for known donors, and a regional average is used for new donors. The report produced by our teams outlines the validity of the counting method used to assess the platelet count of donors. It also mentions the number of donors who provided donations despite a measured platelet count below the minimum value of 150 x 109 PLTs/L and the assessment of the risks incurred by these donors. Scientists and physicians took part in drafting the 2019 follow-up report and the request for clarification of the 2018 follow-up report.

Studying the prevalence of lymphopenia in frequent donors of platelets by thrombapheresis (BEST multicentre study)

At Héma-Québec, most blood platelets destined for transfusion are produced by thrombapheresis. While blood cells other than platelets are returned to the donor at the end of the procedure, there is a stage of leukoreduction that takes place within a chamber (LRS chamber) that retains a large quantity of white blood cells, thereby reducing the amount returned to the donor. Recent observations made by clinician-researchers from the Harvard Medical School showed that some donors of platelets by apheresis had lower levels of white blood cells than normal (lymphopenia) without their health being affected. As part of this project, titled the BEST multicentre study (Biomedical Excellence for Safer Transfusion, a group of international experts in transfusion medicine), we wanted to know more about the levels of white blood cells, especially those of T lymphocytes in our regular platelet donors (i.e., donors who make 20 or more donations a year), and to compare them with the levels found in control donors. These control donors are whole blood donors who have made only a few donations in their lifetime and whose age and sex correspond to that of the platelet donors in the study. We also wanted to establish the risk factors for developing lymphopenia associated with thrombapheresis in donors based on age, number of donations, platelet production, and other parameters.

We recently began measuring the number of white blood cells of the recruited participants using two instruments currently in use in the laboratory: the first (a haematology counter) provides an overall picture of the proportion of various sorts of white blood cells contained in the participants' blood, and the second (a flow cytometer) gives a more accurate measurement of T lymphocytes. We will also measure the amount of immunoglobulin G (an antibody that defends against infections) to complete our evaluation of the immune system.

Mitigating blood-borne infectious diseases

Reviewing criteria governing MSM – men who have sex with men

Our medical and scientific teams took part in drafting the submission to Health Canada for the reduction of the exclusion period from 12 months to three months for men who have sex with men (MSM), and the responses to Health Canada's requests for clarification. Health Canada approved the request in April 2019, and the new criterion was implemented in June 2019. The request was made jointly with Canadian Blood Services (CBS).

We also took part in modelling the risks of HIV transmission through transfusion for a three-month exclusion period for MSM donors. Results of this modelling were presented to Health Canada as part of the submission to change the MSM criterion. The modelling project is part of an initiative by the International Society of Blood Transfusion (ISBT), within the SRAP (Surveillance, Risk Assessment & Policy) subgroup of the TTID (Transfusion Transmitted Infectious Diseases) group, and the project is supported by federal MSM research funds.

A modelling of the risks of HIV transmission through transfusion was done for an exclusion period of less than three months or with no exclusion period combined with the use of pathogen reduction technology (Intercept by CSL Behring). The modelling project is also part of an ISBT initiative, within the SRAP subgroup of the TTID group. The project is supported by federal MSM research funds and is being conducted in collaboration with Université de Sherbrooke.

In addition, this same group, led by Héma-Québec, is looking into the possibility of allowing MSM to give blood within the context of the use of pathogen reduction technology (PRT) without additional exclusion. In this study, this group is seeking to improve and develop new modelling strategies to assess the residual risk of HIV, HBV and HCV infection transmitted through transfusion, in the absence of or less restrictive MSM exclusion criteria in the context of implementing the PRT. The use of PRT to reduce or inactivate the viruses in blood products could also reduce the residual risk of infected donations by MSM donors. As an alternative solution to policies excluding MSM blood donors, safety might rely even more on the efficacy of PRT to eliminate the viruses present in blood products.

Funding has been obtained, and a student has been recruited to carry out the project. The results will be presented at the 2020 AABB conference and the 2020 ISBT congress.

Our medical and scientific teams took part in drafting the submission to Health Canada for the reduction of the exclusion period from 12 months to three months for men who have sex with men.

Emergence of babesiosis

In North America, babesiosis is a disease caused primarily by the zooparasite Babesia microti, which multiplies in red blood cells. The vector of this disease is the tick, more specifically Ixodes scapularis, the same tick that is responsible for the transmission of Lyme disease. The effects of babesiosis are highly variable. Most of the time, it is silent. When symptoms are present, they resemble the flu, which means that the disease often goes undiagnosed or is poorly diagnosed. But for persons who are immunocompromised, young children, the elderly and persons with an enlarged spleen, this disease can have serious and even deadly consequences. Its silent nature and its replication in the red blood cells make babesiosis the most frequent infectious disease transmitted through blood transfusion in the United States.

