

Monitoring International Trends December 2021 – January 2022

The National Blood Authority (NBA) monitors international developments that may influence the supply and 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.

Some key topics that have appeared in news media, online publications, and industry and research updates in this report include:

- <u>Blood Supply:</u> The COVID-19 pandemic is having a significant and ongoing effect on blood donation worldwide. The United States Red Cross declared a 'blood crisis' for the first time in its history as the COVID-19 Omicron surge reduced the number of blood donors. Lifeblood reviewed the minimum deferral period for blood donors that have contracted COVID-19 to bring it in line with policies for other infections.
- <u>Blood Disorders:</u> There has been a focus on testing and analysing the effectiveness of treatments for haemophilia in a variety of real-world settings. In addition, this month's report covers treatment news for anaemia, sickle cell disease, leukemia and the use of immunoglobulin in the treatment of Kawasaki disease.
- <u>Transfusion</u>: The COVID-19 pandemic has had a significant impact on blood supply, in particular short shelf-life products such as platelets. There has been a focus on reports that have researched platelet storage, blood management and blood policy throughout December and January.
- Gene Therapy: A highlight of this report is the success story of one of the first sickle cell patients treated
 with CRISPR gene technology in an on-going study. Potential treatments for haemophilia, anaemia and
 thalassemia are also highlighted.
- <u>COVID-19</u>: The Omicron variant of COVID-19 is now the dominant variant in Australia, with the Delta variant still circulating in the community. The Novavax COVID-19 vaccine has been provisionally approved for use in Australia by the Therapeutic Goods Administration.
- Other items of interest: The Australian Government confirmed a four-year investment in permanent telehealth services and opened a \$14 million grant opportunity through the Medical Research Future Fund called the 2021 Optimising the Clinical Use of Immunoglobulins.



Contents

1	Bloo	d supply	3
	1.1	Blood supply - Australia	3
	1.2	Blood supply – United States of America	3
	1.3	Blood supply - World news	3
	1.4	Regulatory and donation criteria changes	4
	1.5	Storage and management	4
	1.6	Blood donor characteristics and donation effects	5
2	Bloo	d disorders and treatments	6
	2.1	Haemophilia	6
	2.2	Anaemia	7
	2.3	Sickle cell disease	8
	2.4	Leukemia	8
	2.5	Immune system and immunotherapy	9
3	Tran	sfusion	9
	3.1	Paediatrics	9
	3.2	Obstetrics	9
	3.2	Management	10
	3.3	Research	11
4	Gene	e therapies	12
	4.1	Blood related gene therapies	12
	4.2	Regulatory and industry developments	12
5	G COVID-19		13
	5.1	COVID-19 News	13
	5.2	COVID-19 Impacts	13
	5.3	COVID-19 Policy and Industry	14
	5.4	COVID-19 Research	15
6	Othe	r items of interest	16
	6.1	Government & Industry	16
	6.2	Emerging Technology	16
	6.2	Other diseases and developments	17
	6.2.1	Malaria	17
	6.2.2	Dengue	17
	6.2.3	Ebola	17
	6.2.4	Avian influenza outbreaks	18
	6.2.5	Other	18



1. Blood supply

This section contains news articles and government agency statements on blood supply. The negative effects of the COVID-19 pandemic on donation rates has led to blood drives and conversations in the United States, Canada and Australia about the need to revise donation criteria.

1.1 Blood supply - Australia

In Australia, people were encouraged to get out and donate blood for Australia Day and around Christmas.

- Red Cross Lifeblood calls for thousands more blood donors over Christmas break
- Extra blood Lower Hunter donors needed around Australia Day public holiday
- Bloody legends needed in Port Macquarie this Australia Day
- Easy wins: want to save three lives in 10 minutes? Give blood
- 9,000 blood donors urged to give life this Christmas
- Australian Red Cross Lifeblood asks for Rockingham blood and plasma donors this Christmas
- 3,200 blood donors needed now
- Call out for more blood donors in the Illawarra amid nationwide shortfall
- More donors needed as blood donations plummet

1.2 Blood supply – United States of America

There was a critical shortage of blood in the United States caused by a falling donation rates resulting from local weather events, COVID-19 infection rates and the holiday season. The American Red Cross announced its first ever critical shortage after confirming that their supply was at its lowest level in more than a decade.

- "It's really a dire situation" Red Cross facing worst blood shortage in over ten years
- Red Cross sees highest blood shortage in a decade
- Emergency blood shortage persists, Red Cross says, seeking donors
- COVID-19 surge impacting blood donors, community blood supply
- <u>US faces worst blood shortage in over a decade amid pandemic</u>
- Blood donors urgently needed during national blood donor month and throughout the Winter
- <u>Lifeline joins national joint blood bank reserve</u>
- The Blood Connection joins nation's first emergency blood
- Blood drive supports Maury County Public Library
- American Red Cross Blood Supply at Historic Low, Donors needed Urgently
- Upper Peninsula facing severe blood shortage, residents encouraged to donate
- National blood donation shortage could impact Northeast Ohio hospitals
- Blood shortage impacting sickle cell patient care
- <u>Devastating tornadoes activate national Blood Emergency Readiness Corps</u>
- Blood shortage prompts hospitals to plan for surgery cancellations
- Austin-Travis County EMS launches pilot program to carry Type O blood on response vehicles
- Winter storms hamper blood donations amid shortage

1.3 Blood supply - World news

COVID-19 and the impact on blood availability and transfusion practices in low- and middle-income countries

A survey sent to blood collecting agencies in 26 'low and middle income' countries sought to determine how the pandemic had impacted supply. Collectively, 77.4% of respondents experienced a 10% to 50% decline in blood availability.

HIV incidence and compliance with deferral criteria over three progressively shorter time deferrals for men who have sex with men in Canada

In Canada, the deferral for men who have sex with men (MSM) has been progressively reduced from a permanent deferral to 3 months. Between 2010 and 2021, researchers conducted four anonymous online surveys each time deferral time lessened and found that as deferral periods were shortened, HIV residual risk was unchanged.



The contribution and potential of older blood donors in Asia Pacific regions

This study investigated the blood supply contribution of older donors in five Asia Pacific regions, and found that older donors were loyal and regular but under-represented in all the regions studied.

