NATIONAL BLOOD AUTHORITY
AUSTRALIA

Monitoring International Trends

July – September 2022

The NBA monitors international developments that may influence the management of blood and blood products in Australia including but not limited to:

- potential new product developments and applications
- global regulatory and blood practice trends
- events that may have an impact on global supply, demand and pricing
- emerging risks and relevant issues.

The following key topics have appeared in news media, online publications, industry, and research updates and have been included in this report:

Blood supply: The deferral of previous UK residents from donating blood due to concerns of infection with Bovine Spongiform Encephalopathy (mad cow disease) ceased on the 26 July 2022. Since then, the Australian Red Cross Lifeblood has confirmed almost 21,000 people have booked in for their first blood donation. The US Food & Drug Administration (FDA) has also amended its blood donation recommendations relating to the potential risk of infection from previous residents of the UK, France and Ireland.

Blood disorders: Roche have announced the primary analysis of a phase 3 study which showed that emicizumab (Hemlibra) continues to demonstrate a favourable safety profile and effective bleed control in people with moderate or mild haemophilia A.

Transfusion: Studies in the UK and Finland looked at ways to address shortages of Group O RhD-negative red blood cells (RBCs). The UK study looked at the impact of three pre-hospital transfusion strategies (RhD-negative RBCs, RhD-positive RBCs and no transfusion) on the quality-adjusted-life-years of trauma patients, with particular focus on RhD-negative females under 50 years of age. The Finnish study sought to identify areas where policy changes could alleviate the shortage.

Product Management: Researchers tested a novel method to extend platelet storage using xenon gas (Xe) under high pressure and refrigeration and found that storage with the storage method could feasibly extend platelet storage to 14 days.

Immunoglobulin: A systematic review evaluated the efficacy of intravenous immunoglobulin for the treatment of recurrent spontaneous abortion.

Gene therapy: The recent approval of two gene therapies BioMarin's Roctavian (for haemophilia A) in the EU and Bluebird Bio's Zynteglo (for beta thalassemia) in the US, have highlighted the costs associated with outcomes-based pricing models for longer lasting gene therapies.

COVID-19: The National Cabinet agreed to end mandatory isolation for people who test positive for COVID-19 from 14 October 2022. The decision came after the Australian Chief Medical Officer advised that the combination of high vaccination rates, immunity from infections and reduced case numbers suggested there was no longer a need for an enforced period of isolation.

Other items of interest: Successful applicants under the *Medical Research Future Fund (MRFF) 2021 Research and Data Infrastructure Grant Opportunity and 2021 Optimising the Clinical Use of Immunoglobulins Grant Opportunity* were confirmed Allocations included $2.9 million for the Monash University National Transfusion Dataset Team to expand the national transfusion dataset (NTD) from five to approximately 20 hospitals nationally. The program will link data to provide a more comprehensive view of transfusion practice and outcomes.

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Contents

1 Blood supply

This section contains news articles and government agency statements on blood supply in Australia and around the world.

1.1 Blood supply - Australia

The deferral of previous UK residents from donating blood due to concerns of infection with Bovine Spongiform Encephalopathy (BSE or "mad cow disease") ceased on 26 July 2022. Australian Red Cross Lifeblood confirmed almost 21,000 people booked in for their first donation since the removal of deferral rules.

- Grass becomes greener for Australian blood and plasma supplies as thousands of former UK residents step up to donate
- Evidence shows virtually zero risk of 'mad cow' from blood donations in Australia
- Lifeblood: A rare request beyond borders
- Urgent call for blood donors
- Lifeblood: Change to pooled platelet components

1.2 Blood supply – United States

The US FDA has removed the indefinite deferral for donors possibly exposed to Creutzfeldt-Jakob disease through time spent in the UK from 1980-1996, France and Ireland from 1980-2001.

- FDA: Recommendations to reduce the possible risk of transmission of Creutzfeldt-Jakob disease and variant Creutzfeldt-Jakob disease by blood and blood components
- Thousands more people eligible to donate blood after FDA makes historic change to donor regulations
- Blood conservation strategies at United States hospitals during the COVID-19 pandemic
- Celebrating a major upgrade coming to CSL Plasma centres
- HHS announces new campaign to increase U.S. blood and plasma donations

1.3 Blood supply - World news

The European Commission has proposed new rules for donating or receiving vital substances of human origin including blood products, tissues and cells. The new regulation aims to facilitate cross-border circulation of these health products.

The Canadian Blood Service signed a commercial agreement with pharmaceutical company Grifols. The agreement will see the first renumerated collection of blood products in Canada since the creation of the Canadian Blood Service in 1998.

- Europe: EU proposes new blood, tissues and cells regulation
- UK: First-ever amber alert issued by NHS over blood supplies as they fall critically low
- Canada: Grifols enters into agreement with Canadian Blood Services to accelerate self-sufficiency in immunoglobulins for Canada
- Nepal: Spike in dengue cases leads to acute blood shortages
- China: Two persons with rarest 'Golden Blood' found in East China

1.4 Regulatory and donation criteria

Blood donor notification of variant Creutzfeldt–Jakob disease risk: Lessons in communicating donor deferral and risk

In 2005, the blood service in England notified 101 donors by letter that they may be at risk of variant Creutzfeldt–Jakob disease (vCJD) because a recipient of their blood later developed vCJD. This study looked at the donors' responses and continuing attitudes four years later, highlighting the need for ongoing support in donor notifications.

Blood donation behaviour and attitudes towards the 12-month deferral policy among gay and bisexual men in New Zealand

Researchers in New Zealand explored interest in blood donation among gay and bisexual men, including attitudes towards donor deferral policies. An estimated 10% of the sample did not report compliance with the 12-month deferral policy in New Zealand for men who have sex with men. They found that negative attitudes towards the deferral policy were common and noted that there could be a potential increase in the risk to the blood supply if compliance reduced further.

Blood conservation strategies at United States hospitals during the COVID-19 pandemic: Findings from a multi-institutional analysis

Researchers sent an anonymous survey to transfusion medicine specialists across the United States to determine the extent of conservation strategies across the country during the COVID-19 pandemic. Respondents to the survey reported a product shortage in 98% of responses, with 90% of respondents reporting red blood cell shortages. This led to 35.3% of responding institutions altering the composition and/or number of blood product suppliers, and an 100% increase in the number of institutions acquiring blood from organisations that connect hospital transfusion services with blood collection centres.

Monkeypox and the safety of the blood supply

This study investigated the presence of the monkeypox virus in blood components, to measure the risk of infection from otherwise qualified donors. The found that the impact of universal leukoreduction is unknown but noted that disease transmission by intravenous inoculation has been observed in animals, including nonhuman primate models. Researchers suggest that it may be necessary to use specific questions to determine exposure to monkeypox during donor screening.

"Please help us with important research": A retrospective analysis examining the impact of research invitation and participation on subsequent blood donor behavior

Researchers compared donors who were invited to participate in one of 17 blood research projects alongside a control group who were not invited, to test the impact of participation on subsequent willingness to donate. They found that donors were significantly more likely to create an appointment within 14 days of receiving an invitation to participate in a study and were more likely to return to donate within 1-6 months. The results suggest that contacting donors for research purposes does not negatively impact blood collection or willingness to donate.

Haematological patients' perception of home transfusions: Effect of the COVID-19 pandemic

Researchers surveyed haematology patients who receive transfusions in a hospital day care facility during the COVID-19 pandemic. The survey aimed to determine the burden of day care transfusions and whether there was a preference for home transfusions among patients. Results were compared with a similar survey conducted before the pandemic. Researchers found a slight decrease in the proportion of patients willing to receive home transfusions during the pandemic while fewer patients reported that hospital transfusion impaired their quality of life.

1.5 Blood donor characteristics and donation effects

Lipid and haematologic profiling of regular blood donors

This study investigated the effect of blood donation on the health of blood donors by comparing lipid and haematological profiles of regular and first-time blood donors in the National Blood Bank Service of Ethiopia. The study looked at 104 blood samples split evenly between regularly and first-time donors and found that blood donation had a significant health benefit.

Subclinical infection occurs frequently following low dose exposure to prions by blood transfusion

Researchers used an established model of variant Creutzfeldt-Jakob disease in sheep to determine the prevalence of subclinical infection following exposure by blood transfusion from infected donors. Many recipient sheep survived for years post-transfusion, with no clinical signs and no disease-associated prion protein found in post-mortem tissue samples.

A typology of strategies that recognize, reward, and incentivize blood donation

Survey data from 1028 voluntary whole blood and plasma donors was used to determine the effect of incentives on likelihood to donate. This study was conducted in Australia as a voluntary non-remunerated blood donation jurisdiction with a single service, Lifeblood, responsible for all blood collections. Lifeblood's national donor recognition policy include milestone badges and donation certificates, as well as intermittent gifts of appreciation. Researchers were able to develop a framework to organise and synthesise findings from the existing literature to help international blood collection agencies develop recognition, reward and incentive policies that are likely to be successful.

Detection frequencies and viral load distribution of parvovirus B19 DNA in blood and plasma donations in England

Infections with human parvovirus B19 (B19V) are transmissible by blood components and plasma-derived medicines. In this study researchers investigated the level of B19V present in samples collected in England from 2017 prior to the re-introduction of plasma sourced in the United Kingdom.

Using the Health Action Process Approach to predict blood donation intentions and return behavior following a vasovagal reaction for whole blood and plasma donors

Vasovagal reactions (VVRs), such as fainting, are common acute complications related to blood donation. This study used the Health Action Process Approach to identify predictors of donation intention and returns amongst Australian whole blood and plasma donors who experienced a VVR. Researchers found that self-efficacy, positive and negative outcome expectancies, and social support were significant predictors of intentions to return.

Providing extra information increases blood donor return after deferral while offering an alternative good deed does not: Results from a field randomized controlled trial

In this study researchers investigated if offering deferred donors an alternative ‘good deed’ such as volunteering or providing them with additional information about deferral, would increase their likelihood to return after their deferral period. Researchers conducted a trial at 10 Dutch blood donation centres offering alternative good deeds after deferral but found that it did not significantly increase donor return. Providing information about the reasons for deferral increased the chances of whole blood donor return.

Explainable haemoglobin deferral predictions using machine learning models: Interpretation and consequences for the blood supply

Researchers created a model that predicts haemoglobin deferral for whole blood donors with the aim of reducing deferrals, while increasing efficiency and donor motivation. Researchers suggest a model where donors are invited when their haemoglobin levels are safe for donation. They suggest that the number of blood bank visits would increase by 15%, while deferral rates would decrease by 60%.