In 2013, Héma-Québec took part in a seroprevalence study in collaboration with Canadian Blood Services (CBS) and the American Red Cross (ARC) to evaluate the extent of babesiosis in Canada and the urgency of taking preventative measures to protect recipients of blood products. To date, all the results have been negative. Since this first study, we have observed an increase in the number of ticks carrying the parasite in Canada, especially in Manitoba. In Québec, Ixodes scapularis is primarily found in the Montérégie region.

We participated in a second Canada-wide study on the prevalence of babesiosis in blood donors, again in collaboration with CBS and the ARC. Using the Procleix® Babesia Assay kit on the Panther platform by Grifols, a total of 20,000 donations from Héma-Québec and 30,000 donations from CBS originating from targeted areas were tested to detect nucleic acid (NA). The sample of donors chosen for this study represented the areas at highest risk for the presence of the tick.

Results of this study showed no positive blood donor in Québec and six positive donors in Canada (four in Ontario and one in Manitoba, none of whom had a history of travel). These results indicate that this pathogen does not pose a threat to transfusion safety in Québec and that there is no need at the moment to implement specific measures to prevent transmission through transfusion.

In addition to this study, we are taking part in another modelling launched in Canada in collaboration with CBS, Public Health Canada, and Johns Hopkins University to assess the risks of transmission of babesiosis through transfusion.

Hepatitis E Virus — risk-based decision making

The Hepatitis E virus (HEV) is transmitted mainly through the ingestion of inadequately cooked meat, the consumption of contaminated water, and much more rarely through blood transfusion. In healthy individuals, this does not result in a serious infection. However, it could cause serious complications for some populations of recipients at risk. Two studies have already been conducted in collaboration with CBS to determine if the frequency of this infection in blood donors in Canada would justify additional measures to protect the blood supply. During the 2019–2020 fiscal year, we took part in risk-based decision making (RBDM) held by CBS as part of the evaluation of the risk posed by the HEV. This process is rooted in the 2016–2017 study of HEV prevalence among blood donors. One of two HEV screening scenarios was performed. The study's conclusions showed that the prevalence of Hepatitis E is lower in North America than in countries that screen for HVE and that, if a screening test were added, the projected costs would be disproportional to the expected benefits. Following the RBDM process, it was decided not to add the test but, instead, to raise awareness among the medical community while continuing surveillance of this pathogen.

Héma-Québec took part in a seroprevalence study in collaboration with Canadian Blood Services and the American Red Cross to evaluate the extent of babesiosis in Canada and the urgency of taking preventative measures to protect recipients of blood products.

West Nile Virus

Neurological forms of West Nile virus (WNV) infection sometimes go unrecognized by clinicians. In 2018, in collaboration with public health authorities, we evaluated the rate of under-recognition of this neurological disease, using prevalence data of infection detected in blood donors. The study showed a significant reduction in this rate compared with the previous epidemic of 2012.

Biomedical Excellence for Safer Transfusion

We took part in two projects by Biomedical Excellence for Safer Transfusion (BEST) related to HIV. The focus of the first project was a comparison of the rates of incidence, prevalence, and positive tests for nucleic acid (NA), which were negative in serology tests for HIV between various authorities. We received data from 13 authorities and began analyzing them. The focus of the second project was an international comparison of the sexual habits of blood donors within the framework of relaxed criteria for MSM donors. The aim of the project was to compare the percentage of donors who reported risky sexual behaviour between the participating countries and the percentage of donors who felt uncomfortable answering these questions. This project was a follow-up to a similar survey conducted in Canada in 2018. Five centres were recruited in Canada, England, the Netherlands, and Denmark.

Héma-Québec's teams also contributed to the work of BEST into the effect of the age and sex of first-time donors on their rate of return. Results show the impact sex and age had on the rate of return of first-time donors, with women having a higher rate of return than men, and older and young donors having a higher rate of return than donors in the median age group.

We are also involved in the BEST project comparing hemoglobin eligibility criteria and exclusion rates due to low hemoglobin between several authorities. Results indicate that differences in eligibility criteria, especially longer minimum wait times between donations and the taking of iron supplements by women, are associated with a lower exclusion rate for low hemoglobin levels.


MONIT

ORING

THE ENVIRONMENT OF OUR ACTIVITIES

Bench test

Using a bench test enables us to establish special collaborations with companies operating in our various activity sectors. The latter encourages us to keep a forward-thinking connection to the discovery, assessment and development of innovative techniques and products, and remain at the cutting edge of technology and industry best practices. The expertise and equipment available from the offices of our vice presidents also puts us in an advantageous position through the bench test service we offer to outside clients. During the past year, we tested technology to measure the deformability of red blood cells in a microfluid system. This technology, developed by Hemanext (formerly New Health Sciences, headquartered in Lexington, Massachusetts), could eventually be adopted by suppliers of blood components who are always searching for significant reliable indicators of the quality of red blood cells.

