

Monitoring International Trends

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The NBA monitors international developments that may influence the management of blood and blood products in Australia. Our focus is on:

- Potential new product developments and applications;
- Global regulatory and blood practice trends;
- Events that may have an impact on global supply, demand and pricing, such as changes in company structure, capacity, organisation and ownership; and
- Other emerging risks that could put financial or other pressures on the Australian sector.

Summary

Some recent matters of interest appear on pages 8 to 26. Highlights are listed below:

Safety and Patient Blood Management (begins page 8)

Appropriate transfusion; bleeding risk (p8)

- A trial has shown that a lower transfusion threshold for pre-term newborns with thrombocytopaenia reduces their risk of death and major bleeds.
- Researchers investigating the use of a dopamine bolus as a vasoconstrictor found that it was correlated with an increase in venous return and reduction in the need for fluid replacement during and after cardiopulmonary bypass in patients undergoing coronary artery bypass grafting.
- Octapharma announced the publication of data demonstrating that its fibrinogen concentrate is an effective alternative to cryoprecipitate for patients with severe bleeding during cardiac surgery.
- Scientists working on prion detection have demonstrated that their synthetic-molecule-based approach can isolate prion proteins in body fluids sampled from infected animals. This may offer a means of testing donor blood for prions.
- A study has concluded that patients who restart their blood thinners after a gastrointestinal bleed have a lower risk for dying within the next two years even though they have a higher risk for recurrent gastrointestinal bleeding.
- Researchers found that for patients undergoing a radical cystectomy “there are no significant differences in short-term or long-term patient outcomes between those who did and did not receive an intraoperative cell salvage transfusion”.
- Researchers found that haemostasis with a balloon urinary catheter is a safe and effective means of preventing postoperative bleeding following vacuum-assisted breast biopsy.
- Researchers compared intravenous versus combined intravenous and intra-articular tranexamic acid administration in patients undergoing simultaneous bilateral total knee arthroplasty. They found that adding intra-articular tranexamic acid did not decrease perioperative blood loss compared with placebo.
- A review has concluded that “the administration of intravenous tranexamic acid can safely and effectively reduce perioperative blood loss and allogeneic blood transfusions in revision surgery for Vancouver type B periprosthetic femoral fractures, without increasing the risk of symptomatic venous thromboembolism”.

- Swedish researchers reviewed 517,874 pregnancies and deliveries. Two hundred and seventy-seven women required massive blood transfusion. The highest risk was for women with abnormal placentation.
- Data has been reported from a safety trial of lyophilized platelets.
- Tranexamic acid has been found to reduce the risk of mortality in patients with traumatic brain injury.
- Researchers analysed the outcomes for critically bleeding trauma patients who were managed with a 'major haemorrhage protocol' at the Royal London Hospital Major Trauma Centre between 2008 and 2017. The study's lead author said: "Changes in transfusion and resuscitation practice for traumatically injured patients that are rooted in research have led to remarkable improvements in survival".
- NASA-sponsored research is directed towards discovering if freeze dried blood can be rehydrated in a zero-gravity environment.
- Simultaneous use of nonsteroidal anti-inflammatories and oral anticoagulants could increase the risk for major bleeding.

Other (p10)

- Researchers have found that conjoining a healthy mouse and a mouse with Alzheimer's plaques will cause the healthy mouse to begin developing plaques of beta-amyloid protein in its own brain. This raised questions of whether Alzheimer's can be spread through blood transfusions and surgical procedures.
- AstraZeneca presented detailed results from Phase III trials showing that roxadustat significantly increased haemoglobin levels in both non-dialysis-dependent and dialysis-dependent patients with anaemia from chronic kidney disease.
- Researchers have reported that platelet-rich plasma is superior to platelets or plasma for wound healing *in vitro*.
- An international Phase III study of rivaroxaban versus standard anticoagulants for venous thromboembolism in children has found similar efficacy and safety in both treatment arms.
- A study found that early initiation of plasma transfusion during the first 60 minutes of persistent postpartum haemorrhage, compared with no plasma or later plasma, did not lead to adverse maternal outcomes.
- Researchers found that luspatercept reduced the severity of anaemia compared with placebo among a specific category of patients with lower-risk myelodysplastic syndromes.
- Researchers set out to determine the effect of preoperative anaemia on the prognosis of patients with upper tract urothelial carcinoma (UTUC) following radical nephroureterectomy. They found that "preoperative anaemia is an independent risk factor for cancer-specific survival and overall survival."
- Sean Pirkle and colleagues reviewed bleeding and thrombotic complication rates in elective spine surgery patients.
- CytoSorbents Corporation announced the first patient enrolment in the company-sponsored Ticagrelor CytoSorb Hemoadsorption study in the UK.
- Study results showed Andexxa helped produce high rates of haemostasis in patients with major gastrointestinal bleeding.