The effectiveness of iron education through a mobile application on donor return after deferral for low haemoglobin

This study looked at the effect of a mobile education initiative for donors deferred for low haemoglobin in Malaysia. Donors were divided equally into a control group and an intervention group. The return rate was higher in the intervention group, with 81.2% of the donors returning in the seven months of follow-up compared to 66% of the control group. Researchers found that repeat donors were most likely to return to donate, followed by those with a tertiary level of education, and those given the mobile application.

Why the majority of on-site repeat donor deferrals are completely unwarranted

Researchers aimed to determine if the practice of deferring low haemoglobin (Hb) donors was warranted given the variability in typical donor Hb levels. Historical data from 439,376 new donors in the Netherlands was collated and showed that 92% of all deferrals were unnecessary as most were within the range of expected variability. Researchers noted that measurement variability may not only result in unnecessary on-site deferrals but may also result in donations by donors that do not comply with donor eligibility criteria.

Exploring blood donation challenges in the COVID-19 pandemic

This study explored blood donation challenges in North China during the COVID-19 pandemic's first wave. Data was collected from eight blood donors, six potential donors, three blood donation station leaders, and two government officials, through semi-structured interviews. Researchers found the major challenge for blood supply was decreased blood donations, owing to lockdown restrictions and donor apprehension. Researchers noted that 'mobilisation' through social pressure alleviated supply issues but may have had a negative effect on individual attitudes towards donation.

Scientists find new set of blood types

Scientists have described the different mutations of the Er blood group antigen, including two previously unknown versions, taking the number of known genetic variations of the Er antigen to five.

2 Blood disorders and treatments

This section includes published new media, research and industry statements on the progress of blood disorder treatments across various conditions.

2.1 Haemophilia

Sanofi and Sobi present effective bleeding treatment

Pharmaceutical companies Sanofi and Sobi have presented initial results from a phase 3 study evaluating the safety, efficacy and pharmacokinetics of the factor VIII replacement therapy efanesoctocog alfa. The study found that use once weekly provided meaningful bleed protection for people with severe haemophilia.

Sanofi gets FDA priority review for haemophilia A candidate

The FDA has accepted a submission by pharmaceutical companies' Sanofi & Sobi, to prioritise the review of their haemophilia A prophylactic treatment efanesoctocog alfa. The prophylactic is the first factor VIII therapy designed to circulate in plasma independently of the von Willebrand factor, which imposes a half-life limitation on current factor VIII therapies.

New data shows improved prophylactic effectiveness with Sobi's Elocta

This 24-month multi-centre study included more than 350 participants in 45 European treatment centres who were treated with the haemophilia A prophylactic efmoroctocog alpha (Elocta). Researchers found that Elocta was well-tolerated with no inhibitors occurring, including in patients with a previous inhibitor history.

Novo Nordisk release results from haemophilia treatment study

Novo Nordisk has announced initial results from a phase 3 study evaluating the efficacy and safety of prophylactic treatment with concizumab in people living with haemophilia A or B. Concizumab is a monoclonal antibody bypass therapy, that binds tissue factor pathway inhibitor TFP1. The results showed an 86% reduction in treated spontaneous and traumatic bleeds when patients were treated with concizumab.

New data from phase III HAVEN 6 study reinforce favourable safety and efficacy profile of Roche's Hemlibra in people with moderate or mild haemophilia A

Roche announced results from a primary analysis of the phase 3 study, which show that emicizumab (Hemlibra) continued to demonstrate a favourable safety profile and effective bleed control in people with moderate or mild haemophilia A.

Real-world data on emicizumab prophylaxis in the Milan cohort

Researchers conducted an observational study of 21 patients with severe haemophilia A, with and without inhibitors, who switched to emicizumab (Hemlibra) prophylaxis at a haemophilia centre in Italy. Researchers found that Hemlibra was associated with an overall dramatic reduction in annualised bleeding rate, with no increase in the bleeding tendency at the beginning of prophylaxis.

Effect of emicizumab prophylaxis on bone and joint health markers in people with haemophilia A without factor VIII inhibitors in the HAVEN 3 study

Researchers explored the effect of emicizumab (Hemlibra) prophylaxis on bone/joint health in people with haemophilia A (PHA) without FVIII inhibitors. Researchers found some improvement in joint health markers in younger PHA and those with target joints after 48 weeks of Hemlibra, but biomarkers of bone/joint health did not show significant changes during 72 weeks of Hemlibra prophylaxis.

Surgical outcomes in people with haemophilia A taking emicizumab prophylaxis

This study investigated the impact of emicizumab (Hemlibra) prophylaxis on the surgical outcomes of people with haemophilia A (PwHA). Data from phase 3 clinical trials were pooled to provide a summary of PwHA with or without factor VIII inhibitors, receiving Hemlibra prophylaxis and undergoing surgery. The doses of FVIII concentrate or bypassing agent (rFVIIa) for treatment of post-operative bleeds following minor surgery were low, with most minor procedures performed without additional prophylactic factor concentrate. No surgery resulted in death, thrombosis, thrombotic microangiopathy or new FVIII inhibitor development.

Emicizumab in children: bleeding episodes and outcome before and after transition to Emicizumab

Researchers investigated the effect of switching to emicizumab (Hemlibra) on 13 paediatric patients with haemophilia A. They found that Hemlibra was safe and effective in children with haemophilia A, including those who had received minimal or no previous treatment.

Emicizumab for the treatment of acquired haemophilia A

This study reviewed the results of 11 acquired haemophilia A (AHA) patients treated with emicizumab (Hemlibra), in conjunction with rituximab (Rituxan) for four weeks at a single US institute. After an average follow-up period of 14 months, eight patients had achieved complete remission, two patients achieved a partial remission, and one patient experienced a recurrence of the disease.

Fitusiran prophylaxis leads to 61% reduction in bleeds among people with haemophilia A or B

Research results into the haemophilia prophylactic fitusiran (Alnylam) found that monthly treatment resulted in significantly fewer bleeding episodes compared with episodic-based on-demand treatment among males with haemophilia A or B. Almost two-thirds of participants in the phase 3 study had no treated bleeds while receiving the treatment.

Exercise capacity in people with haemophilia: A systematic review

Researchers conducted a systematic review to analyse the exercise capacity of people with haemophilia (PWH), as measured in standardised laboratory or field tests. They found that that PWH have lower exercise capacity but noted the necessity of emphasising exercise in treatment.

Switching from standard to extended half-life FVIII prophylaxis in haemophilia A: Comparison of factor product use, bleed rates and pharmacokinetics

This study compared the clinical and laboratory outcomes between standard (SHL) and extended half-life (EHL) FVIII prophylaxis. The study included 38 patients and found that after switching to EHL prophylaxis, median weekly infusions decreased by 29% while factor consumption for prophylaxis decreased by 17%. Weekly infusions decreased in 71% and FVIII utilization in 55% of patients. The findings suggest a successful switch to EHL FVIII products is possible, with decreased infusion frequency, factor consumption and clinical efficacy.

Efficacy, safety and pharmacokinetics of recombinant human coagulation factor VIII (omfiloctocog alfa) in previously treated Chinese children with severe haemophilia A

This study investigated the efficacy, safety and pharmacokinetics of omfiloctocog alfa in Chinese paediatric patients with severe haemophilia A. A total of 69 patients were enrolled and mean exposure to omfiloctocog alfa was 78.9 days. In total, patients experienced 127 bleeding episodes and 27 patients did not experience any bleeding episodes. Researchers found that omfiloctocog alfa was well tolerated and assisted in the prevention and treatment of bleeding in patients with severe haemophilia A.

Efficacy, safety and bioequivalence of the human-derived B-domain-deleted recombinant factor VIII TQG202 for prophylaxis in severe haemophilia A patients

Researchers evaluated the safety and efficacy of a new B-domain deleted recombinant FVIII TQG202 produced by human-derived cells for prophylaxis in severe haemophilia A patients. It compared the bioequivalence with another B-domain deleted recombinant FVIII Xyntha. Researchers suggest that TQG202 had similar results to Xyntha in patients who received the treatment and was well tolerated.

Socioeconomic participation of persons with haemophilia: Results from the sixth haemophilia in the Netherlands study

This study assessed participation in education, the labour market, and social participation for persons with haemophilia compared with the general male population in the Netherlands. Clinical characteristics were extracted from electronic medical records of 1009 participants and general population data were extracted from Statistics Netherlands. Researchers found that educational attainment was higher for people with haemophilia than the rest of the male population, but employment outcomes were worse overall.

Orphan drug designation granted for etranacogene dezaparvovec, CSL Behring's gene therapy for haemophilia B

The Therapeutic Goods Administration has granted orphan drug designation for etranacogene dezaparvovec (EtranaDez), a late-stage gene therapy candidate developed for haemophilia B by CSL Behring.

Time between inhibitor detection and start of immune tolerance induction: association with outcome in the BrazIT Study

This study evaluated the association between the time elapsed from the detection of inhibitors and treatment with immune tolerance induction (ITI) on the patients with haemophilia A. They found that delayed ITI was not associated with failure of the treatment and concluded that ITI should be offered to patients regardless of the time elapsed from the detection of inhibitors.

Haemophilia patients treated with marstacimab see fewer bleeds
Treatment with marstacimab, an experimental antibody-based therapy developed by Pfizer, reduced the number of bleeds in patients with severe haemophilia who took part in a phase 1b/2 clinical study. The result was the same for patients with haemophilia A or haemophilia B, regardless of inhibitors.

Factor IX inhibitors in haemophilia B: A report of National Haemophilia Registry in China
Researchers analysed haemophilia B inhibitor patients' characteristics, factor IX (FIX) genotypes, treatment strategies and outcomes to explore the risk factors for FIX inhibitor development. The study looked retrospectively at patients registered on the Chinese National Registry and Patient Organisation Registry. Researchers found large deletions and missense mutations of the FIX gene were most significantly associated with inhibitor development and that low-dose immune tolerance induction (ITI) therapy might be feasible for FIX inhibitor eradication.

Clinical experience of switching patients with severe haemophilia to rVIII-SingleChain or rIX-FP
This report summarises the clinical experience of different haemophilia treatment centres in managing the switch to rVIII-SingleChain or rIX-FP in haemophilia patients. Researchers found that the physician plays an important role in the motivation of patients to switch based on their individual needs and expectations.

Elective surgery in patients with inherited bleeding disorders: A retrospective analysis
This study evaluated the outcomes of adult patients with inherited bleeding disorders, who received factor replacement for elective surgery in NSW and the ACT. Researchers reported a total of 1065 surgeries on 571 patients between 2000 and 2018. Bleeding complications were reported in 14 surgeries and 19 patients received factor replacement beyond standard duration of prophylaxis. Approximately 50% of all surgeries were performed in a haemophilia treatment centre.