Activity sectors

Scientific surveillance is done in direct link with our activity sectors, i.e., labile blood products, stable products, human tissues, and mother's milk. The environment of the RSCL's activities is also monitored, more specifically serology tests, genotyping, red blood cell antigens, leukocyte antigens, platelets, rare blood, and in vitro production of red blood cells. The scientific field of stem cells from cord blood and adult blood is also part of our areas of interest.

By drawing on the best publicly accessible information resources, surveillance also enables us to track signs or indices that reveal major changes.

Practices

The various sectors of our organization are players in the monitoring process. At Medical Affairs and Innovation, surveillance of our environment and associated practices is part of our culture, through medical monitoring, which guarantees the safety of blood donors and recipients, and scientific monitoring, which is indispensable to innovation and leading-edge research for the benefit of the community. At various levels, be it scientific or medical teams, monitoring is done in successive stages: knowledge of one's environment or field, selection of themes and surveillance subjects, use of surveillance tools and automatic alerts if necessary, information analysis, and dissemination of content.

Persons in the field or who have the appropriate expertise can contribute to choosing information deemed to be important, put it into perspective and forward it in an adapted format up the ladder to the various levels of the organization.

Surveillance platform

Out of our analysis of monitoring practices by sector came possible improvements, especially methods for disseminating and sharing surveillance. Actions were also taken with our Information Technology colleagues to put in place a dedicated platform integrated into our Intranet.

One of the targeted goals of the platform is to reduce the silo effect and make monitoring a means of communication between teams, divisions, and offices of vice presidents, so that information can flow and be accessible in a lasting way, and that all members can derive benefits beyond the capacity of existing electronic messaging systems.

This platform's operating principle is that information posted on it is accessible to all. These posts are the responsibility of the contributors who disseminate it.

The platform became operational in 2019, after a pilot trial phase. Within a year, 64 monitoring posts were drafted by many contributors from Medical Affairs and Innovation, and Regulatory Affairs in 15 different categories associated with our activities and product lines. Several hundred one-time visitors consulted many thousands of pages over a 12-month period.

Organizational monitoring contributes to a broader sharing of information from experts or specialized analyses through a structured digital platform integrated into the organization.

Risk management

Managing biological risks

Human immunodeficiency virus (HIV), the agent responsible for acquired immunodeficiency syndrome (AIDS), was the first emerging infectious disease (EID) to have a major impact on the safety of blood products. The lessons learned from this epidemic made us aware of the need to be alert to emerging infections that could have repercussions on the safety of the supply system of blood products.

The objective of biological risk management at Héma-Québec is to provide all the necessary tools to recognize, describe, and prioritize the pathogens that present a real or potential risk of transmission through transfusion (as well as for stem cells, human tissues, and mother's milk), and to quantify these risks.

To ensure proactive biological risk management, systemic monitoring and surveillance of emerging pathogens that could threaten and harm the safety of recipients was implemented.

A list of pathogens under surveillance is updated monthly, and trends regarding these pathogens and the updating of the table are discussed with the medical people in charge. This list is

presented periodically to Héma-Québec's Board of Directors, as well as to the Safety Advisory Committee.

Emerging pathogens present in our local and international environment are tracked through epidemiological bulletins, information databases, and social networks and media.

Finally, we monitor trends for diseases that require mandatory reporting to Quebec Public Health authorities (MADO) and that can pose a threat to transfusion safety.

Risk management participation in the organization

Medical Affairs and Innovation actively participates, with other offices of vice presidents, in the integrated risk management process. In close collaboration with the Division of Integrated Risk Management, we are responsible for identifying, assessing, handling, and following up risks related to pathogens and toxins used in the context of research, as well as risks associated with products and donors.


PURSUING
BUSINESS
DEVELOPMENT
EF


FORTS

Patent and commercialization

Combining mild hyperthermia and UM171: pursuing national and regional requests

In 2015, a research team from the Division of Innovation discovered that mild hyperthermia (cultured at 39°C) and certain pyrimidine composites had a synergistic effect on the proliferation of hematopoietic stem cells. In a culture medium favourable to megakaryocyte differentiation, the synergistic effect between mild hyperthermia and the pyrimidines was even stronger. Since this discovery was deemed to be patentable while having promising commercialization potential, three provisional patent applications asserting this invention were filed in the United States, i.e., two in June 2015 and one in May 2016. An international patent application asserting the priority of these three provisional American applications were filed in June 2016. In December 2017, national and regional phases were filed in Canada, the United States, Europe, Japan, South Korea, Australia, New Zealand, Israel, Singapore, China, and Hong Kong. These national and regional applications are currently under review. The review process is moving forward smoothly: we are awaiting the granting of some patents in 2020–2021.