Effect of the first year of COVID-19 pandemic on the collection and use of blood components in Colombia monitored through the national haemovigilance system

A Colombian study looked at the effect of the COVID-19 pandemic on blood donation and blood product use within the country from March 2020 to March 2021. The authors found that there was a reduction in blood donations (16.7%) and deferrals (33.7%), with the majority of donors (60.5%) aged in the 20-39 age range. There was also a drop in administration of blood products to transfused patients and patients requiring blood components (-8.7% and -13.9% respectively).

Blood unit segments accurately represent the biophysical properties of red blood cells in blood bags but not haemolysis

Current practices in transfusion medicine are to store red blood cell (RBC) units for up to 42 days, and to use these units on a first-in first-out basis. The study suggests that the ability to perform interim testing on RBC units during storage, without compromising the blood product, could have a major impact on selecting RBC units for chronic transfusion recipients.

1.4 Regulatory and donation criteria changes

CSL Behring to appeal after losing challenge to Mexican donor ban

Biotech company CSL Behring has lost a bid to overturn a United States customs decision to ban donors from entering the United States from Mexico to donate plasma.

Democratic Representatives, LGBTQ advocates call on FDA to revise blood donation policy for gay men

The blood supply shortage in the United States has triggered calls review the deferral period for homosexual men to donate blood.

<u>Podcast: Red Cross Lifeblood in desperate need of new blood donors after COVID-19 lockdowns affect donation</u> supply (ABC radio Melbourne recording)

Lifeblood Australia's Executive Director of Donor Services, Cath Stone, has said the number of new blood donors in Australia would have to increase by 45% next year to meet hospital demand. COVID-19 lockdowns have affected the number of people needing blood, while also leading to many appointment cancellations.

Lifeblood to change rules to allow blood donations sooner after having COVID-19

Lifeblood Australia is changing the rules the deferral to for resuming donations after donors have recovered from COVID-19. People who have had the virus will need to wait seven days before booking an appointment, down from waiting 28 days after recovery before being eligible to donate blood.

1.5 Storage and management

Time from apheresis platelet donation to cold storage: Evaluation of platelet quality and bacterial growth

Cold storage reduces posttransfusion survival of platelets, however it can improve platelet activation, lower risk of bacterial contamination, and extend shelf-life compared to room temperature storage. This study evaluated the impact of time from platelet component collection to cold storage on in vitro properties and bacterial growth. Researchers suggest that extending time from extraction to cold storage from 2 to 8 hours after collection does not significantly increase bacterial growth while platelet component quality and function is maintained.



<u>Evaluation of platelet concentrates prepared from whole blood donations with collection times between 12 and 15 minutes</u>

In many countries, whole blood (WB) donations with collection times between 12 and 15 minutes are not allowed to be used for platelet concentrates (PC). Since the development of guidelines, many process-related changes have been introduced. This study aimed to determine the effect of WB with long collection times on PC quality. This study provides evidence that 12–15 minute donations should not be excluded for PC preparation and justifies to readdress the guidelines to <15 min instead of <12 min of collection in line with current practice in some countries.

Impact of product platelet count reduction on platelet demand in Canada

This discussion piece outlines the Canadian experience of reducing the minimum in apheresis platelet products to reduce platelet shortages. The author notes that reducing the platelet count did not lead to a significant increase in demand but allowed blood operators to more flexibly collect multiple platelet doses while meeting quality standards for platelet count year-round.

<u>Impact of different pathogen reduction technologies on the biochemistry, function, and clinical effectiveness of platelet concentrates:</u> An updated view during a pandemic

The study suggests that pathogen reduction technologies add a level of safety to current donor screening and regulated testing for known pathogens. The authors note that these technologies increase patient safety but do so at the expense of platelet functionality and survival in clinical trials.

Exploring the causes of wastage of blood and its components in a tertiary care hospital blood bank

This study from Pakistan found a discard rate of 8.87%, with the majority of waste being platelet products, due to short shelf life. Leakage of blood bags remained a predominant cause for the discard of blood components. Seropositivity for hepatitis B, C, and human immunodeficiency virus (HIV) was reported in almost 30% units of donated blood.

Impact of the pathogen inactivation process on the migration of di(2-ethylhexyl) phthalate from plasma bags

Di(2-ethylhexyl) phthalate (DEHP) is a plasticizer that is commonly used in the manufacture of polyvinyl chloride (PVC) blood bags that can migrate from the bag into the blood plasma. Pathogens in plasma must be inactivated, but this process may increase DEHP migration. The researchers assessed the impact of illumination-based pathogen inactivation on the migration of DEHP from PVC bags into plasma and investigated the impact of the pathogen inactivation process on the DEHP exposure rate. The authors suggest that the pathogen inactivation process did contribute to DEHP leachability.

Acquired platelet storage container leaks and contamination with environmental bacteria: A preventable cause of bacterial sepsis

Environmental contamination of apheresis platelets is rare but can cause sepsis. Container damage provides a pathway for contamination after culture screening, point-of-issue bacteria testing, or pathogen reduction. Researchers reviewed a single blood container manufacturers' records which showed 23 US reports of leaks involving 24 containers attributed to post manufacturing damage, at a rate of 44 per million distributed storage containers. Analysis of returned containers showed evidence of scratches, impressions, and/or piercings.

1.6 Blood donor characteristics and donation effects

A methods review of the "healthy donor effect" in studies of long-term health outcomes in blood donors

The "healthy donor effect" (HDE) is an important consideration when investigating the effect of blood donation. The effect suggests that donors that have fewer health issues tend to donate more, thus a true randomized sample is difficult to obtain when investigating ongoing health effects of donations. The review notes the importance of HDE being considered in the design phase of any studies.

Who donates? Patterns of blood donation and donor characteristics at a university-affiliated hospital-based donor center

This recent study published in the journal Transfusion looked at the patterns and demographics of people that donated at the University of California, Los Angeles (UCLA) Blood & Platelet Centre. The study found that the demographics of donors reflected that of the local university demographic.



Weekly Group O Blood Supply Report

The Association for the Advancement of Blood & Biotherapies (AABB) provides weekly supply estimates data for Group O blood. They estimate a weekly US nationwide average supply of approximately 2.4 days for O-negative red blood cells and 2.3 days for O-positive RBCs. The link also includes a trend graph of type O blood supply since 2017.

It is about who you know (and how you help them): Insights from staff and donors about how to recruit and retain a panel of committed anti-D donors

Anti-D immunoglobulin donors in Australia are motivated by multiple factors, including knowing who the recipient is, and dedicated staff who are integral to building donors' commitment through education and support. The findings of this study suggest the current approach to recruitment could be broadened to include all donors who meet formal selection criteria and rewarding the motives identified for donating.