2.2 Von Willebrand disease (VWD)

Clinical, economic, and health-related quality of life burden associated with von Willebrand disease in adults and children: Systematic and targeted literature reviews
This review investigated the prevalence and burden of clinical complications, the impact on health-related quality of life and the economic burden associated with VWD. Researchers found that VWD patients experienced a high burden of clinical complications, reduced quality of life and high healthcare costs. They also found that haemarthrosis is more common in severe VWD than is often assumed, and that bleeds (including haemarthrosis) can reduce quality of life.

Recombinant von Willebrand factor prophylaxis in patients with severe von Willebrand disease
This study reported the results of prophylactic recombinant von Willebrand factor (rVWF) treatment for people with VWD. Researchers found the participants demonstrated a decrease in annualised bleed rate compared with on-demand therapy and prophylaxis with plasma-derived VWF.

2.3 Congenital fibrinogen deficiency (CFD)

Efficacy and safety of fibrinogen concentrate for perioperative prophylaxis of bleeding in adult, adolescent, and paediatric patients with congenital fibrinogen deficiency
Researchers reported results and dosing considerations for human fibrinogen concentrate (HFC) treatment in perioperative bleeding management in patients with CFD. They found that in patients with fibrinogen deficiency, HFC treatment for haemostatic management during and after minor or major surgery was successful, with efficacy comparable across different age groups.

2.4 Factor VII deficiency

Reproductive health and haemostatic issues in women and girls with congenital FVII deficiency

Congenital factor VII (FVII) deficiency is an inherited bleeding disorder, with heterogenous bleeding symptoms. This review evaluated the prevalence and management of bleeding symptoms associated with gynaecological and obstetric issues in women with FVII deficiency. They found that women with congenital FVII deficiency had an increased risk of heavy menstrual bleeding, ovarian bleeding and postpartum haemorrhage, which significantly impacted quality of life.

2.5 Thalassemia

Efficacy and safety of hydroxyurea as adjuvant therapy in paediatric patients of transfusion dependent beta-thalassemia major

This study looked at the efficacy and safety of hydroxyurea as adjuvant therapy in paediatric cases of transfusion-dependent beta-thalassemia. The study included 110 initial participants divided into two groups, with one group receiving hydroxyurea in addition to blood transfusion and chelation therapy. Researchers found that hydroxyurea improved mean haemoglobin levels, reduced the number of blood transfusions per year and decreased serum ferritin levels.

Red blood cell alloimmunisation and other transfusion-related complications in patients with transfusion-dependent thalassaemia: A multi-center study in Thailand

This study investigated the occurrence of red blood cell (RBC) alloimmunisation and other transfusion-related complications in patients with transfusion-dependent thalassaemia (TDT) in eight medical centres across Thailand. Researchers found that transfusion-related complications, especially alloimmunisation, were common among Thai patients with TDT.

Safety and efficacy of mitapivat, an oral pyruvate kinase activator, in adults with non-transfusion dependent α-thalassaemia or β-thalassaemia: an open-label, multicentre, phase 2 study

In this phase 2 study, researchers measured the safety and efficacy of mitapivat (Pyrukynd) for the treatment of alpha and beta thalassaemia. Twenty participants (15 with beta-thalassaemia and 5 with alpha-thalassaemia) received Pyrukynd. Sixteen patients had a haemoglobin response, 17 patients had a treatment-emergent adverse event and 13 had a treatment-emergent event that was considered to be treatment related.

Luspatercept for the treatment of anaemia in non-transfusion-dependent beta-thalassaemia

In this phase 2 study, researchers assessed the safety and efficacy of luspatercept (Reblozyl) versus a placebo in patients with non-transfusion-dependent beta-thalassaemia. Seventy-four of the 96 patients in the Reblozyl group and zero in the placebo group had an increase of at least 1·0 g/dL in haemoglobin concentration. The proportion of patients with serious adverse events was lower in the Reblozyl group than in the placebo group.

2.6 Sickle cell disease (SCD)

Clinical management of the acute complications of sickle cell anaemia: 11 years of experience in a tertiary hospital

Researchers studied admissions for acute complications in patients with SCD under 16 years of age in Spain between 2010 and 2020. Researchers aimed to determine the type of diagnoses experienced by people with SCD in an environment with less experience in the diagnosis and treatment of the disease. The study recorded 71 admissions for 25 patients and noted that despite the prophylactic and therapeutic measures provided to patients, many continue to suffer acute complications that require hospital management.

Reduced red cell transfusions and hospitalisations in sickle cell patients treated with voxelotor

The authors of this study report on the outcome of treating patients in their clinic with voxelotor (Oxbryta). The data of 13 patients collected over two years was analysed, with researchers observing 20 fewer hospitalisations and 91 fewer red cell transfusions, suggesting that Oxbryta treatment is a clinically and economically effective treatment option.

Multi-organ dysfunction secondary to abrupt discontinuation of voxelotor in a patient with severe sickle cell disease

The authors report the case of a woman with SCD and multiple other health related complications. The authors report that the woman abruptly (and accidentally) discontinued voxelotor (Oxbryta) therapy on two separate occasions which led to an acute worsening of anaemia, an increase in lactate dehydrogenase, acute kidney injury, severe hypoxia, and heart failure.

Early hydroxyurea use is neuroprotective in children with sickle cell anaemia

Researchers analysed the cognitive status of SCD patients, who began hydroxyurea between the age of three and five years old, to determine ongoing effects on cognitive performance. Researchers found that children with SCD treated with hydroxyurea from an early age had a similar cognitive performance compared to unaffected matched controls.

Implementation of national blood conservation recommendations at an adult sickle cell centre

This study described the outcomes of the implementation of blood conservation changes in a single SCD centre in the US during the COVID-19 pandemic. Changes to the treatment of 53 patients who remained on chronic exchange treatments resulted in the conservation of 854 red blood cell units, without significantly affecting haemoglobin levels or the number of acute care presentations. Five patients who transitioned to predominantly simple transfusions, experienced difficulty maintaining haemoglobin levels. The researchers suggest that in a blood shortage crisis, optimising the exchange procedure itself may be the safest means of conserving blood in a population of adult patients with SCD.

Measurement of post-transfusion red blood cell survival kinetics in sickle cell disease and beta-thalassemia

In this study researchers looked at the survival of transfused RBCs in people with SCD or beta-thalassemia to investigate factors that determine cell survival. RBC survival and the influence of donor and patient characteristics were assessed by simultaneous transfusion of two allogeneic RBC populations. The transfused RBCs groups were chemically labeled (with biotin) to allow them to be tracked during the study. Most patients demonstrated a non-linear trend in RCS that was different from the observed RBC survival kinetics in healthy volunteers. The data collected indicates that patient-related factors largely determine post-transfusion RCS behavior, while donor factors have a negligible effect.

HLA Class II regulation of immune response in sickle cell disease patients: Susceptibility to red blood cell alloimmunisation

SCD patients are commonly treated with RBC transfusion, meaning that alloimmunisation to RBC antigens can be a common complication in chronically transfused patients. This study evaluated the association between human leukocyte antigen polymorphisms and the possible risk of developing RBC alloantibodies. They found that SCD patients carry an increased risk of producing RBC alloantibodies and suggested that a strategy to prevent this is to select RBC units by phenotype for susceptible SCD patients receiving multiple transfusions.

Adherence to NHLBI guidelines for the emergent management of vaso-occlusive episodes in children with sickle cell disease

In 2014 the US National Heart, Lung, and Blood Institute (NHLBI) released guidelines to direct the care of patients presenting with vaso-occlusive episode (VOE) to improve the consistency of treatment across service providers. Researchers looked at the practices of academic, paediatric emergency departments in the US and Canada to determine adherence to the 2014 NHLBI recommendations. They found significant delays in the adherence to recommendations particularly in the time of treatment with parenteral opioids for pain relief.

Hyperhaemolytic crisis following transfusion in sickle cell disease with acute hepatic crisis

In this report, researchers outline a case of hyperhaemolysis syndrome in which a patient was initially admitted and treated for a SCD pain crisis, but then developed signs of acute haemolysis after receiving a blood transfusion.

The role of MRI-R2 in the detection of subclinical pancreatic iron loading among transfusion-dependent sickle cell disease patients and correlation with hepatic and cardiac iron loading

This study aimed to measure pancreatic iron load among transfusion dependent SCD patients. Sixty-six SCD patients were assessed with results indicating moderate-to-severe hepatic iron overload in 65.2% of cases. Normal-to-mild iron overload was present in the pancreas in 86% of cases, and 50% had elevated serum ferritin. Patients with higher levels of haemolysis markers and lower pre-transfusion haemoglobin levels showed moderate-to-severe pancreatic iron overload.

Pulmonary hypertension screening in children with sickle cell disease

This study examined the utility of screening for pulmonary hypertension (PHT) in children with SCD by using multiple methods to determine the best approach for discovery. Children aged 8-18 were screened but found that PHT symptoms were not consistent with current suggested screening methods.

Ferriprox safely, effectively lowers iron load in SCD patients

Researchers have confirmed that long term treatment with deferiprone (Ferriprox) is safe and effectively reduced iron load in SCD patients experiencing transfusion induced iron overload.

Sickle cell disease could be treated with common plant, study finds

Scientists at Aberystwyth University in Wales isolated a chemical in the Alchornea cordifolia plant, also known as the Christmas Bush. The chemical could help relieve the symptoms of SCD, a life-threatening and painful disease suffered by 15,000 people in the UK.

2.7 Human immunodeficiency virus (HIV)

Combination anti-HIV antibodies provide sustained virological suppression

In this study researchers report the results of a clinical trial involving administration of two HIV-specific broadly neutralising monoclonal antibodies (bNAbs) in a group of HIV infected people compared with a group receiving a placebo. Researchers found that compared with placebo, the combination bNAbs maintained complete suppression of plasma viral markers (for up to 43 weeks) after analytical treatment interruption. This suggests that sustained virological suppression is achievable with intermittent administration of combination bNAbs.

Long-lasting HIV prevention drug could be game changer — but who will pay?

The World Health Organization has recommended the use of a treatment that protects people at high risk of HIV infection. Cabotegravir (also known as CAB-LA) was approved by the FDA in December 2021. A producer of this treatment, ViiV, announced that it would allow up to three other companies to produce and supply generic versions of the drug for use in 90 of the world's lowest-income countries, where the majority of new HIV cases occur.

Gilead breaks through with first approval for new HIV drug

A long-acting HIV treatment Sunlenca has received approval for use in Europe. The decision authorises Sunlenca for patients whose current treatment regimen can no longer keep their HIV infection at bay and will be added to other antiviral drugs to boost patients' immune response and reduce levels of virus in the body.