Commercialization

We contacted some organizations that were likely to be interested in acquiring a licence to use this patented technology. Preliminary talks were held with two of them. Medical Affairs and Innovation will be on the lookout for new opportunities to commercialize this patented technology.


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REACH

External outreach — the dissemination of knowledge acquired throughout the exploratory or applied research process — is often the final stage of all research and development.

Since the fundamental part of research at Héma-Québec takes place in Medical Affairs and Innovation, it is logical that this vice president office contributes significantly to the organization's scientific outreach.

Following the merger of the vice presidents of Medical Affairs and Research and Development offices in 2017, external outreach was consolidated within a single administrative unit. This consolidation resulted in the introduction of data entry, compilation, and outreach dissemination tools to better coordinate and promote this activity.

Internal outreach

Transfer of internal knowledge

Many tools and communication channels are used to transfer knowledge arising out of the research work of Medical Affairs and Innovation for the benefit of the entire organization. Beyond the results of their research work, researchers contribute to the continuous education of staff from other sectors of the organization by organizing training sessions for them. During 2019–2020, two training sessions were offered by research staff to colleagues in other divisions. Employees of the Laval GLOBULE Centre received training on the characterization of granulocytes destined for transfusion. A second training session, held in conjunction with the Division of Human Tissues Day, explained the NovaSterilis technology evaluation process as a method of cleaning and sterilizing musculoskeletal tissues. In addition to these training sessions, and recently implemented tools and communication channels, is a wealth of information from international and external sources made available to Héma-Québec's employees. These tools are described in greater detail in the "Surveillance platform" and "Internal communications" sections, and "@lexandrie."

Internal communications

Héma-Québec employees have access to many communication venues and platforms, on which Medical Affairs and Innovation staff provide content. These tools include, among other things, Les Mots d'Héma plus, the online journal of Héma-Québec staff, accessible through I@rtère. In addition to this, Medical Affairs and Innovation regularly organizes lunchtime talks, titled the "Rendez-vous curieux des Affaires médicales et innovation". Invited speakers are drawn from Héma-Québec staff or from outside the organization. In the case of internal speakers, the lunch-hour "Rendez-vous curieux" is an opportunity for staff to introduce fellow Héma-Québec employees to their mandate, work team, and colleagues' achievements. External speakers are generally scientific researchers who present their work, stimulate knowledge sharing, and encourage outside collaborations. The "Rendez-vous curieux" take place at our Quebec City or Montréal facilities and are broadcast live on the Web for all the facilities' employees, thereby providing access to as many as possible. An audio recording of most of the presentations is also made and uploaded to C@AMPUS, the online learning platform that is also accessible through I@rtère. The increasing use of digital tools is part of an effort to tap into the full potential of these new technologies and foster effective communication to the greatest number of employees.

Developing digital tools

@lexandrie

For many years, the Office of the Vice President, Medical Affairs and Innovation has compiled information on an ongoing basis, for use in Héma-Québec's outreach activities. This includes published scientific articles, guest lectures, convention presentations, internal reports, patents, external funding, outside collaborations, and edited manuscripts and funding or grant requests. Up to now, this information was collected in a simple Excel file, with the various outreach elements arranged in tabs. This method is efficient for compiling general statistics and preparing related documents, such as annual reports and five-year statements.

The ongoing entry of information into this file led to the development of I@rtère, a repository for a growing number of outreach documents, accessible to all employees. We soon realized that there was information overlap in the Excel file and in I@rtère, and a duplication of data entry tasks. In short, there was room for improvement and efficiency gains in the data entry and dissemination process. In collaboration with the Office of the Vice President, Information Technology and Digital Strategy, the team from Epidemiology, Surveillance and Biological Risk Management worked on designing a digital tool in which the data entry and consultation functions were centralized. Out of this thinking and testing came @lexandrie, a virtual library that assembles and centralizes the fundamental elements of Héma-Québec's outreach. Running SharePoint in the background and accessible through I@rtère, this platform makes it possible to enter, filter and compile data, and access original documents. The official deployment of this virtual library is planned for the coming months. Training sessions will be held for all employees who will be tasked with inputting information and consulting @lexandrie. As well as providing Héma-Québec's staff with ready access to information, @lexandrie will eliminate the duplication of tasks and increase efficiency.