Routine donor red cell antibody screening: Considering the alternate strategy

This Australian study looked at the current Lifeblood practice of performing red blood cell antibody screening on every whole blood donation and looks at the risks involved with an alternate strategy whereby an antibody screen is performed on the first donation and only repeated following pregnancy, transfusion or a significant break between donations (>2 years). Researchers concluded that while the alternate strategy is a more cost-effective option within the Australian setting, the additional residual risk was not deemed to be acceptable.

2. Blood disorders and treatments

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

2.1 Haemophilia

UniQure and CSL Behring announce trial updates for hemophilia B gene therapy

UniQure and CSL Behring recently announced that 'etranacogene dezaparvovec', an investigational haemophilia B gene therapy currently in clinical trials, has matched comparable treatments in the control of annualised bleeding rates (ABR) 18-months post commencement.

<u>Immune tolerance induction in the era of emicizumab – still the first choice for patients with haemophilia A and inhibitors?</u>

This study surveyed centres representing 17 countries in the Europe/Middle East region treating a total of 4,955 haemophilia patients. The study found that Immune Tolerance Induction (ITI) remains the preferred method for treatment of patients with haemophilia A with inhibitors, but noted that the treatment 'emicizumab' has become a preferred first-line approach to protect against bleeds and represents an alternative to ITI in certain patient groups.

<u>Fitusiran significantly reduced bleeding in haemophilia A and B with inhibitors</u>

Fitusiran is an investigational small interfering RNA (siRNA) treatment that targets antithrombin in the blood to restore thrombin generation and improve coagulation. The study found that Fitusiran significantly reduced bleeding rates among patients with haemophilia A or B with inhibitors.

Reduced cardiovascular morbidity in patients with haemophilia: Results of a 5-year multinational prospective study

Life expectancy of people with haemophilia has increased with the availability of new clotting treatments, while the incidence of cardiovascular disease (CVD) in these people has increased. The study found that there was no significant relation between severity of haemophilia and incidence of CVD.



The relationship between chronic pain and psychosocial aspects in patients with haemophilic arthropathy

This study suggests that higher intensity of pain in patients with haemophilic arthropathy is correlated with anxiety, catastrophism, and the degree of kinesiophobia (fear of movement). The perception of quality of life in patients with haemophilia, especially the physical component, negatively correlates with intensity of pain.

Arthropathy in people with mild haemophilia: Exploring risk factors

This study examined the risk factors associated with arthropathy (joint disease) in 85 patients with mild haemophilia. It found that patient age and clotting factor levels appear to be the most determinant risk factors associated with the development of arthropathy in mild haemophilia. The authors suggested that physical activities with a low risk of bleeding are recommended for patients with arthropathy.

Emicizumab does not interfere with the activated clotting time

Emicizumab (Hemlibra), is a treatment for bleeding prevention in haemophilia A patients. The treatment acts like activated Factor III (FVIII) that is present in non-haemophiliacs but does not need prior activation and so is expected to shorten activated clotting time (ACT). ACT has typically been used as a useful marker of unfractionated heparin (UFH) activity, in order to monitor patient clotting potential during cardiopulmonary bypass or cardiac catheterization. The study examined whether ACT can reliably monitor UFH activity in emicizumab-treated patients and found that emicizumab does not interfere with UFH-induced ACT prolongation.

Effects of replacement therapies with clotting factors in patients with haemophilia: A systematic review and meta-analysis

Different prophylactic and episodic clotting factor treatments are used in the management of haemophilia. The authors looked at nine randomized controlled trials (RCTs), which compared different factor replacement therapies in patients with haemophilia and suggested that prophylactic treatment (at either low, intermediate, or high doses) is superior to episodic treatment for bleeding prevention.

2.2 Anaemia

Retrospective evaluation of preoperative anaemia management at a Melbourne metropolitan hospital: a framework for quality improvement

An evaluation was undertaken of the patient blood management systems in a Melbourne metropolitan hospital. This assessed the prevalence of anaemia and the current blood management practices of each surgical unit, to create recommendations for a hospital wide implementation. It was found that the orthopaedic unit had the most effective method for treating preoperative anaemia, and the whole hospital should adopt the system as well as address specific barriers identified within each unit.

<u>Perinatal risk factors associated with severity of haemolytic disease of the foetus and newborn due to Rh</u> maternal-foetal incompatibility: A retrospective cohort study

A retrospective cohort study was conducted in Paris and the surrounding area, between 2013 and 2015. The study looked at the severity of haemolytic disease (quick destruction of red blood cells) in foetus and newborns where there is maternal incompatibility of Rh blood types. Researchers concluded neonatal anaemia is caused by anti-c alloimmunisation (the third red blood cell antibody responsible for haemolytic disease in foetus and newborns).

Mortality and morbidity in non-transfusable and transfusable patients: A systematic review and meta-analysis

At a certain degree of anaemia, known as the transfusion threshold or trigger, allogeneic red cell transfusions are administered with the purpose of reducing the increased morbidity and mortality observed. This review investigated how the transfusions were affected by Patient Blood Management (PBM) practices and whether there were adverse effects for patients that were unable to receive a transfusion. The researchers found that patients unable to receive allogeneic blood transfusions had similar clinical outcomes to patients that received transfusion. The results of their meta-analysis may also provide further incentives to deliver more aspects of PBM to transfusable patients.



2.3 Sickle cell disease

Mitapivat (AG-348) demonstrates safety, tolerability, and improvements in anaemia, haemolysis, oxygen affinity, and haemoglobin S polymerization kinetics in adults with sickle cell disease

This trial looked at the drug 'Mitapivat' developed by Agios Pharmaceuticals and found that the treatment improved anaemia, reduced markers of hemolysis, improved oxygen affinity, and decreased in red blood cells sticking or clumping together, signaling its potential to improve clinically meaningful outcomes in the treatment of sickle cell disease.

FDA approves drug to treat sickle cell disease in patients aged 4 up to 11 years

The FDA has granted accelerated approval for 'Oxbryta' (voxelotor) tablets to treat sickle cell disease in pediatric patients aged from 4 to 11 years old.

Perinatal outcomes in women with sickle cell disease: a matched cohort study from London, UK

The study reviewed pregnancies in women with sickle cell disease that received maternity care between 2007 and 2017 at a tertiary referral centre in London, UK. Researchers found that women with sickle cell disease had a persistently higher risk of adverse perinatal outcomes compared with other patients.