2.8 Kawasaki disease (KD)

Infants, older patients with Kawasaki disease demonstrate different complication risks

Researchers have found that unresponsiveness to IVIg and the development of coronary artery abnormalities differ between infants and older patients with KD. Researchers suggested that care providers should address residual risk factors for KD-related coronary artery abnormalities, other than initial unresponsiveness to IVIg, especially in infants.

Intravenous methylprednisolone pulse therapy versus intravenous immunoglobulin in the prevention of coronary artery disease in children with Kawasaki disease

Researchers conducted a randomised, single-blind clinical trial on 40 patients with KD aged six months to five years to evaluate the effect of intravenous methylprednisolone pulse (IVMP) therapy in preventing coronary artery lesions (CAL). Patients were randomised into two groups and treated with either IVMP or intravenous immunoglobulin (IVIg). After two weeks the frequency of CAL was 20% in the IVMP group and 45% in the IVIg group, with no significant difference between the two groups after two weeks and two months. This suggested that IVMP as an initial line therapy effectively controlled systemic and vascular inflammation and decreased coronary artery damage.

Predictors for intravenous immunoglobulin resistance in patients with Kawasaki disease

To identify risk factors for IVIg resistance, researchers performed a retrospective analysis of medical records of KD patients from two medical centres in South China from January 2015 to December 2017. The study found that patients presenting with coronary artery lesions in the acute phase and a C-reactive protein level >100 mg/L at diagnosis were associated with IVIg resistance in KD.

Therapeutic window of intravenous immunoglobulin (IVIG) and its correlation with IVIG-resistant in Kawasaki Disease: a retrospective study

Researchers sought to determine the best time for initial IVIg treatment in KD patient to reduce the likelihood of resistance. They found that IVIg therapy within seven days of illness was more effective for reducing the risk of coronary artery abnormalities than after seven days of illness. This suggests that IVIg treatment within the first seven days of illness is the optimal therapeutic window for KD patients.

2.9 Cold agglutin disease (CAD)

Sanofi gets EMA Committee recommendation for approval of Enjaymo for haemolytic anaemia in adult patients with cold agglutinin disease

The European Medicines Agency's (EMA) has recommended approval for sutimlimab (Enjaymo) in the treatment of haemolytic anaemia in adult patients with CAD. Enjaymo has been found to ease anaemia, reduce fatigue and the need for blood transfusions in people with CAD.

2.10 Postpartum haemorrhage (PPH)

Association of maternal perfluoroalkyl substance exposure with postpartum haemorrhage in China

Prenatal exposure to perfluoroalkyl substances (PFASs) in women has been linked to pregnancy disorders and adverse birth outcomes. This study aimed to explore the associations of maternal PFAS exposure with the risk of PPH and found that the risk increased with increased exposure to a PFAS mixture.

Implementation of postpartum haemorrhage emergency care using a bundle approach at a tertiary care hospital in North India

This study investigated whether implementing a PPH bundle of care reduced maternal morbidity and mortality in an Indian hospital. A total of 1304 women gave birth from January 2021 to January 2022 with 107 of these women diagnosed and treated for PPH. Researchers reported a significant increase in the use of tranexamic acid (p=0.041) and a significant reduction in blood transfusion rates (p=0.032) after the implementation of bundled care.

Hospital-level variation in rates of postpartum haemorrhage in California

Researchers performed a cross-sectional study examining live births in California hospitals to examine the extent of hospital-level variation in risk-adjusted rates of PPH. Over three years, the cohort comprised of 1,904,479 women who had a live birth delivery at 247 hospitals. Researchers found wide variability in the rate of PPH across hospitals in California which were not attributable to patient factors, hospital teaching status or annual delivery volume.

2.11 Hereditary angioedema

HAE patients see benefits following 1-year of treatment with Takhzyro

In this study researchers found that half of the participants with hereditary angioedema treated with lanadelumab (Takhzyro) for at least a year, prolonged their dosing interval and used significantly less on-demand treatments.

HAE attacks safely prevented by NTLA-2002 gene therapy

The Phase 1 trial of Intellia Therapeutics gene therapy for hereditary angioedema 'NTLA-2002' has confirmed that the drug is well tolerated at two different doses and reduced the number of swelling attacks in people with hereditary angioedema. Phase 2 is expected to begin in the first half of 2023.

2.12 Immune system and immunotherapy

Population pharmacokinetic modelling of intravenous immunoglobulin treatment in patients with Guillain–Barré syndrome

Researchers developed a model to predict the pharmacokinetics of a standard 5-day IVIg course (0.4 g/kg/day) in patients with Guillain–Barré syndrome. This is the first population-pharmacokinetic model for standard IVIg treatment in Guillain–Barré syndrome and provides a new tool to predict the pharmacokinetics of alternative regimens of IVIg in Guillain–Barré syndrome.

Using a scenario approach to assess for the current and future demand of immunoglobulins: An interview and literature study from The Netherlands

Researchers explored the current and future demand of immunoglobulins globally and specifically for the Netherlands using a mixed mode assessment. They identified neurology, immunology, and haematology as the main drivers of Ig demand along with four groups of transformational factors that may impact demand.

CAR-T therapy effective in youngest kids with ALL

Researchers examined the real-world outcome of treatment with tisagenlecleucel (Kymriah) in younger children and infants with acute lymphoblastic leukaemia (ALL) at 15 different hospitals in Europe. Patients received a single intravenous infusion of tisagenlecleucel with overall survival at 6 and 12 months after infusion being 88% and 84% respectively, while event-free survival was 75% and 69%.

3 Transfusion

This section includes published research on transfusion procedures to improve patient outcomes.

3.1 Paediatrics

Red blood cell volume, but not platelet or plasma volume is associated with mortality in neonatal ECMO

This study investigated the relationship between blood product components and mortality in newborns receiving extracorporeal membrane oxygenation (ECMO) support. Researchers reviewed data taken from a children's hospital in the United States from 2002 to 2019 and suggest that red blood cell (RBC) volume rather than platelet or plasma volume, was associated with mortality in newborns on ECMO.

Blood transfusion is associated with increased mortality for neonates with congenital diaphragmatic hernia on extracorporeal membrane oxygenation support

Researchers performed a single centre review of all newborns with congenital diaphragmatic hernia (CDH) undergoing surgical repair with extracorporeal membrane oxygenation (ECMO) to determine the impact of platelet transfusion on patient outcomes. Researchers found that major bleeding and platelet transfusions in the post-operative period were associated with increased mortality for neonates on ECMO for CDH repair.

3.2 Clinical Practice

Surgical indication and approach are associated with transfusion in hysterectomy for benign disease

In this study researchers investigated the pre-operative and intraoperative risk factors associated with the need for RBC transfusion among women undergoing hysterectomy. Patients receiving blood transfusion between January 2011 – December 2017 within 30 days of surgery, were compared to patients who did not receive any transfusion. Researchers found that indicators such as body mass index, smoking, bleeding disorders and pre-operative sepsis were more accurate in predicating likelihood of transfusion.

Modelling the outcomes of different red blood cell transfusion strategies for the treatment of traumatic haemorrhage in the prehospital setting in the United Kingdom

Researchers analysed the potential benefits of prehospital transfusion (PHT) of trauma haemorrhage patients with O RhD-positive RBCs compared to no PHT to determine if these units could be a suitable replacement for the high demand group O RhD-negative. They found that while the use of RhD-positive RBCs carries risks, the benefits are higher than if no PHT is administered, even for women of childbearing age. Researchers concluded that the use of group O RhD-positive RBCs could be considered in the case of a national shortage of RhD-negative RBCs.

Over-transfusion with blood for suspected haemorrhagic shock is not associated with worse clinical outcomes

Researchers evaluated patient outcomes after early, small volume RBC transfusion for patients presumed to be undergoing haemorrhagic shock. A total of 3,121 patients who received RBC transfusion within the first 24 hours were included in the study. Researchers found that there was no difference in the risk of acute kidney injury (AKI), acute respiratory distress syndrome (ARDS), infection, cardiac arrest, venous thromboembolism or stroke for patients receiving 1–3 units compared to a non-transfused group or 4–9 units group. Compared to those receiving ≥10 units, the 1–3 units group had a significantly lower risk of AKI, ARDS, and cardiac arrest.

Haematological support of patients with significant anaemia who decline red blood cell blood transfusion

This study proposes a protocol to support patient populations who declined blood transfusions, by looking at baseline characteristics at the time of severe anaemia, the various treatment strategies implemented and patient outcomes.

Incidence and characteristics of hypotensive transfusion reaction: 10-year experience in a single centre

Researchers reviewed hypotensive transfusion reactions (HyTR) across a period of 10 years, using haemovigilance data from a Korean tertiary care hospital. Researchers identified 37 HyTRs incidents in 35 patients with the highest incidence occurring with filtered random donor platelets, with more than half of the HyTRs occurring within 15 minutes of start of transfusion. All cases recovered without severe complications.

Whole blood transfusion and paroxysmal nocturnal haemoglobinuria meet again: Minor incompatibility, major trouble

Researchers report a case study of a patient who received a standard low-titre group O whole blood transfusion during pre-hospital transportation. Following the transfusion, the patient suffered a haemolytic transfusion reaction with researchers suggesting that haemolysis was likely due to minor incompatibility between the plasma from the transfused whole blood and the patient's paroxysmal nocturnal haemoglobinuria red cells.

Attitudes of American women toward accepting RhD-mismatched transfusions in bleeding emergencies

Researchers measured the willingness of women in the United States to accept urgent but incompatible transfusions when considering the potential for future pregnancy complications. A total 309 responses to a postal survey were analysed with at least 90% of the respondents agreeing that they would accept an urgent incompatible transfusion when the absolute risk reduction in maternal mortality was greater than or equal to 4%.

Multi-national survey of transfusion experiences and preferences of patients with myelodysplastic syndrome

Researchers conducted a web-based cross-sectional multi-national survey to audit real world transfusion practices and understand the experiences and preferences of patients with myelodysplastic syndrome requiring RBC transfusion. The survey was distributed to patients in the US, Canada, and UK. Patients surveyed identified two main changes to their transfusion care that they believed would improve their quality of life: self-administered point of care testing of haemoglobin and higher haemoglobin transfusion thresholds. Researchers also found variability in the haemoglobin thresholds for transfusion by country.

Effect of high vs low dose tranexamic acid infusion on need for red blood cell transfusion and adverse events in patients undergoing cardiac surgery

In this study researchers investigated the effect of tranexamic acid infusion on the need for RBC transfusions in patients undergoing cardiac surgery with cardiopulmonary bypass. Researchers found that high-dose tranexamic acid infusion significantly reduced the proportion of patients who received RBC transfusion. The rate of a composite safety end point of 30-day mortality, seizure, kidney dysfunction, and thrombotic events was 17.6% in a high-dose group and 16.8% in a low-dose group. Among patients who underwent cardiac surgery with cardiopulmonary bypass, high-dose compared with low-dose tranexamic acid infusion resulted in a modest, statistically significant reduction in the proportion of patients receiving RBC transfusion and met criteria for noninferiority with respect to a composite safety end point.