Internal reports

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Laforce-Lavoie A, Ducas É, de Grandmont MJ, Cloutier M. Volume maximal de prélèvement et suivi de température du traitement de tissus cutanés (GEO-158/33208). Final report presented to Étienne Fissette (Devision of Human Tissues Operations, Office of the Vice President, Medical Affairs and Innovation), May 2, 2019.

Boyer L, Brouard D. Évaluation du système thermorégulateur ITEGA pour le transport de tubes de prélèvements à 2–8 °C (GEO-111/33064). Final report presented to France Bernier (Division of Product Qualification, Office of the Vice President, Quality and Development), May 3, 2019.

Allard MÈ. Détermination de la tar e du dispositif de prélèvement de plasma sur PCS2 (GEO111/2019J). Final report presented to Kheng Ly Oueng (Division of Projects and Compliance, Office of the Vice President, Blood Products and Mother's Milk), May 7, 2019.

Cayer MP, de Grandmont MJ, Nolin MÈ, Brouard D. Essais de performance du dispositif de prélèvement T5 proposé par la compagnie Macopharma. Impact sur la qualité du plasma (GEO-147B/33240). Final report presented to Luc Lévesque (Office of the Vice President, Blood Products and Mother's Milk), May 7, 2019.

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Ducas É, Laforce-Lavoie A, Cloutier M. Caractérisation du support refroidissant pour les allogreffes cutanées (GEO-158/33208). Final report presented to Étienne Fissette (Division of Human Tissues Operations, Office of the Vice President, Medical Affairs and Innovation), August 14, 2019.

Cayer MP, de Grandmont MJ, Girard M. Optimisation de la récupération des granulocytes avec l'utilisation de l'agent de sédimentation VoluvenMD (GEO-111/2019P/33064). Final report presented to Alexandre Beaudry (Division of Permanent Centre and Mobile Blood Drive Operations, Office of the Vice President, Blood Products and Mother's Milk), September 6, 2019.

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Girard M, Gaussen A. Fortification du lait maternel – État de la situation. Final report presented to Pierre Noël (Office of the Vice President, Blood Products and Mother's Milk), November 6, 2019.

Cayer MP, de Grandmont MJ, Fournier MJ, Brouard D. Évaluation de la performance de l'appareil ADAM-rWBC2MC pour le dénombrement des leucocytes résiduels dans les produits sanguins (GEO-168/33302). Final report presented to Diane Fournier (Division of the Stem Cell Donor Registry and Reference and Stem cell Laboratories, Office of the Vice President, Medical Affairs and Innovation), November 8, 2019.

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Conferences, convention presentations, workshop facilitation

Users Committee, March 3, 2019 and April 17, 2019

Lecture by invitation

Bonnaure G. "La leucoréduction de nos produits : une source de cellules pour l'immunothérapie."

2019 CACMID-AMMI Canada Annual Conference, Ottawa, Canada, April 3–6, 2019

Poster

Lewin A. « Banked human ingestion and Bacillus cereus infection in preterm: Case reports ».

2019 Annual Conference of the Canadian Society for Transfusion Medicine (CSTM), Calgary, Canada, May 30–June 2, 2019

Lectures by invitation

Cayer MP, Fournier MJ, de Grandmont MJ, Brouard D. « Characterization of the NanoEnTek ADAM-rWBC2 performances for residual white blood cell quantification in leukoreduced blood components ».

Cloutier M. « Aggregates in apheresis platelet concentrates: Can it be predicted from the donor's history? ».

Girard M, Fernandes M. « Granulocytes, this unknown and misunderstood blood product ».

Rhéaume MÈ, Rouleau P, Tremblay T, Loubaki L. « Shortterm exposure of umbilical cord blood CD34+ cells to human platelet lysate and cytokines enhances engraftment ».

Robidoux J, Yoshida T, Wolf M, Shevkoplyas S, Brouard D. « Red blood cell deformability: Development of a microfluidic device to characterize red blood cell deformability ».

Robitaille N. « RhD determination: Quebec's experience ».

Posters

Boyer L, Allard MÈ, Fournier MJ, de Grandmont MJ, Brouard D. « Thermoregulation container for blood component logistics operations: A shelf life and performance study ».

Cayer MP, de Grandmont MJ, Fournier MJ, Kim MS, Lee HS, Jacques A, Brouard D. « Performances of the NanoEnTek ADAM-rWBC2 in residual white blood cell quantification in leukoreduced blood components ».

Laforce-Lavoie A, de Grandmont MJ, Constanzo-Yanez J, Allaire N, Loiselle S, Bourgoin L, Robitaille N, Cloutier M. « Processing red blood cell products obtained from sickle-cell trait donors with the ACP 215 ».