Malaria protection due to sickle haemoglobin depends on parasite genotype

This early release study published in the December edition of Nature, found that specific changes in three regions of the malaria parasites' genome could be responsible for malaria infections in people with sickle cell disease.

Burden of central nervous system complications in sickle cell disease: A systematic review and meta-analysis

Sickle cell disease (SCD) patients are at high risk of central nervous system (CNS) complications and may experience significant morbidity. This review included 32 studies published from January 2000 to 2020, evaluating humanistic and economic outcomes of SCD. The review suggests that SCD individuals with CNS complications experience decreased cognitive function and incur substantial health care costs compared with the general populations and SCD sufferers without CNS disease.

<u>Procedural adverse events in paediatric patients with sickle cell disease undergoing chronic automated red cell exchange</u>

Chronic automated red cell exchange (RCE) is increasingly employed for sickle cell disease. This study investigated the incidence of adverse events associated with RCE and potential patient and procedural risk factors. In a study of 38 patients, the authors demonstrated that approximately 20% of chronic automated RCE procedures were associated with adverse outcomes but that the majority of these events were asymptomatic (hypocalcaemia and less commonly hypotension), requiring only simple medical intervention.

2.4 Leukemia

<u>Five-drug combination for ultra-high-risk bone marrow cancer identified</u>

A combination of five drugs have been shown to successfully slow the progression of a highly aggressive myeloma. Myeloma occurs in the plasma cells in bone marrow, causing bone pain in the chest or spine, weakened bones, fatigue, nausea, constipation, frequent infections and weight loss. The study suggests that a combination of bortezomib, lenalidomide, daratumumab, dexamethasone and cyclophosphamide chemotherapy allow people with ultra-high-risk multiple myeloma to live longer before their disease progressed.

Adverse outcomes in chronic myeloid leukemia patients treated with tyrosine kinase inhibitors

In a large cohort-study, the authors assessed morbidity in 1328 Swedish chronic myeloid leukemia (CML) patients that were treated with <u>tyrosine kinase inhibitors (TKIs)</u>. The authors found a number of adverse events in CML patients subjected to prolonged treatment with TKI (in particular with 2nd generation drugs), as compared to outcomes for carefully matched controls. The study noted that the full clinical implications of the findings were unclear, but may provide important novel insights into the long-term morbidity and mortality of CML patients.



2.5 Immune system and immunotherapy

Alternate-day dosing of caplacizumab for immune-mediated thrombotic thrombocytopenic purpura

Caplacizumab in combination with plasma exchange, steroids and rituximab is a standard of care for immune-mediated thrombotic thrombocytopenic purpura (ITTP). ITTP is a rare but life-threatening autoimmune disease caused by autoantibodies against the von Willebrand-factor. This study looked at the timing and outcome of dosing of caplacizumab in a cohort of 25 ITTP patients, finding that alternate-day dosing was successful in the majority of patients suggesting that it may be safely considered after three to four weeks of daily treatment.

3. Transfusion

This section includes peer reviewed research and industry publications on transfusion procedures to improve patient outcomes and reduced wastage of blood products.

3.1 Paediatrics

<u>Granulocyte transfusions made with modified fluid gelatin in paediatric and adolescent patients with prolonged</u> neutropenia

Granulocyte transfusions are used to treat progressive systemic or local infections in prolonged neutropenic patients (low count of a type of white blood cell) with antibiotic or antifungal resistance. Granulocytes are most commonly collected from whole blood by apheresis using hydroxyethyl starch (HES) as the red blood cell sedimentation agent. The study tested a modified fluid gelatin in place of HES and suggests that it provided an effective alternative with a reduced chemical half-life in the body.

Two-year follow up shows delaying umbilical cord clamping saves babies' lives: A minute's delay could make a lifetime of difference

Researchers found that delaying umbilical cord clamping reduces a child's relative risk of death or major disability in early childhood by 17 per cent, the study also found that 15 per cent fewer infants needed blood transfusions after birth.

<u>Impact of Early Treatment with High-Dose Intravenous Immunoglobulin on Incidence of Kawasaki Disease</u>
Complications in Iranian Children

Kawasaki disease causes inflammation in blood vessels throughout the body and mostly affects children under 5 years. This study looked at the impact of administering high-dose intravenous Immunoglobulin with acetyl; salicylic acid therapy to prevent heart lesions and assess the impact on hearing. Researchers found the majority of patients recovered from coronary artery lesions while none of the patients experienced hearing loss.

Haemostatic efficacy of pathogen-reduced platelets in children undergoing cardiopulmonary bypass

Paediatric patients undergoing cardiopulmonary bypass (CPB) often require blood component transfusions. Pathogen-reduction (PR) of platelets reduces the risk of microbial contamination. This research looked at the haemostatic efficacy of PR platelets in children undergoing CPB and found that patients receiving PR platelets did not have more blood loss or require more transfusions than those who received standard platelets.

3.2 Obstetrics

Autotransfusion of vaginally shed blood as a novel therapy in obstetric haemorrhage: A case series

The study aimed to report outcomes in a cohort of women who received autotransfusion (receiving one's own blood) of vaginally shed blood and to describe the feasibility of blood collection and cell salvage processing at the time of vaginal haemorrhage. Researchers found that in 64 cases where autotransfusion of vaginally shed blood occurred, autotransfusion was well tolerated and suggest that autotransfusion of vaginally shed blood is a feasible technique to employ during severe obstetric haemorrhage.



3.3 Management

Blood unit segments accurately represent the biophysical properties of red blood cells in blood bags but not haemolysis

Blood unit segments provide a simple and non-destructive way to sample red blood cells (RBCs) in clinical studies of transfusion efficacy, but it is not known whether RBCs sampled from segments accurately represent the biophysical properties of RBCs in blood bags. The study found that RBCs sampled from blood unit segments accurately represent the biophysical properties of RBCs in blood bags but not haemolysis.

The continued decline of plasma transfusions in Taiwan: An 11-year population-based study

This study found that plasma utilisation rates in Taiwan declined over the previous 11 years. However inappropriate plasma use remained high while the use of alternative therapies remained low in services such as gastroenterology.

Transfusion practice in the bleeding critically ill: An international online survey

Researchers conducted a survey among physicians working in ICU environments. Transfusion practice in massively and non-massively bleeding patients was examined, including transfusion ratios, thresholds, and the presence of transfusion guidelines. The study found that half of the centres associated with respondents had no massive transfusion protocol available and that transfusion practice in massively bleeding critically ill patients is highly variable.