Low volume blood product transfusion patterns and ratios after injury

This retrospective analysis of the American College of Surgeons Trauma Quality Improvement Program database was performed to identify adult trauma patients who received one or more units of packed RBCs four and 24 hours after admission. Blood products received were used to calculate plasma and platelet ratios. Researchers found that plasma and platelet ratios were closer to the target 1:1 ratio for four or less units of pRBCs while plasma and platelet ratios increased for those receiving between five to ten units pRBCs, demonstrating increasingly unbalanced resuscitation.

The abrogated role of premedication in the prevention of transfusion-associated adverse reactions in outpatients receiving leukocyte-reduced blood components

Researchers at a hospital in Taiwan investigated if a program could improve the understanding of physicians related to the unnecessary use of premedication and what impact premedication had on outpatients developing transfusion-associated adverse reactions (TAARs). Researchers compared data from the eight months prior to and after the program was implemented. The premedication rate significantly decreased from 92.4% to 76.7% after the educational program. Researchers also found that decreased premedication was not associated with increased incidence of TAARs in outpatients.

Platelet transfusion and mortality in patients with sepsis-induced thrombocytopenia

This study explored the association between platelet transfusion and mortality in patients with sepsis-induced thrombocytopenia. A total of 1733 patients were included in the study of which 296 patients were included in the platelet transfusion group and 1437 patients were included in the non-platelet transfusion group. Researchers found that platelet transfusion was associated with increased in-hospital mortality in septic patients with severe thrombocytopenia, however, it was not associated with 90-day mortality, or the length of ICU stay.

First report of transfusing low-titre cold-stored type O whole blood to an extremely low birth weight neonate after acute blood loss

This study reports on an emergency transfusion of re-warmed low-titre cold-stored type O whole blood using a fluid warmer for the resuscitation of a hypotensive 25-week gestation foetus following acute and severe placental abruption. Researchers found that the transfusion was tolerated well, without evidence of haemolysis or other complications.

Incidence of transfusion-related acute lung injury temporally associated with solvent/detergent plasma use in the ICU: A retrospective before and after implementation study

This retrospective study in the Netherlands investigated the incidence of transfusion-related acute lung injury (TRALI) in intensive care units, following the replacement of quarantined fresh frozen plasma (qFFP) by solvent/detergent pooled plasma (SDP). Researchers reviewed patients who received ≥1 plasma units and developed hypoxemia within 24 h. They found that implementation of SDP lowered the incidence of TRALI in which plasma products were implicated, though not significantly.

Hormones, age, and sex affect platelet responsiveness in vitro

Researchers investigated the effect of testosterone on platelet responses in the body to determine the effect of sex and age on response to trauma-induced coagulopathy. Apheresis platelets were collected from males and females of differing ages and incubated with testosterone or estradiol and stimulated with buffer, adenosine diphosphate, platelet activating factor or thrombin. Researchers found that testosterone decreases platelet function dependent on the stimulus, age, and sex. Platelet metabolism had varying responses to sex hormones dependent upon sex and age.

Interventions to reduce infections in patients with haematological malignancies: a systematic review and meta-analysis

This study assessed the safety and efficacy of prophylactic immunoglobulin (Ig), antibiotics and vaccination in adult patients with haematological malignancies commonly associated with acquired hypogammaglobulinemia. The analysis of the randomized controlled trials found that prophylactic antibiotics did not reduce the risk of clinically documented infections (CDIs) and while prophylactic Ig reduced the risk of CDIs, it also increased risk of adverse events.

Prophylactic platelet transfusions versus no prophylaxis in hospitalised patients with thrombocytopenia: A systematic review with meta-analysis

This review compared reports of hospitalised patients who received prophylactic platelet transfusion with patients who received no prophylaxis for the treatment of thrombocytopenia. The researchers found that prophylactic platelet transfusion reduced the proportion of patients with at least one episode of clinically important bleeding. However, the authors noted the overall certainty of evidence collected was low.

Health-related quality of life after restrictive versus liberal RBC transfusion for cardiac surgery: Sub-study from a randomised clinical trial

In this study of Australian patients, researchers investigated whether a restrictive transfusion strategy was inferior to a liberal transfusion strategy on long-term health-related quality of life (HRQOL) up to 24 months post cardiac surgery. A total of 617 Australian patients were identified for the study with data available for 208 restrictive and 217 in liberal transfusion recipients. Researchers found that restrictive transfusion resulted in inferior HRQOL outcomes at 12 months after surgery, suggesting that a liberal transfusion strategy improved patient outcomes.

Estimating the effect of donor sex on red blood cell transfused patient mortality: A retrospective cohort study using a targeted learning and emulated trials-based approach

This study investigated the effect of donor sex on RBC transfused patient mortality using the RBC transfusion database from the Capital Region of Denmark, which contains records of over 900,000 transfusion events. Patients were at least 18 years old, had received a leukocyte-reduced RBC transfusion, and had no history of RBC transfusions prior to baseline. Researchers found that male patients had a 28-day survival rate of 2.06 percentage points higher when treated with RBC units exclusively from male donors compared with exclusively from female donors. There was no evidence of differing outcomes for female patients who were administered exclusively male or female RBCs. The researchers concluded that sex-matched transfusion policies may improve patient outcomes.

4 Product management

This section includes published research on product management to improve patient outcomes and reduce wastage of blood products.

4.1 Storage

Hyperbaric treatment of platelets extends in vitro storage to 14 days

Researchers tested a novel method to extend platelet storage using xenon gas (Xe) under high pressure and refrigeration. Apheresis platelets (APU) prepared in 65% platelet additive solution were stored under standard conditions at 20°C–24°C to day 5. Paired APUs were prepared with Xe and stored to day 14 at 2°C–6°C. Researchers found that platelet storage with the xenon/hyperbaric/cold method is a feasible candidate for extension of storage to 14 days based on in vitro characteristics.

Minimal impact of anticoagulant on in vitro whole blood quality throughout a 35-day cold-storage regardless of leukoreduction timing

This study assessed the impact of white blood cell removal from whole blood either after 3–8 hours or 18–24 hours after collection. In vitro quality was assessed after filtration and throughout five weeks of storage at 4°C. Researchers found that in vitro whole blood quality seems to be independent of the choice of anticoagulant and filtration timing and suggest whole blood hold-times are effective up to 24 hours, allowing for greater flexibility for transfusion services.

Validated transport conditions maintain the quality of washed red blood cells

Researchers compared washed RBC quality in 'ideal' storage conditions in a blood bank refrigerator to a 'real-world' simulation of unit transport, including holding in a transport cooler. Twelve RBC units were washed and allocated evenly into either condition. Measurements revealed that placement in a transport cooler was associated with higher unit temperature prior to 12 hours. However, researchers also found that certain measures of unit quality, including extracellular potassium, pH, lactate, and free haemoglobin were indistinguishable between conditions. Researchers concluded that washed units stored under approved transport conditions may be returned to inventory up to 24 hours after washing.

In vitro quality and haemostatic function of cold-stored CPDA-1 whole blood after repeated transient exposure to 28°C storage temperature

This study aimed to investigate if changing temperatures resulted in a measurable effect on common quality parameters and viscoelastic haemostatic function of cold stored CPDA-1 whole blood. Eight bags of whole blood were exposed to five weekly 4 hour long transient temperature changes to 28°C and 8 bags were stored continuously at 4°C as a control. Researchers found that CPDA-1 whole blood repeatedly exposed to 28°C did not show reduced quality compared to the control group up to day 35, however two units had haemolysis of 1.1% and 1.2%.

Cold-stored platelets are effective in an in vitro model of massive transfusion protocol assessed by rotational thromboelastometry

In this study researchers explored the effect of using cold-stored platelets (CPs) versus room temperature stored platelets (RPs) in an in vitro transfusion model based on a massive transfusion protocol. RPs and CPs were individually combined with RBCs and plasma in a 1:1:1 volume ratio to make transfusion packages. Both transfusion packages restored the clot characteristics of haemodiluted or hyperfibrinolytic whole blood. Only transfusion packages made with CPs significantly reduced the maximum clot lysis of hyperfibrinolytic whole blood. Plasminogen activator inhibitor-1 activity in CPs transfusion packages were also significantly higher.

Intervening on the storage time of RBC units and its effects on adverse recipient outcomes using real-world data

Researchers estimated the comparative effect of transfusing exclusively older vs fresher RBC units on mortality, and thromboembolic events. The research suggests that transfusing exclusively older RBC units stored for more than one or two weeks increases the 28-day recipient mortality and risk of thromboembolism or death compared with transfusing fresher RBC units.

4.2 Treatment

Transfusion outcomes between regular and low yield pathogen reduced platelets across different patient populations in a single institution

This study reviewed platelet transfusions at Stanford Hospital to determine the effect of pathogen reduction technology (PRT) on patient outcomes. Comparisons were made between PRT-treated regular (PRT-PR) and low (PRT-PL) yield platelets. Researchers found that platelet utilisation per patient remained mostly unchanged even when the frequency of PRT-PL transfusion increased suggesting that units may be used in an equivalent manner to maintain adequate platelet inventory.

Cold-stored platelet function is not significantly altered by agitation or manual mixing

Researchers assessed cold-stored platelets stored for 21 days with or without agitation and then with or without daily manual mixing to determine aggregate formation and potential effects of sedimentation. Agitation resulted in macroaggregate formation while no agitation caused film-like sediment. No substantial differences were found in cold-stored platelet function between storage conditions. Surface receptor expression, thrombin generation, aggregation, and clot formation were relative in different storage conditions. Researchers found storage duration (not condition) impacted phenotype and function and concluded that cold-stored platelets may be able to be stored with or without agitation, and with or without daily mixing with minimal changes to haemostatic function.

Optimisation of human platelet lysate production and pathogen reduction in a public blood transfusion centre

Human platelet lysate (HPL) has been proposed as a safe and efficient xeno-free alternative to fetal bovine serum (FBS) for large-scale culturing of cell-based medicinal products. This study evaluated the impact of applying a pathogen reduction treatment (PRT) based on riboflavin and ultraviolet irradiation on the raw materials of a human platelet lysate (HPL) product. The application of a PRT on the starting materials significantly altered the protein composition while growth promoting rates were unaffected when compared with FBS.