Ramirez-Arcos S, Allen J, Bhakta V, Bower L, Cardigan R, Girard M, Howell A, Kou Y, McDonald C, Nolin MÈ, Sawicka D, Sheffield W. « Challenging the 30-minute rule for thawed plasma ».

Robidoux J, Laforce-Lavoie A, Brouard D. « Red blood cell deformability: proof-of-concept study of a microfluidic method to characterize red cell concentrates derived from various processing methods ».

Tremblay T, Loubaki L. « Daudi stroma to eliminate anti-CD38: Related interference in pretransfusion testing ».

29th Regional Congress of the ISBT, Bâle, Suisse, June 22–26, 2019

Oral presentations

Ramirez-Arcos S, Allen J, Bhakta V, Bower L, Cardigan R, Girard M, Howell A, Kou Y, McDonald C, Nolin MÈ, Sawicka D, Sheffield W.« Challenging the 30-minute rule for thawed plasma ».

Lewin A, Grégoire Y, Houle-Aubé « TT-HIV and the use of pathogen reduction technology. New approach for deferral of plasma MSM donor ».

Poster

Grégoire Y. « Estimated residual risk of HIV with a three-month deferral for men who have sex with men in Canada ».

WMDA-NetCord & FACT Cord Blood Day, 2019 Cord Blood Connect Congress, Miami Beach, United States, September 12, 2019

Lecture by invitation

Delage G. "Cord blood transplantation and emerging pathogens. Is there reason for concern?"

Cord Blood Connect, Miami, United States, September 13–15, 2019

Posters

Simard C, Trépanier P, Néron S, Fournier D. « Rapid determination of potency in cord blood and in mobilized peripheral blood stem cells by flow cytometry ».

Fournier D. « What's in The Bag: Cord Blood Unit Potency Assessment Using a Novel Rapid Flow Cytometry Assay ».

Maheux A. « Validation of the MacoPress SMART for Volume Reduction of Cord Blood Units at Héma-Québec's Cord Blood Bank ».

BBTS Annual Conference 2019, Harrogate, United Kingdom, September 18–20, 2019

Poster

Allen J, Sawicka D, Maddox V, Ramirez-Arcos S, Howell A, Girard M, Nolin MÈ, Bhakta V, Bower L, Cardigan R, Kou Y, Sheffield W, McDonald C. « Applying the 30-minute rule to plasma products: Do room temperature exposures increase bacterial risk? ».

AABB Annual Meeting, San Antonio, United States, October 19–22, 2019

Lecture by invitation

Delage G. « bioMérieux Product & Innovation Theater. Delayed-sampling large-volume culture of platelets: Experience of one blood establishment ».

Posters

Baillargeon N, Éthier C, Robitaille N, Constanzo-Yanez J, Boileau M, Parent C, Lavoie J. « Anti-Hr0 identified during pregnancy: A case study ».

Cayer MP, de Grandmont MJ, Fournier MJ, Kim MS, Lee HS, Brouard D. « Performance evaluation of the ADAM-rWBC2 for the quantification of residual leukocytes in RBC and platelet concentrates ».

Drews SJ, Stramer SL, Proctor MC, Tonnetti L, Bres V, Linnen JM, Bernier F, Delage G, Gaziano T, Grégoire Y, Labrie J, Bigham M, Hawes G, Scalia V, Fearon M, O'Brien SF. « Use of laboratory data and recipient outcomes to determine case classification in five Canadian blood donors with reactive Babesia laboratory results ».

Ducas É, Cayer MP, de Grandmont MJ, Cloutier M. « A scoring system for platelet aggregates: Get your apheresis platelet concentrates back on the fast track ».

Laforce-Lavoie A, de Grandmont MJ, Constanzo-Yanez J, Allaire N, Loiselle S, Robitaille N, Cloutier M. « Sickle-cell trait donors: Can we process red blood cell products with the ACP 215? ».

O'Brien SF, Roy É, Myhal G, Goldman M, Osmond L, Robillard P. « Men who have sex with men: Are alternative risk-targeting questions practical? ».

Rhéaume MÈ, Rouleau P, Tremblay T, Loubaki L. « Short-term exposure of umbilical cord blood CD34+ cells to human platelet lysate and cytokines enhances engraftment ».

Robidoux J, Brouard D. « Red blood cell deformability as a quality marker to distinguish whole blood processing methods ».

Tremblay T, Loubaki L. « Daudi stroma to eliminate anti-CD38: Related interference in pretransfusion testing ».