Assessment of bacterial growth in leukoreduced cold-stored whole blood supports overnight hold at room temperature prior to filtration

The authors suggest that whole blood transfusion has 'regained attention' in the treatment of trauma patients, citing several studies suggesting that whole blood transfusion in certain situations can result in equitable outcomes to blood component transfusion. The study notes that bacteria able to resist immune clearance can grow in whole blood (WB) held at room temperature prior to leukoreduction by filtration, but the bacteria that grow in cold-stored WB do not reach clinically significant levels after 21 days of storage and that transfusing cold-stored leukoreduced WB may not pose a major bacterial contamination safety risk to transfusion patients.

Cutting through the hype on platelet-rich plasma

A <u>study</u> undertaken by Australian researchers has called into question the use of platelet-rich plasma for treating osteoarthritis pain and joint structural damage, suggesting that the treatment was no more effective than placebo for treating knee osteoarthritis pain.

Estimating the risks of prehospital transfusion of RhD-positive whole blood to trauma patients who are bleeding in England

Haemolytic disease causes faster destruction of red blood cells in new born babies. It occurs when a mother and baby have a different blood type and Rh factor status. This study assessed the risk of harm resulting from a proposal to transfuse low-titre D-positive red blood cells, when O D-negative red blood cells are not available, and blood group is unknown. The authors found that the risk of transfusing RhD-positive blood is low in the prehospital setting.

<u>Incorporating the entity of under-transfusion into hemovigilance monitoring: Documenting cases due to lack of inventory</u>

The authors of this report state that under-transfusion is an underreported entity within hospitals and hemovigilance systems. An 11-member working group of the AABB (Association for the Advancement of Blood and Biotherapies) Hemovigilance Committee was formed in October 2020 in the US to study the topic of under-transfusion. The working group proposed four incident codes that can be used by hemovigilance systems to appropriately document instances of under-transfusion due to lack of supply.

Association of *Staphylococcus aureus* in platelet concentrates with skin diseases in blood donors: Limitations of cultural bacterial screening

Bacterial contamination in platelet concentrates is a major problem in transfusion medicine. Contamination with *Staphylococcus aureus* (*S. aureus*) is occasionally missed. Researcher isolated *S. aureus* from nasal specimens and from the arm skin specimens of three donors with atopic dermatitis. In the study, *S. aureus* showed irregular detectability over 24 to 48-hour post-spike periods, whereas the three other bacterial species were detected in all culture bottles after a 24-hour post-spike period.



3.4 Research

<u>Short-term high-dose intravenous iron reduced peri-operative transfusion after staggered bilateral total knee</u> arthroplasty

This study looked at the use of high dose intravenous iron around the time of surgery for patients receiving knee replacements. Researchers suggest that immediate post-operative, high-dose intravenous iron treatment may contribute to reduced transfusion rates, facilitate haemoglobin recovery, and minimise the development of moderate to severe anaemia.

Individualised or liberal red blood cell transfusion after cardiac surgery: a randomised controlled trial

This randomised study in two French academic hospitals looked at 164 patients who were admitted to ICU after cardiac surgery. Transfusion guidelines in these ICUs are based on haemoglobin threshold, with limited consideration of oxygen delivery or consumption. The study found that individualising treatment based on the oxygen supply returning to the heart would allow for a more restrictive red blood cell transfusion strategy with limited impact on postoperative morbidity or 6-month mortality.

Association of red blood cell transfusion volume with postoperative complications and mortality in neonatal surgery

This study looked at patients' outcomes in the American College of Surgeons, 'National Surgical Quality Improvement Program' paediatric database. The authors suggest that total red blood cell transfusion (RBCT) volume is associated with worse postoperative outcomes in newborns with a significant increase in 30-day mortality.

<u>Bleeding outcomes of inpatients receiving therapeutic plasma exchange: A propensity-matched analysis of the National Inpatient Sample</u>

Used in the treatment of autoimmune conditions, neurologic, and hematologic diseases, therapeutic plasma exchange (TPE) removes coagulation proteins. The process also inadvertently removes platelets, which further contributes to haemostatic abnormalities. The study was designed to determine bleeding outcomes of inpatients treated with TPE. The authors concluded that the use of TPE in the inpatient setting is positively associated with bleeding; however, with low prevalence.

3D printing of blood plasma may speed up wound healing

Platelet-rich plasma (PRP) is a natural healing substance in our blood. This study explores ways of enhancing the wound healing process by extracting PRP from blood and manipulating it through 3D printing.

Effects of dual chelation therapy with deferasirox and deferoxamine in patients with beta thalassaemia major

Patients with thalassaemia experience complications related to iron overload. In Australia currently, the two main options for iron chelation (iron extraction therapies) are 'deferasirox' and 'deferoxamine'. This study looked at the effect of combining both therapies as a 'dual chelation therapy' (DCT) and suggest that DCT is an effective way to reduce iron levels in patients with beta thalassaemia.

Thrombomodulin (THBD) gene variants and thrombotic risk in a population-based cohort study

The protein C anticoagulant system plays a key role in maintaining haemostatic balance. Studies have identified thrombomodulin gene (THBD) variants among venous thromboembolism (VTE) patients. This study aimed to determine the thrombotic risk of rare and common THBD variants in a large population-based cohort of middleaged and older adults and found that rare qualifying THBD variants were associated with VTE, suggesting that rare variants in THBD contribute to development of VTE.



4. Gene therapies

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

4.1 Blood related gene therapies

CRISPR gene-editing treated her sickle cell disease and she's still thriving

The first patient treated for sickle cell disease utilising CRISPR gene technology is reporting positive results a year on from the administration of the therapy. Doctors have now treated at least 45 patients with sickle cell and beta thalassemia, reporting that half of the patients are experiencing positive results.

Gene Therapy for transfusion-dependent β-Thalassemia

Transfusion-dependent beta-thalassemia is caused by mutations in the β -globin gene, which may cause significantly reduced or absent adult haemoglobin production. This can result in severe anaemia and lifelong dependence on RBC transfusions. The study found that 91% of subjects who were treated with betibeglogene autotemcel (beti-cel) gene therapy, including six of seven patients under the age of 12, achieved transfusion independence in the short term.

<u>Intellia therapeutics announces first patient dosed in Phase 1/2 clinical trial of NTLA-2002 for the treatment of hereditary angioedema</u>

Intellia is has commenced trials on its gene therapy 'NTLA-2002' to treat hereditary angioedema (HAE) a rare, genetic disorder characterized by severe, recurring and unpredictable inflammatory attacks in various organs and tissues of the body.