- Research found that people with "metabolic syndrome" are vulnerable to recurring blood clots.

Products and Treatments (begins page 12)

Treating haemophilia (p12)

- Updates were made available for a number of gene therapies being developed for haemophilia.
- A report on the results of a 10-year gene therapy study in dogs has rekindled past concern that, by using a virus to insert therapeutic genes into the human genome, scientists may inadvertently be triggering cancer in the treated cells.
- Researchers have conducted direct comparative studies that shed light on the pharmacokinetic differences between extended half-life factor IX products, including the number of injections and overall factor concentrate consumption.
- Researchers found that, amongst children with von Willebrand Disease (VWD), boys may be more likely to report bleeding incidents and to use treatment products for the condition than girls.

Treating beta thalassemia and sickle cell disease (p14)

- Nova Laboratories launched its new liquid formulation of hydroxycarbamide for sickle cell disease.
- Researchers report that iron chelation therapy with a combination of deferasirox and deferoxamine may improve bone mass in patients with transfusion-dependent beta thalassemia at the same time as it reduces serum ferritin levels.

Treating other conditions (p14)

- Rocket Pharmaceuticals reported long-term follow-up data from the Phase I/II study of its gene therapy for Fanconi anemia. Rocket said it represented the first evidence of long-term improvement.
- A meta-analysis suggests Iron chelation therapy may reduce mortality and leukemia transformation risk among patients with myelodysplastic syndrome (MDS).
- Apellis Pharmaceuticals announced positive Phase III results for Pegcetacoplan in adults suffering from paroxysmal nocturnal haemoglobinuria (PNH).
- Akari Therapeutics reported positive interim data from its Phase III PNH CAPSTONE study in complement inhibitor naïve, transfusion-dependent patients.
- A recent paper suggests a general approach to the diagnosis and management of thrombocytopenia in pregnancy.
- Researchers found that initial treatment with low-dose aspirin and intravenous immunoglobulin is not associated with an increased risk for recurrent fever relative to high-dose aspirin in children with Kawasaki disease.
- Protagonist Therapeutics initiated a Phase II study of its hepcidin mimetic in patients with hereditary haemochromatosis.

Regulatory matters (begins page 15)

- BioCryst Pharmaceuticals submitted a new drug application to the US Food and Drug Administration (FDA) for a once daily, oral treatment to prevent hereditary angioedema attacks.

- The FDA approved Celgene and Acceleron's Reblozyl for the treatment of anaemia in adult patients with beta thalassemia who need regular red blood cell transfusions.
- The FDA awarded Fresenius Medical Care a breakthrough device designation for a new haemodialysis system designed to prevent blood clots.
- The FDA awarded rare paediatric disease designation to Aruvant, Roivant Sciences' gene therapy for sickle cell disease and beta-thalassemia.
- Biomarin announced the submission of a Biologics License Application to the FDA for its AAV gene therapy, valoctocogene roxaparvovec, for adults with haemophilia A. This is the first marketing application submission in the US for gene therapy for any form of haemophilia.
- FibroGen announced the submission of a New Drug Application to the FDA for roxadustat for the treatment of anaemia of chronic kidney disease in both non-dialysis-dependent and dialysis-dependent patients.
- In India, Pharmazz submitted an application for Marketing Authorization of centhaquine for the treatment of patients with hypovolemic shock and excessive blood loss.
- Samsung Bioepis Co.Ltd. and AffaMed Therapeutics announced that the China National Medical Products Administration has approved the Clinical Trial Application for a biosimilar candidate referencing Soliris (eculizumab). The approval permits initiation of a Phase III clinical study at Chinese sites. The drug is designed to treat paroxysmal nocturnal haemoglobinuria.