Baillargeon N, Éthier C, Robitaille N, Constanzo-Yanez J, Boileau M, Parent C, Lavoie J. « Anti-Hr0 Identified During Pregnancy: A Case Study ».

51st Congress of the International Society of Paediatric Oncology (SIOP), Lyon, France, October 23–26, 2019

Poster

Arbitre C, Gaucher N, D.Trottier ED, Bourque CJ, Darilus J, Sanon PN, NDabirabe L, Robitaille N, Pastore Y « Patients' and Caregivers' experience with pain management in children and teenagers with Sickle Cell Disease requiring admission for vaso-occlusive crisis ».

Pédiatrie de 1re ligne, Montréal, Canada, November 20, 2019

Lecture by invitation

Robitaille N. "Urgences hématologiques."

61st ASH Annual Meeting & Exposition, Orlando, United States, December 7–10, 2019

Oral presentation

Azouzi S, Mikdar M, Hermand-Tournamille P, Gautier ÉF, Salnot V, Willemetz A, Nicolas G, Vrignaud C, Raneri A, Mayeux P, Bole-Feysot C, Nitschke P, Cartron JP, Colin Aronovicz Y, Hermine O, Jedlitscky G, Cloutier M, Constanzo-Yanez J, Éthier C, Robitaille N, St-Louis M, Le Van Kim C, Peyrard T. « The multidrug transporter MRP4/ABCC4 involved in the leukemia clinical course specifies the novel PEL human blood group system ».

2020 ABC Annual Meeting, Arlington, United States, March 9–11, 2020

Lecture by invitation

Delage G. "How we do risk management at Héma-Québec."

Patents granted, retained and current, and patent requests retained and under review

"A new method of expanding cord blood cells." Patents granted in Canada (CA2562760C), the United States (US7452662B2) and Europe (EP1743024B1; validated in Germany, France, and the United Kingdom). Dupuis N, Proulx C, inventors. Héma-Québec, assignee. Expiry: 04-25-2025.

"Method for polyclonal immunoglobulin production by human B cells." Patents granted in Canada (CA2738176C) and the United States (US8703486B2). Néron S, Roy A, Fecteau JF, inventors. Héma-Québec and Université Laval, assignees. Expiry: 08-17-2029.

"Rapid cooling to and maintaining of whole blood at 20 to 24°C for processing." Patents granted in Canada (CA2770657C) and the United States (US8192924B1); application under review in Europe (issued under EP2514308A3). Barakat M, Thibault L, Haarmann KH, Beauséjour A, Alleva A, Tremblay M, Lapointe S, inventors. TCP Reliable Inc., Héma-Québec, assignees. Expiry: 10-17-2031.

"Fabricating a phase change blood cooling system." Patent request to extend Patent US8349552B1, granted in the United States (US8802364B2). Haarmann KH, Alleva A, Bringas TL, Thibault L, Beauséjour A, Tremblay M, inventors. TCP Reliable Inc., Héma-Québec, assignees. Expiry: 10-17-2031.

"Extracellular mitochondrial components for detecting inflammatory reactions and conditions." Patent granted in the United States (US9945853B2). Boilard É, Boudreau L, Thibault L, Gelb MH, inventors. Université Laval, Héma-Québec, University of Washington, assignees. Expiry: 10-10-2034.

"Methods for culturing and/or differentiating hematopoietic stem cells into progenitors and uses thereof." Patent applications under review in Canada (issued under CA2987974A1), the United States (issued under US2018147239A1), Europe (issued under EP3303570A1), Japan (issued under JP2018516089A), South Korea (issued under KR20180023947A), Australia (issued under AU2016273439A1), New Zealand (issued under NZ738216), Israel (issued under IL256093), Singapore (issued under SG11201710067U), China (issued under CN107922926A), and Hong Kong (issued under HK1253792). Laganière J, Dumont N, inventors. Héma-Québec, assignee. Expiry of patents eventually granted: 06-03-2036.

Commitment to the scientific and medial community

As a national supplier of blood components, Héma-Québec actively participates in and collaborates on committees, stakeholder groups, and national and international associations concerning blood, transfusion medicine and stem cells. These groups include, among others, the National Advisory Committee on Transfusion Medicine (NACTM), the Recipient Epidemiology and Donor Evaluation Study (REDS), the International Society of Blood Transfusion (ISBT) (in particular the Transfusion-Transmitted Infectious Diseases – Surveillance, Risk Assessment & Policy (TTID-SRAP) subgroup), the Foundation for the Accreditation of Cellular Therapy (FACT), the AABB, the World Marrow Donor Association (WMDA), the Biomedical Excellence for Safer Transfusion (BEST) Collaborative, the Canadian Standards Association (CSA Group), the ThéCell Network, the Canadian Donation and Transplantation Research Program (CDTRP), and Canadian Blood Services (CBS). Many Héma-Québec representatives who sit on these entities come from the Office of the Vice President, Medical Affairs and Innovation, which is a testimony to the commitment of this office's staff to the community of experts interested in Héma-Québec's product lines and activities.