GlaxoSmithKline aim for HIV cure by 2030

Following recent approval of an injectable HIV-1 treatment from the National Institute for Health and Care Excellence (NICE), GlaxoSmithKline has high hopes in developing a cure for the virus in the next decade.

In vivo delivery of CRISPR-Cas9 using lipid nanoparticles enables antithrombin gene editing for sustainable haemophilia A and B therapy

In this study using mice, researchers hypothesized that CRISPR gene editing may represent a long-term and versatile therapeutic option for treating haemophilia A and B.

BioMarin announces stable and durable annualized bleed control in the largest Phase 3 gene therapy study in adults with severe haemophilia A

BioMarin Pharmaceutical has reported positive results from its ongoing global Phase 3 GENEr8-1 study of valoctocogene roxaparvovec, an investigational gene therapy for the treatment of adults with severe haemophilia A.

BioMarin plans return to FDA with updated data on haemophilia gene therapy

BioMarin is expected to take their treatment 'Roctavian' to the Food and Drug Administration later this year with clinical trial results providing evidence its gene therapy for haemophilia can prevent bleeding. The data from BioMarin's study, are meant to meet requirements laid out by the FDA when it rejected the company's previous approval application a year and a half ago.

4.2 Regulatory and industry developments

<u>Importation of plasma and use of apheresis platelets as risk reduction measures for variant Creutzfeldt-Jakob</u> disease: The SaBTO review

Following recognition that blood, blood components, tissues and organs donated by infected donors could transmit infectious proteins causing variant Creutzfeldt-Jakob Disease (vCJD), several risk reduction measures were introduced in the UK. The Advisory Committee on the Safety of Blood, Tissues and Organs (SaBTO) established a working group to review the measures in place. Factors considered included: ethical issues around the current provisions and potential changes; operational issues for blood establishments and hospitals; a review from the Advisory Committee on Dangerous Pathogens (ACDP) showing the downward trend in the estimated number of future cases of vCJD; and cost-effectiveness.



Assessment the knowledge of blood transfusion in Iranian nurses of Tehran's hospitals

This study of 325 Iranian nurses found the majority lacked knowledge in pre-transfusion activities. The analysis also revealed there was a significant correlation between the knowledge score and academic degree. Out of all nurses, 48% (156) declared that they need further training in haemovigilance and a large proportion of the involved nurses were unaware of the risk of improper identification.

5. COVID-19

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

5.1 COVID-19 News

The Centers for Disease Control and Prevention (CDC) in the United States has released a comparative study of outcomes for the COVID-19 Omicron variant in relation to previous outbreaks. The US Food and Drug Administration has approved new treatment for patients that have contracted COVID-19, while limiting the use of certain monoclonal antibody treatments. In Australia states are initiating return to school plans for students, with only Queensland delaying the start of the first term. In Australia the Novavax COVID-19 vaccine was provisionally approved by the Therapeutic Goods Administration, and National Cabinet agreed that there will be no reduction in the seven-day isolation period for people that test positive to COVID-19. In world news, the WHO has recommended two new drugs to treat COVID-19 infected patients. Here are some news articles relating to the pandemic:

- Omicron COVID-19 variant: Experts say vaccine protection against severe disease remains high, but spread will continue
- Vaccines appear weak at blocking Omicron, better against severe disease
- WHO recommends booster for people with health problems
- The Novavax COVID-19 vaccine has been approved for use in Australia
- National Cabinet agrees to keep seven-day COVID-19 isolation period
- WHO recommends two new drugs to treat COVID-19
- COVID-19 disruption to the economy as shortages continue
- Trends in disease severity and health care utilization during the early Omicron variant period compared with previous COVID-19 high transmission periods
- With new trial, Pfizer and BioNTech will test whether an omicron vaccine is needed
- Coronavirus (COVID-19) Update: FDA limits use of certain monoclonal antibodies to treat COVID-19 due to the Omicron variant
- ATAGI statement on Omicron variant

5.2 COVID-19 Impacts

Podcast: Post-vaccination COVID-19 in patients with haematologic malignancies

The podcast discusses immune response to vaccination, risk factors and short-term outcomes of COVID-19 in patients with lymphoma and multiple myeloma.

Incidence of venous thromboembolic events in COVID-19 patients after hospital discharge

During the COVID-19 pandemic, investigations have reported a high incidence of venous thromboembolic (VTE) events in hospitalized patients with COVID-19. The risk of hospital-associated VTE extends from the time of admission to 90 days after discharge. Researchers found that the incidence of VTE among COVID-19 patients after hospital discharge was 1.8% higher than most other patient groups.



Trigger of rare blood clots with AstraZeneca jab found by scientists

A report <u>published in Science Advances</u> claims to have found "the trigger" that leads to extremely rare blood clots after receipt of the Oxford-AstraZeneca COVID-19 vaccine. Researchers suggest that in a small number of pre-disposed individuals the binding of viral vector as a complex with platelet factor 4 results in a misplaced immunity, building antibodies that bind to and activate platelets, causing them to aggregate and cause thrombosis. <u>Australian haematologists have reacted cautiously to the news</u>, noting that further research was needed to prove the link to vaccine-induced immune thrombotic thrombocytopenia (VITT).

Myocarditis cases reported after mRNA-Based COVID-19 vaccination in the US from December 2020 to August 2021

This study looked at reported cases of myocarditis in the United States after receiving mRNA based COVID-19 vaccinations. Researchers found that the risk of myocarditis after receiving mRNA-based vaccines increased across multiple age and sex strata and was highest after the second vaccination dose in adolescent males and young men.

Genentech's tocilizumab shortage due to COVID-19 now hits CAR-T recipients, with FDA offering alternatives to help

Tocilizumab, is an immunosuppressive drug, used for the treatment of rheumatoid arthritis and systemic juvenile idiopathic arthritis that has been used as a treatment for patients hospitalised with inflammation due to COVID-19. The use of the drug for COVID-19 treatment has resulted in multiple manufacturers reporting supply shortages.

Anti-COVID-19 Immunoglobulin G concentration expected to peak in October 2021

A study sought to model the concentration of anti COVID-19 Immunoglobulin G which could be expected in the plasma pool and final-product batches of CSL Behring's Immunoglobulin product Privigen. The study predicted that anti-COVID-19 Immunoglobulin G concentration would have peaked in batches produced in mid-October 2021.