New ultraviolet C light-based method for pathogen inactivation of red blood cell units

This study proposes a new approach to inactivating pathogens in RBC units by employing ultraviolet C (UVC) light. Researchers used whole blood-derived leukoreduced RBCs suspended in additive solution, as test samples and controls. They performed vigorous agitation and haematocrit reduction by diluting the RBCs with additional additive solution during illumination to ensure that UVC light penetrated and inactivated the nine bacteria and eight virus species tested. They found that UVC treatment of RBCs in the additive solution did not alter RBC antigen expression, but significantly influenced some in vitro parameters. Compared to controls, haemolysis was higher in UVC-treated RBC units, but was still below 0.8% at 36 days of storage.

Contamination of platelet concentrates with Staphylococcus aureus induces significant modulations in platelet functionality

Platelet concentrates (PCs) contaminated with *Staphylococcus aureus (S. aureus)* can escape detection during PC screening, causing septic transfusion reactions. In this study researchers investigated the impact of *S. aureus* contamination on platelet metabolism and functionality during PC storage. They found that contamination with *S. aureus* exacerbates platelet storage lesions in contaminated PCs but only when contamination has reached clinically significant levels.

Laser incubation for the rapid detection of red cell alloantibodies in human blood samples

Pre-transfusion antibody screening requires the detection and identification of immunoglobulin G (IgG) antibodies against RBCs. Researchers compared a laser incubation method to the more typical heating block technology when conducting an indirect antiglobulin test. Presence of an alloantibodies were detected after 1-min incubation for 96% of samples with no samples requiring longer than 3 minutes of laser incubation to detect the antibodies. No samples required longer than 5 min to achieve an equivalent result to that of the 5 minute heating block incubation and the laser did not damage cells or antibodies.

4.3 Inventory Management

Plasma transfusion practises: A multicentre electronic audit

This audit was conducted to determine the proportion of plasma transfused without a guideline supported indication and/or at a sub-therapeutic dose in Canadian medical services. Researchers found that in one year, 78% of plasma was transfused without a guideline supported indication or at a sub-therapeutic dose.

How we built a hospital-based community whole blood program

This report outlines the implementation of a whole blood treatment program in a clinical practice setting in the US. While the authors noted that developing a whole blood program is complex, the investments of time, effort, and funding can potentially improve care, save blood bank and nursing effort, and reduce patient charges.

Removal of platelets from blood plasma to improve the quality of extracellular vesicle research

Researchers studied the efficacy of the most commonly used centrifugation protocol to prepare cell-free plasma for the purpose of extra vesicle (EV) research. Plasma was prepared according to the double centrifugation protocol of the International Society on Thrombosis and Haemostasis (ISTH) but researchers were unable to remove all platelets. The researchers noted that because the ISTH centrifugation protocol does not remove all platelets reporting platelet levels and filtration is necessary component of EV research.

A data-driven approach to determine daily platelet order quantities at hospitals

Researchers developed a prediction model to guide the daily ordering quantity of platelet units at a hospital that ordered units from a central supplier. The model places orders at the end of each day to bring the platelet inventory to the predicted demand for the next day while also factoring in inventory costs of wastage and shortage.

Use of O RhD-negative red blood cells: A nationwide, prospective audit

Researchers in Finland investigated the utilisation of O RhD-negative RBCs to understand clinical use and identify areas where policy changes could help alleviate the shortage of O RhD-negative RBCs. They found that 47% of O RhD-negative units were issued to non-O RhD-negative patients with 67.5% of the units being issued for non-urgent transfusions. Researchers noted that the most common reason for issuing O RhD-negative units was inventory management, as most of the units were issued close to expiry.

5 Immunoglobulin

This section includes published research and industry publications on the use of immunoglobulin therapies to improve patient outcomes

5.1 Subcutaneous immunoglobulin

Usefulness of subcutaneous immunoglobulin therapy in the management of myasthenia gravis: a retrospective cohort study

This retrospective study aimed to determine the utility of subcutaneous immunoglobulin (SCIg) therapy in the management of myasthenia gravis (MG) at the neuromuscular referral centre in Bordeaux. The duration of disease progression did not appear to affect the response to SCIg therapy. The number of hospital days per month was significantly reduced after SCIg compared to before, and the number of days in intensive care unit and the number of days of orotracheal intubation (OTI) were also reduced. Only minor adverse effects were noted, and 80% of patients were in favor of continuing SCIg. The researchers concluded that SCIg appears to be a well-tolerated and useful treatment in MG but that further large-scale prospective studies are needed to confirm the results.

5.2 Intravenous immunoglobulin

A retrospective comparative analysis of factors affecting the decision and outcome of initial intravenous immunoglobulin alone or intravenous immunoglobulin plus methylprednisolone use in children with the multisystem inflammatory syndrome

In this study researchers determined the impact of the combined treatment of intravenous immunoglobulin (IVIg) and methylprednisolone on fever, length of hospital stay and admission to paediatric intensive care units in children with multisystem inflammatory syndrome (MIS-C). Researchers compared the results of children treated with IVIg and methylprednisolone to children who were treated with only IVIg and found the combined treatment lowered the severity of MIS-C but increased hypotension. The incidence of fever did not differ significantly between patient groups.

Comparative Efficacy of Rivaroxaban and Immunoglobulin Therapy in the Treatment of Livedoid Vasculopathy: A Systematic Review

Researchers conducted a literature review of 20 treatment reports to compare the patient outcomes of people with livedoid vasculopathy when treated with the drug rivaroxaban or IVIg therapy. Researchers found both treatments were good therapeutic options and suggested that there may be potential benefits in utilising both in a combination therapy.

Efficacy of intravenous immunoglobulin in the treatment of recurrent spontaneous abortion: A systematic review and meta-analysis

Researchers conducted a meta-analysis of 15 studies to evaluate the efficacy of IVIg in the treatment of patients with recurrent spontaneous abortion (RSA). A total of 902 patients were included in analysis. Researchers found that IVIg increased the live birth rate of RSA patients, however, when divided into primary and secondary abortions for subgroup analysis, they found no statistical difference.

Efficacy and safety of intravenous immunoglobulin in patients with lupus nephritis: A systematic review of the literature

This review evaluates the evidence for IVIg in the care of patients with lupus nephritis (LN). IVIg was found to be between 60% to 70% effective in patients with LN. Few adverse reactions were identified, however the authors noted caution should be exercised when using IVIg for patients with the class V variant of LN.

Paediatric Acute-onset Neuropsychiatric Syndrome (PANS) and intravenous immunoglobulin (IVIG): comprehensive open-label trial in ten children

Researchers conducted an open-label study to review the effect of intravenous immunoglobulin (IVIg) treatment for children with paediatric acute-onset neuropsychiatric syndrome (PANS). The trial included ten children with PANS, who received IVIg treatment monthly for three months. Researchers found considerable improvements in symptoms and clinical impairments in all participants. Moderate to severe transient side effects were recorded in three cases.

Efficacy, safety and pharmacokinetics of a new 10% normal human immunoglobulin for intravenous infusion, BT595, in children and adults with primary immunodeficiency disease

Researchers evaluated the efficacy, safety and pharmacokinetics of a new, highly purified 10% IVIg, Yimmugo (also known as BT595) administered in people with primary immunodeficiency diseases. Participants were switched from their previous IVIg replacement therapy to Yimmugo with patients receiving doses for approximately 12 months at intervals of three or four weeks. Only one of the 67 participants experienced a serious bacterial infection suggesting that Yimmugo is an effective replacement therapy in patients with primary immunodeficiency disease for preventing infections.

Intravenous Immunoglobulin May Accelerate Platelet Count Stabilisation, Recovery in Obinutuzumab-Related Thrombocytopenia
Researchers have reported that IVIg treatment may accelerate platelet count stabilisation and recovery in anti-CD20 monoclonal antibody related thrombocytopenia.

Reduced risk of infections with the intravenous immunoglobulin, IgPro10, in patients at risk of secondary immunodeficiency-related infections
A retrospective database analysis was conducted to assess treatment patterns and infection rates in patients at risk of secondary immunodeficiency (SID) related infections, with or without the immunoglobulin replacement therapy (IgRT), 'gPro10' exposure. Despite being sicker at baseline, the group receiving IgPro10 demonstrated fewer infections post-index than the non-IgRT cohort. This suggests that IgPro10 may be an effective option for infection prevention in patients at risk of SID.

6 Gene therapies

This section includes industry updates and research on the progress of gene therapies though regulatory bodies as well as gene therapy safety.

6.1 Gene therapies: blood and bleeding disorders

Phase 1–2 trial of AAVS3 gene therapy in patients with haemophilia B
This multicentre, open-label, phase 1–2 trial assessed the safety and efficacy of varying doses of FLT180a in patients with severe or moderately severe haemophilia B.

BioMarin presents abstract on vector DNA transmission risk at ISTH
Pharmaceutical company Biomarin has recommended that haemophilia A patients receiving their gene therapy valoctocogene roxaparvovec (Roctavian) use contraception for six months following treatment to reduce the chance of vector shedding. Gene therapies such as valoctocogene roxaparvovec use adeno-associated viruses (AAVs) vectors to deliver a functioning factor VIII gene to cells in the patient's liver. This allows patients to produce factor VIII, however the viral vector can be transmitted through bodily fluids until the clearance of vector DNA.

Two Zolgensma deaths bring gene therapy safety to spotlight
Novartis recorded two deaths after treatment with its spinal muscular atrophy gene therapy onasemnogene abeparvovec-xioi (Zolgensma). Two patients in Russia and Kazakhstan died of liver failure (a known side effect) within six weeks of receiving Zolgensma.

FDA approves first cell-based gene therapy to treat adult and paediatric patients with beta-thalassaemia who require regular blood transfusions
The FDA has approved betibeglogene autotemcel (Zynteglo), for the treatment of patients with beta-thalassaemia who require regular red blood cell transfusions. Zynteglo is a one-time gene therapy product administered as a single dose.

With two new expensive gene therapy approvals, outcomes-based pricing deals grab the spotlight again
The recent approval of two gene therapies for bleeding disorders, BioMarin's Roctavian (for haemophilia A) in the EU and Bluebird Bio's Zynteglo (for beta thalassemia) in the US, has highlighted the costs associated with outcomes-based pricing models for longer lasting gene therapies.

Pfizer, Sangamo set to resume gene therapy study after safety delay
Pfizer and Sangamo will restart the phase 3 trial of their haemophilia A gene therapy giroctocogene fitelparvovec, after the FDA lifted a clinical hold on the study. The trial was paused voluntarily after patients treated with the therapy produced higher than expected levels of Factor VIII.