Commitment to the university community

University affiliations

Some Medical Affairs and Innovation staff members are adjunct professors at Québec universities, where they oversee the work of master's and PhD students. At present, five Office of the Vice President members are adjunct professors at Université Laval, i.e., four in the department of biochemistry, microbiology and bioinformatics, and one in the department of chemistry. Another Medical Affairs and Innovation staff member is affiliated with the department of obstetrics and gynecology at Université de Sherbrooke, while a member of the transfusion medicine team is a clinical associate professor in the department of pediatrics at Université de Montréal. These affiliations ensure synergy and promote collaboration between Héma-Québec and the Québec university community.

Mentoring students and interns

The Office of the Vice President, Medical Affairs and Innovation plays a central role in Héma-Québec's mandate to train the next generation of specialists in the biology of blood and its components, human tissues, stem cells, and mother's milk. As such, this office takes an active role in mentoring students and interns. In the past year, its staff has overseen the work of seven master's and PhD students, and two postdoctoral interns. Students from various teaching institutions in Québec and elsewhere are also regularly welcomed into our laboratories to complete an internship as part of the requirements of their studies program. In 2019–2020, Medical Affairs and Innovation enabled four students to complete an internship in its research laboratory.

Medical Affairs and Innovation also welcomed three physicians who were taking specialized training in transfusion medicine.

University courses

Girard M, Loubaki L. "La greffe de cellules souches." Training offered to students as part of the "MCB-4016 – Immunologie et pathogenèse microbienne" course in the department of biochemistry, microbiology and bioinformatics, faculty of sciences and engineering, Université Laval, November 29, 2019.

Antoine Lewin teaches a seminar in biostatistics in the department of obstetrics and gynecology at Université de Sherbrooke.

Nancy Robitaille has taught courses on sickle cell anemia and IVIG use for hemolytic disease of the newborn to Université de Montréal residents. She is also a contributor to the pediatric hematology-oncology residency program and the pediatric intensive care residency program, teaching the theories of apheresis and sickle cell anemia and severe complications.

Funded research projects

$710,985 research grant from the Canadian Institutes of Health Research (CIHR) to Alexey V. Pshezhetsky (lead investigator) and Renée Bazin (co-investigator), valid from 2017 to 2022.

$45,000 research grant from the MITACS Accelerate Fellowship to Jean-Sébastien Delisle (Hôpital Maisonneuve-Rosemont) (lead investigator) and Sonia Néron (co-investigator), valid from June 1, 2018 to May 1, 2020.

$14,994 research grant from the Foundation of Stars to Jean-Charles Pasquier (lead investigator) and Antoine Lewin (co-investigator), valid from September 1, 2018 to September 1, 2019.

$39,618 grant from the MSM Research Program (Canadian Blood Services (CBS)) to Antoine Lewin (lead investigator), valid from January 3, 2019 to March 19, 2021.

$30,000 grant from the Blood Efficiency Accelerator Program (Canadian Blood Services (CBS)) to Maria Fernandes (Centre de recherche du CHU de Québec) (lead investigator) and Mélissa Girard (co-investigator), valid from February 1, 2019 to February 1, 2020.

$30,000 research grant from the MITACS Accelerate Fellowship to Éric Biron (lead investigator) and Lionel Loubaki (co-investigator), valid from May 1, 2019 to June 30, 2021.

$30,000 research grant from the MITACS Accelerate Fellowship to Maria Fernandes (Centre de recherche du CHU de Québec) (lead investigator) and Mélissa Girard (co-investigator), valid from September 1, 2019 to August 1, 2021.

$100,000 research grant from the Canadian Institutes of Health Research (CIHR) to Nathalie Auger (lead investigator) and Antoine Lewin (co-investigator), valid from October 10, 2019 to October 10, 2020.

$10,000 research grant from MSM Knowledge Mobilization Funding (Canadian Blood Services (CBS)) to Antoine Lewin (lead investigator), valid from March 20, 2020 to March 21, 2021.

$189,900 research grant from the Canadian Institutes of Health Research (CIHR), Project Scheme to Jacques Lacroix, Marisa Tucci, Simon Stanworth, and Stéphane Leteurtre (lead investigators) and Nancy Robitaille (co-investigator), valid from July 1, 2019 to June 30, 2020.

This report is published by the Office of the Vice President, Medical Affairs and Innovation.

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February 2021