New research on immune responses in patients with kidney failure after receiving different COVID-19 vaccines Research reveals that patients on kidney dialysis typically have an impaired response to COVID-19.

More than half a billion people pushed or pushed further into extreme poverty due to health care costs

New evidence suggests that the COVID-19 pandemic is likely to halt progress towards the World Health

Organization's goal of Universal Health Coverage.

<u>Psychological impact of the COVID-19 pandemic on young professionals in blood banks and transfusion services:</u> <u>A global cross-sectional survey</u>

This survey looks at the psychological impact of the COVID-19 pandemic on staff working in blood banks and transfusion services.

Belief in having had COVID-19 linked with long COVID-19 symptoms

This study looks at the effect of extended COVID-19 symptoms and found that these 'long' effects may have some psychological components.

5.3 COVID-19 Policy and Industry

WHO lists 9th COVID-19 vaccine for emergency use with aim to increase access to vaccination in lower-income countries

The WHO has given emergency approval for the use of 'Covovax' produced by the Serum Institute of India under license from 'Novavax'. It is hoped that the approval will increase access to COVID-19 vaccination particularly in lower-income countries.

FDA finds 3 COVID-19 tests that fail to detect the Omicron variant

The FDA has identified three COVID-19 molecular tests that are not able to detect the Omicron variant, stating that mutations in the viral targets for some tests could result in false negative results.



Senegal expects waste of 400,000 COVID-19 vaccines by year-end; Nigeria to destroy a million expired vaccines

Logistical issues associated with the roll out of COVID-19 vaccination will result in the destruction of 1,000,000 vaccination doses in Nigeria and 400,000 in Senegal.

FDA panel, after debate, narrowly backs Merck COVID pill

An FDA advisory panel has confirmed the benefits of Merck & Co's new drug 'molnupiravir', despite concerns that the treatment may not be as effective as previously stated.

European Medicine Agency (EMA) receive marketing authorisation application for molnupiravir

The EMA has begun evaluating an application for marketing authorisation of 'molnupiravir' using an accelerated pathway with a decision possible within weeks.

EMA approves Pfizer-BioNTech COVID-19 vaccine for young children

Emergency use of the Pfizer-BioNTech COVID-19 vaccine in children aged 5 to 11 years old has been approved by the EMA.

5.4 COVID-19 Research

WHO recommends against the use of convalescent plasma to treat COVID-19

The World Health Organisation (WHO) has advised against using convalescent plasma to treat patients regardless of the severity of their symptoms. The process takes blood from recovered patients to administer to critically ill patients to help fight off the disease. The WHO made their determination after reports demonstrated that convalescent plasma treatment had no impact on any of the critical or important outcomes for patients diagnosed with COVID-19. The WHO advised strongly against the use of the treatment in all but research settings.

Risk of hospital stay 40% lower with Omicron than Delta, UK data suggests

A report from the United Kingdom has suggested that hospitalisation after contracting the Omicron variant is lower when compared with the previous Delta variant. The study suggests a moderate reduction in the chance of hospitalisation overall but warned that this may be offset by the amount of infections expected from Omicron.

Antibody Response and Variant Cross-Neutralization After COVID-19 Breakthrough Infection

This study investigated the effects of breakthrough infections after vaccination against COVID-19 showing substantial boosting of immunity after breakthrough infection, despite predominantly mild disease symptoms.

The coronavirus infects fat cells, study suggests

Scientists examined fatty tissue from patients who died from COVID-19 infections and found coronavirus particles in the tissue that surrounded various organs. The study (in pre-print) suggests that human fatty tissue is more permissive to COVID-19 infection and when infection occurs it elicits an inflammatory response.

Most COVID-19 vaccines will work as boosters, study suggests

In a comparison of seven different brands, researchers found that most shots give a strong boost, even in mixand-match combinations.

<u>UK study shows mixing Pfizer and AstraZeneca COVID-19 vaccines with Moderna elicits better immune response</u>

A British study mixing COVID-19 vaccines has found that people had a better immune response when they received their first dose of AstraZeneca or Pfizer-BioNTech shots, followed by Moderna nine weeks later. Findings from this trial demonstrate that the immune response of same or different third dose boost with all tested vaccines was superior to controls regardless of which vaccine had been received in the initial course.

Like the flu vaccine every year, the FDA could move quickly on a variant-targeted COVID-19 vaccine

In much the same way that the flu vaccine is signed off every year without a requirement for large clinical trials, the USA's Food and Drug Administration (FDA) may employ a similar strategy in authorising variant-focused versions of the mRNA vaccines.

Antibody response and variant cross-neutralization after COVID-19 breakthrough infection

Vaccinated patients that had a breakthrough COVID-19 infection showed substantial boosting of antibody mediated immunity after infection, despite having mild disease symptoms.



Plant-based vaccine trialled for COVID-19

A new plant-based vaccine is showing an overall efficacy rate of 71%, with the developer Medicago planning to seek regulatory approval to proceed to more advanced trials. According to the World Health Organisation plant-derived vaccines have several advantages. They can be produced cheaply in very high amounts, carrier plants such as potatoes and corn are readily accepted by patients and antigens derived from them are stable and can be stored for long periods of time.

6. Other items of interest

This section contains general industry and regulator updates as well as developments in non-blood and non-COVID-19 related diseases that may have flow on affects to the blood industry.

6.1 Government & Industry

Permanent telehealth for all Australians

The Australian Government has confirmed a four-year investment to support permanent telehealth services, allowing GPs, specialists and allied health professionals to continue consulting with their patients by phone or online.

\$276 million to back Australia's brightest health scientists

The Australian Government has opened a \$14 million grant opportunity through the Medical Research Future Fund called the *2021 Optimising the Clinical Use of Immunoglobulins*. It aims to examine the use of antibodies from human blood to address a number of clinical conditions.

Provisional Mortality Statistics, Jan 2020 - Oct 2021

This Australian Bureau of Statistics report looks at the mortality rates for 2020 and 2021 and compares these to the average number of deaths recorded over the previous 5 years (2015-2019).

Australia's CSL to buy drug maker Vifor for \$11.7 Billion

Australian biotech company CSL Ltd. has agreed to buy Swiss drug maker Vifor Pharma AG for an equity value of \$11.7 billion. The acquisition is the largest to date by CSL, which is Australia's sole manufacturer of AstraZeneca COVID-19 vaccine and a primary supplier of commercial blood products in the Australian market.