Now playing catch-up to bluebird, Vertex and CRISPR send in their pitch for blood disorder cell therapy
Vertex and CRISPR Therapeutics are expected to submit their gene therapy exagamglogene autotemcel (Exa-cel) for review by US authorities in the first quarter of 2023 and expect to file for approval in the EU and UK by the end of 2022. Exa-cel is a treatment for sickle cell disease and transfusion-dependent beta thalassemia (TDT).

BioMarin resubmits its haemophilia gene therapy to the FDA
BioMarin Pharmaceutical has resubmitted its haemophilia gene therapy aloctocogene roxaparvovec Roctavian) for approval by the FDA. The FDA declined BioMarin's previous application, but the company has obtained more robust data on the effectiveness of the Roctavian which was recently approved in Europe by the European Medicines Agency.

BioMarin reports cancer case in haemophilia gene therapy trial
BioMarin has reported an instance of a patient receiving the gene therapy Roctavian developing leukemia. Testing indicated that diseased blood cells had low levels of Roctavian vector DNA, suggesting the cancer may have developed separately to the treatment. Details of the assessment were submitted to regulators worldwide, with no authorities currently calling for a hold or modifications to ongoing Roctavian clinical trials.

Decision-making about gene therapy in transfusion dependent thalassemia
Researchers conducted interviews with the parents of children with transfusion dependent thalassemia (TDT), as well as adults with TDT, to understand patient knowledge and decision-making regarding gene therapies. Participants expressed a desire for a cure and cited transfusion independence, chelation reduction and improved quality of life as motivators for considering gene therapy. Knowledge about the process, long-term outcomes, safety, and side effects as well as the potential for death or treatment failure were identified as deterrents. However, reduction in frequency of transfusions, even without elimination of transfusions was deemed to be acceptable for most participants.

Bluebird wins FDA approval of gene therapy for rare brain disorder
The FDA has granted accelerated approval to Bluebird Bio's cerebral adrenoleukodystrophy (CALD) gene therapy, Skysona. CALD is a very rare childhood brain disease which affects young males and results in severe disability or death.

Clinical gene technology in Australia: building on solid foundations
It is just over 20 years since Australia's national gene technology regulatory scheme administered by the Office of the Gene Technology Regulator came into effect. This report provides a snapshot of the evidence for and setbacks to using gene therapy in a clinical setting.

7 COVID-19

This section contains news articles, peer reviewed papers and industry publications on the coronavirus disease (COVID-19) pandemic and management of the virus across the world including effects on blood and related services.

7.1 COVID-19 effect on blood, blood diseases and related services

Neurological consequences of COVID-19: A curious case of delayed onset Guillain-Barre
This report highlights a patient diagnosed with Guillain–Barré syndrome (GBS) five weeks after COVID-19 infection. The authors noted that the delayed onset of GBS and rapid progression of the illness were novel and could indicate a new side effect of recent COVID-19 variants. The patient received a standard five-dose of intravenous immunoglobulin and demonstrated rapid improvement in response to therapy. The authors suggest that healthcare providers should still consider GBS as a possibility in patients with a relatively distant history of COVID-19 infections.

Clinical characteristics of hospitalised COVID-19 patients who have gastrointestinal bleeds requiring intervention: A case-control study

This retrospective analysis of hospitalised adult patients with COVID-19 infection admitted between 1 March 2020 and 5 January 2021 aimed to determine the incidence and outcomes of clinically significant gastrointestinal (GI) bleeding. Researchers found that of the 1,007 patients included in their analysis, 76 (8%) had a GI bleed requiring endoscopic intervention. The authors note that a GI bleed in COVID-19 patients could be from the virus' direct effect on the gut mucosa or stress-induced bleeding like any other severely sick ICU patient.

Anticoagulation in non-ICU patients with COVID-19 at high thrombosis risk

The most severe clinical presentation of COVID-19 is acute respiratory distress syndrome (ARDS). Researchers have suggested the use of full anticoagulation be considered in patients with COVID-19 who are not in the intensive care unit but are at high risk for progression of thrombosis and low risk for bleeding.

Hospital red blood cell and platelet supply and utilisation from March to December of the first year of the COVID-19 pandemic

This study determined how hospital blood supply and blood utilisation was affected by the first wave of COVID-19. Researchers compared weekly red blood cell and platelet inventory, transfusion, and outdate data from 13 institutions in the United States, Brazil, Canada, and Denmark from March to December of 2019 (pre-pandemic) and 2020 Researchers found that despite concerns surrounding reduced donations during pandemic restrictions, RBC and PLT supply was greater than utilisation due to reduced patient care activity.

A case of COVID-19 vaccine-induced thrombotic thrombocytopaenia

Researchers report a case of a 37-year-old female who developed vaccine-induced thrombotic thrombocytopaenia after receiving the Johnson & Johnson COVID-19 vaccination. The patient was treated surgically and received steroids with IVIg, which led to the resolution of the thrombocytopenia.

Development of resistance associated mutations after sotrovimab administration in high-risk individuals infected with the COVID-19 Omicron variant

Researchers looked at the development of resistance associated spike protein mutations after a single treatment with the COVID 19 oral anti-viral sotrovimab (Xevudy). This indicates that treatment of high-risk patients with the monoclonal antibody may be associated with mutation development, especially in immunocompromised patients.

7.2 COVID-19 news

The National Cabinet has agreed to end mandatory isolation for people who test positive for COVID-19 from 14 October 2022. The decision comes after the Australian Chief Medical Officer advised that the combination of high vaccination rates, immunity from infections and reduced case numbers suggested there was no longer a need for an enforced period of isolation. The Australian Technical Advisory Group on Immunisation (ATAGI) recommended the vaccine for young children at high risk of developing severe illness from COVID-19.

- Mandatory COVID-19 isolation periods scrapped from 14 October, emergency response 'finished' says national cabinet
- Letter from the Chief Medical Officer to the Prime Minister about the proposed removal of mandatory isolation for COVID-19
- ATAGI recommendations on COVID-19 vaccine use in children aged 6 months
- COVID-19 cases drop everywhere: WHO
- Australians are dealing with second, third and fourth COVID-19 infections

7.3 COVID-19 policy and industry

The *Lancet* COVID-19 Commission has published a report on the international response to the COVID-19 pandemic. The report investigates and analyses the history and current state of the pandemic with a focus on recommending better responses in the case of potential future pandemics. The WHO has responded to the report, noting that many of the recommendations the *Lancet* proposes align with the WHO's goals.

- The *Lancet* Commission on lessons for the future from the COVID-19 pandemic
- WHO responds to The *Lancet* COVID-19 Commission
- National Cabinet Statement on COVID-19 settings
- $31.5 million to boost support for COVID-19 research
- High blood viscosity may predict mortality in COVID-19 hospitalisation

7.4 COVID-19 research and treatment

Association of COVID-19 vs influenza with risk of arterial and venous thrombotic events among hospitalised patients

Researchers in the United States investigated the incidence of arterial thromboembolism and venous thromboembolism in patients hospitalised with COVID-19. They compared these results to patients hospitalised with influenza, to understand the risk of thrombotic complications after COVID-19 infection. They found that COVID-19 was associated with a higher risk of venous thromboembolism within 90 days when compared to influenza, but not arterial thromboembolism.

Long-term effectiveness associated with the Pfizer COVID-19 vaccine among adolescents in South Korea

Researchers compared the rates of COVID-19 infection and critical infection in South Korea by age, census region, vaccination status, and vaccine doses in all adolescents aged 12 to 18 years, to determine the effectiveness of the Pfizer COVID-19 vaccine, BNT162b2 (Comirnaty). Researchers found that Comirnaty was sufficient for protection against critical COVID-19 infection, but that effectiveness waned over time and offered limited protection 30 days after the second dose.

Nirmatrelvir use and severe COVID-19 outcomes during the Omicron surge

Researchers investigated the efficacy of Pfizer's COVID-19 oral antiviral nirmatrelvir (Paxlovid) in a real world setting. The study, undertaken in Finland, reviewed 3902 cases in which patients received Paxlovid and found that treatment reduced the mortality rate among people over the age of 65 by 81%. However, the study also found that the drug had no significant benefit in terms of hospitalisation or death for patients under 64 years old.

Characterisation of pathogen inactivated COVID-19 convalescent plasma and responses in transfused patients

Researchers evaluated COVID-19 convalescent plasma from donors and recipients using multiple antibody assays. Researchers assessed the characteristics of donated COVID-19 convalescent plasma (dCCP) characteristics, antibody responses, 28-day mortality, and adverse events in recipients of dCCP. They found pathogen reduction technology (PRT) did not impact dCCP anti-virus neutralising activity, but transfusion of unselected dCCP did not impact survival and had no adverse effects. Researchers suggested that the variable dCCP antibodies and post-transfusion antibody responses indicated the need for controlled trials.

Acute-type acquired haemophilia A after COVID-19 mRNA vaccine administration: A new disease entity?

Researchers report a case in which a young patient developed acute acquired haemophilia A (AHA) after receiving an mRNA COVID-19 vaccine but improved rapidly. Researchers compared this case with other reports of AHA after COVID-19 vaccination and suggest that the levels of FVIII inhibitors associated with acute AHA decrease more rapidly in such cases than in idiopathic AHA.

Case reports of management of aplastic anaemia after COVID-19 vaccination: a single institute experience in Taiwan

Researchers discuss four cases of aplastic anaemia (AA) that arose after COVID-19 vaccination in a single Taiwanese hospital and two other such cases identified in a literature review. Researchers noted that AA occurred after receiving either an adenoviral-vectored or a mRNA vaccine, with greater severity noted after the adenoviral-vectored vaccine platform. Researchers highlighted that they were unable to identify a causative relationship between COVID-19 vaccination and AA but noted that the treatment strategies they employed were effective.

Intravenous immunoglobulin (IVIg) therapy in hospitalised adult COVID-19 patients: A systematic review and meta-analysis

Researchers investigated the impact of intravenous immunoglobulin (IVIg) on mortality and length of hospitalisation in adult COVID-19 patients. They reviewed 13 studies, reporting on the use of IVIg therapy in hospitalised adult COVID-19 patients and found that IVIg therapy provided no significant benefit regarding patient mortality or length of hospitalisation. Results indicated that IVIg therapy may increase the length of hospital stay in severe COVID-19 patients.

Worsening general health and psychosocial wellbeing of Australian hospital allied health practitioners during the COVID-19 pandemic

Researchers assessed the psychological health of allied health practitioners using online surveys at three points during the COVID-19 pandemic. The questionnaire used the short form version of the Depression Anxiety Stress Scales (DASS-21), to determine the health of practitioners. Allied health practitioners reporting poor general health significantly increased over time. Anxiety increased significantly between the first and second reporting period, while depression scores increased significantly between the second and third period. These increases in stress scores were recorded across time, suggesting that the COVID-19 pandemic had a significant impact on the mental health of health practitioners.

General practice experiences of Australia's COVID-19 vaccine rollout: lessons for primary care reform

Researchers interviewed owners and managers of general practices in Greater Sydney between June and August 2021 to understand their experiences in delivering Australia's COVID-19 vaccine program. Practices reported early enthusiasm for the vaccine rollout, adjusting staffing and infrastructure to manage the increased vaccination workload. Some practices reported increased income related to vaccination, but nearly all reported increased costs.

Early and out-of-hospital use of COVID-19 convalescent plasma: An international assessment of utilisation and feasibility

Researchers distributed a questionnaire to the International Society of Blood Transfusion COVID-19 convalescent plasma (CCP) working group to determine the extent of existing trials on early and outpatient CCP and out-of-hospital (OOH)/home transfusion (HT) practices. They found that barriers to implementation of OOH/HT included existing legislation, lack of policies pertaining to outpatient transfusion and logistical challenges such as lack of resources.

8 Other items of interest

This section contains general industry and regulator updates as well as developments in non-blood and non-COVID related diseases that may have flow on affects to the blood industry.

8.1 Research and development news

Trends in adverse event rates in hospitalised patients, 2010-2019

This study investigated the instances of adverse events in hospitalised patients in the US over a ten-year period. Researchers found that rates of adverse events in hospitalised patients with acute myocardial infarction, heart failure, pneumonia, and major surgical procedures declined significantly between 2010 and 2019 and for patients with all other conditions, between 2012 and 2019.

How do dangerous blood clots form in space? New insights from a valve model may provide information to protect astronauts

In this study researchers looked at the flow patterns and red blood cell (RBC) movement at the microscopic level to understand why astronauts develop blood clots. In the absence of gravity, body fluids shift from the legs to the upper body and the head. It is thought that the lateral movement of RBCs contributes to the formation and progression of blood clots not only in venous valves, but also in aortic aneurysms and blood-circulating devices.

Study: CRISPR gene editing can lead to cell toxicity and genome instability

Scientists at IRB Barcelona have reported that, depending on the targeted spot of the human genome, CRISPR gene editing can give rise to cell toxicity and genomic instability. Researchers analysed a CRISPR library designed for human cells and detected 3,300 targeted spots that show strong toxic effects. The reports also found that around 15% of human genes contain at least one toxic editing point.

Genetically modified herpes combats advanced cancers

Researchers have modified a version of the herpes simplex virus to treat a range of advanced cancers, with a quarter of treatment recipients experiencing tumour size reduction in early testing.

Alzheimer's: Targeting key protein in blood may slow progression

Researchers have demonstrated that replacing the blood of an Alzheimer's disease mouse model with the blood of another mouse reduced the levels of Alzheimer's brain markers and improved spatial memory in the mouse model.

Is transfusion blood safe? AI holography system checks blood quality without injections

A South Korean research team has developed an AI holography system that automatically extracts important information and inspects the quality of RBCs. The team has suggested that the technology will be able to inspect the quality of RBCs stored for a certain time by combining the 3D structure image data of RBCs.

Blood Type Linked to Risk of Stroke Before Age 60

Researchers have found that a people with blood type A have a higher risk of stroke before the age of 60 than people with other blood types, while people with blood type O are less likely to have an early onset stroke. Researchers did a meta-analysis of 48 studies involving almost 17,000 people who had experienced a stroke and more than 570,000 people with no history of stroke and found that blood type had a reasonable effect on the chances of stroke before 60.

Citrullinated fibrinogen forms densely packed clots with decreased permeability

This study investigated the effect of fibrinogen citrullination on the structure of fibrin clots. Citrullinated fibrinogen has been detected in human plasma and it decreases the decomposition and mechanical resistance of fibrin clots.

8.2 Industry news

There are too many blood cancer cell therapies in development, report says

Data and analytics company, GlobalData, has warned that the development landscape for cancer cell therapies is 'oversaturated' with more than 800 cell therapy prospects for five major blood cancers.

Pfizer to acquire Global Blood Therapeutics for $5.4 billion to enhance presence in rare haematology

Pharmaceutical company Pfizer has signed a deal to purchase the company Global Blood Therapeutics and its sickle cell disease drug, 'Oxbryta'. Pfizer confirmed it will buy the sickle cell disease-focused biotech for USD $5.4 billion.

Moderna sues Pfizer, BioNTech over COVID-19 vaccine technology

Moderna has filed a lawsuit against Pfizer and BioNTech, claiming that the 'Comirnaty' COVID-19 vaccine infringes on patents issued to Moderna between 2010 and 2016. Moderna, who filed the suit in the US and in Germany, are seeking compensation for all alleged use of its intellectual property by Pfizer and BioNTech in developed countries after March 2022.

British Society for Immunology & United Kingdom Primary Immunodeficiency Network (UKPIN) consensus guideline for the management of immunoglobulin replacement therapy

The UK Primary Immunodeficiency Network (UK-PIN) and the British Society of Immunology (BSI) has created a guideline to support the use of immunoglobulin replacement therapy (IgRT) in primary and secondary immunodeficiency disorders in UK.

Novo Nordisk to acquire Forma Therapeutics and expand presence in sickle cell disease and rare blood disorders

Novo Nordisk has agreed to acquire Forma Therapeutics for $20 USD per share in cash, representing a total value of $1.1 billion. Forma Therapeutics is a clinical-stage biopharmaceutical company focused on developing treatments for sickle cell disease and other rare blood disorders.

CSL CEO Paul Perreault determined to grow plasma collection after full-year sales dip

Pharmaceutical company CSL Behring has reported a drop in profits, partly due to reduced plasma donation during the COVID-19 pandemic. CEO Paul Perreault has claimed that they are investigating every possible option to grow plasma collection volumes.

AstraZeneca wins federal class-action suit, judge dismisses shareholders' misleading claims

Pharmaceutical company AstraZeneca has won a lawsuit in the US, brought by company shareholders, alleging the company made misleading statements about the clinical testing of its COVID-19 vaccine.

Therapeutic Goods Administration (TGA): Xembify

The TGA has approved Xembify (normal immunoglobulin human) as a replacement therapy in adult and paediatric patients with Primary immunodeficiency diseases (PID) and Symptomatic hypogammaglobulinaemia secondary to underlying disease or treatment.

8.3 Government & policy

Australian Government Department of Health and Aged Care - New name for Department

The Department of Health is now the Australian Government Department of Health and Aged Care, with the change of name reflecting the importance of aged care to the Australian community and the high priority the Government places on aged care reform.

Cyberattacks refocusing from large health systems to smaller hospitals, specialty clinics

The number of cyberattacks on health care services in the US decreased in 2022, however, attackers are increasingly focused on smaller health care companies and specialty clinics, as larger health services improve their security protocols.

International Society of Blood Transfusion Working Party on Red Cell Immunogenetics and Blood Group Terminology Report of Basel and three virtual business meetings: Update on blood group systems

This report presents the outcomes from the meetings of the Working Party for Red Cell Immunogenetics and Blood Group Terminology. The working party is currently responsible for ratifying blood group systems, antigens and alleles under the International Society for Blood Transfusion.

Therapeutic value of drugs granted accelerated approval or conditional marketing authorisation in the US and Europe from 2007 to 2021

This article looks at the therapeutic value of new drug indications granted accelerated approval or conditional marketing authorisation in the US and Europe. In this cohort study of 146 drugs, 39% of indications granted accelerated approval and 38% granted conditional marketing authorization were rated as having high added therapeutic value.

The AABB releases clinical practice guideline

The Association for the Advancement of Blood and Biotherapies (AABB) has released clinical practice guidelines for the appropriate use of COVID-19 convalescent plasma (CCP) in hospital and outpatient settings. The guidelines provide five specific recommendations for treating patients with COVID-19 and suggest that CCP is most effective when transfused with high neutralizing titers to infected patients early after symptom onset.

$156 million to support innovative medical research

Successful applicants under the Medical Research Future Fund (MRFF) *2021 Research and Data Infrastructure Grant Opportunity* and *2021 Optimising the Clinical Use of Immunoglobulins Grant Opportunity* have been confirmed. The funding included $2.9 million for the Monash University National Transfusion Dataset Team to expand the national transfusion dataset (NTD) from five to approximately 20 hospitals. It also includes over $800,000 for a national registration process to track, collect and evaluate chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) patient outcomes with real world data.

WHO launches guide to safely unlock benefits of the life sciences

The WHO has released its first publication for mitigating risks and governing dual-use research, the *Global guidance framework for the responsible use of the life sciences*. The guide outline ways to prevent the accidental and deliberate misuse of biology and other life sciences.

8.4 NBA - National Blood Sector Research and Development Program

Massive transfusion experience, current practice and decision support: A survey of Australian and New Zealand anaesthetists

This grant from Round 4 of NBA's grant program looked at decision making during massive transfusion and aimed to find efficiencies which could improve outcomes for patients. In an initial scoping review, researchers demonstrated significant variation, lack of benchmarks internationally for massive transfusion protocols (MTP) and minimal evidence to guide practice. Barriers and risks of clinical decision-making were also explored in a survey of 227 respondents across Australia and New Zealand. The research team successfully developed a prototype computerised clinical decision support system to support massive transfusion and will now test this prototype in a surgical massive transfusion setting.

8.5 Other diseases and developments

8.5.1 Malaria

- BioNTech set to take malaria vaccine into clinical trials
- Malarial host-parasite clash causes deadly blood sugar drop
- Australian researchers use mathematical modeling to fight malaria
- Australia pledges $266 million to tackle HIV, TB and malaria
- An epidemiological analysis of imported malaria in Shanghai during a COVID-19 outbreak

8.5.2 Dengue

- Mosquitoes more attracted to people infected with viruses like dengue and Zika
- Study: Viruses can change your scent to make you more attractive to mosquitoes
- Do COVID-19 lockdowns have impacted on global dengue burden? A special focus on India
- Takeda gets first approval for its dengue vaccine
- France reports 16 locally acquired cases of dengue year to date

8.5.3 Japanese Encephalitis

- Vaccine rollout for Japanese encephalitis
- Japanese Encephalitis in Australia — A sentinel case
- Mosquito-borne disease risk increases for river communities facing third La Nina
- Japanese encephalitis outbreak likely six times larger than reported
- NSW expands access to Japanese encephalitis vaccine

8.5.4 Monkeypox

- Monkeypox in 2022—What clinicians need to know
- Monkeypox has been declared a global emergency
- Monkeypox: WHO chief advises at-risk men to reduce number of sexual partners
- What is monkeypox: symptoms, treatments, cases and Australia's response
- Monkeypox outbreak 2022 - Global