Moderna plans mRNA vaccine factory in Australia that can churn out 100M doses per year

Moderna has announced plans to build a production facility in Australia to provide access to a domestically manufactured portfolio of mRNA vaccines against respiratory viruses, including COVID-19 and seasonal influenza.

New PBS listing helps Australians with rare genetic condition

Australians with a rare and potentially deadly condition, hereditary angioedema, are now able to obtain Takhzyro (lanadelumab) through the Pharmaceutical Benefits Scheme (PBS). Hereditary angioedema is a rare, chronic genetic condition occurring in around 1 in 50,000 people. It results from a defect in the gene that controls a blood protein called C1-Inhibitor. This leads to higher levels of a substance called bradykinin in the bloodstream, which causes symptoms such as swelling and pain. Takhzyro® helps to reduce the amount of bradykinin in the bloodstream and prevents symptoms associated with hereditary angioedema.

6.2 Emerging Technology

The transfusion service laboratory in virtual reality

The authors created an interactive, educational 360° virtual reality walkthrough tour of a Transfusion service and Microbiology Laboratory by taking multiple 360° still-images and adding navigation buttons, and other interactive elements. The virtual tours were used for recruitment and education.

Haemolysis contributes to anaemia during long-duration space flight

A study of fourteen astronauts throughout their 6-month missions onboard the International Space Station found that that space flight is associated with persistently increased levels of products of haemoglobin



degradation and carbon monoxide in lung air. The findings suggest that the destruction of red blood cells, haemolysis, is a primary effect of microgravity in space flight and that the anaemia associated with space flight is a haemolytic condition that should be considered in the screening and monitoring of both astronauts and space tourists.

<u>Direct transfer of data of people with haemophilia from the Thai Haemophilia Treatment Centre Registry to the World Bleeding Disorders Registry of the World Federation of Haemophilia</u>

The Thai Society of Haematology has created a 'Haemostasis Registry' to connect with the World Federation of Haemophilia global database on people with haemophilia called the 'World Bleeding Disorders Registry'. The database is set up to connect with the two databases directly enabling data sharing, with necessary controls.

New test can identify if a patient has cancer and if it has spread

The study analysed samples from 300 patients with non-specific but concerning symptoms of cancer, such as fatigue and weight loss, who were recruited through the Oxfordshire Suspected CANcer (SCAN) pathway. The researchers assessed whether the test could distinguish patients with a range of solid tumours from those without cancer. Their results show that cancer was correctly detected in 19 out of every 20 patients with cancer using this test. In those with cancer, metastatic disease was identified with an overall accuracy of 94%. These results make this the first technology to be able to determine the metastatic status of a cancer from a simple blood test, without prior knowledge of the primary cancer type.

6.3 Other diseases and developments

6.3.1 Malaria

Malaria alert issued for South Africa - and these THREE regions are 'high-risk'

South African health authorities have issued an alert to combat a growing malaria outbreak, with concerns that some cases of malaria infection are being misdiagnosed as COVID-19.

6.3.2 Dengue

Cases of mosquito borne diseases in sub-continental Asia rose to abnormally high levels in December before falling in January. The additional effect of COVID-19 on patients has been highlighted as a concern. Reports of Dengue outbreaks in South America increased in January with cases reported in Colombia, Brazil and Paraguay. Researchers have found that the dengue, has a high transmission rate because mosquitos infected with the virus are more attracted to mammals and therefore more likely to bite.

- Brazil: Hundreds of probable dengue cases reported in Minas Gerais during first days of 2022
- Paraguay reports 300 dengue cases weekly in 2022
- Zamboanga City reports first dengue death of the year
- Telangana Reports Cases Of 'Covidengue', Doctors Advice Immediate Medical Care Once Diagnosed
- Dengue hospitalisation in Dec abnormal
- Dengue death toll reaches 100 in Bangladesh
- Delhi adds 285 dengue cases in a week, total tally rises to 9,260
- Ahmedabad: Chikungunya cases see steep rise, 9 times higher as compared to 2019
- Over 76% of suspected deaths in Punjab confirmed as dengue cases
- Dengue cases in Delhi this year mounts to over 8,200
- <u>26 Dengue fatalities & over 33,000 patients in 2021</u>
- Pakistan reports over 52,000 dengue cases in 2021
- Dengue Virus Makes Mosquitoes Bite More Often

6.3.3 Ebola

Ebola outbreak in Democratic Republic of the Congo declared over

Good news from the Democratic Republic of Congo where an Ebola outbreak in the East of the country has ended. The first case was discovered more than two months ago and resulted in 11 infections of which six people died.



6.3.4 Avian influenza outbreaks

The United Kingdom experienced its largest ever bird flu outbreak, which spread across Europe to wild bird populations in Israel. An outbreak of bird flu has also been confirmed in the Burkina Faso and North America. A different strain in Asia has caused the death of multiple people in China but the effect on bird life has been less well reported.

Europe

- Bird flu discovered at Dutch farm; 216,000 chickens to be culled
- Avian flu: Outbreak in Newcastle closes Ouseburn Farm
- Bulgaria reports bird flu outbreak at duck farm
- France says bird flu spreads to southwest duck-breeding region
- Israel detects bird flu among dozens of wild cranes
- Warning as second bird flu case found at Scots nature reserve
- Whole Wild Bird Population of Festetics Castle in Keszthely Had to Be Destroyed
- New bird flu outbreak in Northern France, two more suspected
- France: Farmers ordered to cull 2.5 million animals after outbreaks of bird flu

North America & Africa

- Bird flu outbreak causes N.C. zoo closure, concern from experts
- Eurasian H5 bird flu found in US for first time since 2016
- Avian flu discovered in birds around St. John's, Environment Canada says
- Burkina Faso reports outbreak of H5N1 bird flu

Asia

- China reports additional H9N2 avian influenza case for 2021
- China Confirms 28th Bird Flu Case
- Bird flu hits Kottayam once again
- Bird flu scare on rise in Kerala, mass culling of ducks in Kottayam, Alappuzha
- Five human cases of H5N6 bird flu reported in China

6.3.5 Other

Researchers pinpoint how Zika virus evades cell's antiviral response: Site of virus-host interaction offers new target for antiviral therapeutics

Researchers have discovered that Zika evades the bodies antiviral response by suppressing interferon signalling to gain access to cells.

Pakistan launches anti-polio drive as COVID-19 cases rise

Pakistan, one of only two nations where polio remains endemic, is moving closer to polio free status with mass vaccination programs under way and only one reported case in the country in 2021.