Market structure and company news (begins page 16)

- CSL Behring has partnered with US-based SAB Biotherapeutics to investigate new therapies to treat autoimmune, infectious and idiopathic diseases by leveraging SAB's technology platform.
- The FDA recently finalised a guidance letter concerning platelet storage.
- Sangamo Therapeutics has handed over the development of SB-525, a gene therapy for haemophilia A, to Pfizer, which will now take the therapy into Phase III clinical trials.
- Global Blood Therapeutics and Syros Pharmaceuticals will collaborate to discover, develop, and market new therapies for sickle cell disease and beta thalassemia.
- Generation Bio announced the closing of a \$US 110 million Series C financing to advance development of two liver-targeted gene therapy programs, for haemophilia A and phenylketonuria.

Specific country events (begins page 17)

- Researchers working in Nigeria found "that one in four newborns and one in 10 children in hospital had low blood oxygen, and these children were eight times more likely to die than those with normal blood oxygen."
- In Australia, researchers showed that patient blood management guidelines introduced by the National Blood Authority in 2012 have reduced blood transfusions in cardiac surgery without any adverse impact on patient outcomes.
- US researchers say there may be a significant number of patients with symptomatic, undiagnosed Von Willebrand disease in the commercially insured population.
- In the US, from 2013 to 2016, over 60 per cent of all platelets transfused were apheresis-derived, and 93 per cent were leukoreduced. Patients with leukaemia, myelodysplastic syndrome, or lymphoma accounted for 46 per cent of platelets transfused.

- The Alliance for Regenerative Medicine announced the release of a report arguing that cell and gene therapies can deliver cost savings to health systems.
- Canadian studies suggested a need to undertake more screening for iron deficiency in early childhood.
- A study has found 60 per cent of Indigenous children in remote Far North Queensland communities are affected by anaemia.

Research not included elsewhere (begins page 18)

- US researchers found that adolescent girls with heavy menstrual bleeding appear to have a high prevalence of bleeding disorders.
- A US haematologist reflecting on haemophilia carriers she had tested during her career, said that one in five of the women had factor levels below 30 per cent, which warranted a haemophilia diagnosis to alert healthcare professionals to bleeding risk.
- A Swedish study found women who are haemophilia B carriers have more than three times the risk of bleeding following childbirth than non-carriers.
- Scientists have developed a technique to deliver chemotherapy to the lungs using red blood cells.
- Real-time peer auditing reduced the rate of central-line-associated bloodstream infections by 12 per cent at a hospital in North Carolina.
- Time spent in space has a dose-response relationship with acute and chronic reductions in haemoglobin.
- The ThromboGenomics high-throughput sequencing test may validate recently discovered genetic variants associated with rare bleeding, thrombotic, or platelet disorders.
- Researchers have evaluated the potential of recombinant human platelet-derived growth factor-AB to improve recovery after a heart attack.

Infectious diseases (begins page 20)

Mosquito-borne diseases (p20)

- Drones have been used to spray rice fields with a non-toxic film.
- Scientists have identified molecules that can kill the malaria parasite *Plasmodium falciparum*.
- Takeda's tetravalent dengue vaccine has been found effective in healthy children and adolescents.
- Cases of dengue declined where mosquitoes carrying *Wolbachia* were released.
- Valneva SE announced an End of Phase II meeting with the FDA for its single-shot chikungunya vaccine candidate.

Influenza (p21)

- The Scientists have identified antibodies that protect against multiple strains of the influenza virus.
- BiondVax Pharmaceuticals completed enrolment in the Phase III trial of its universal influenza vaccine candidate.
- The US Centers for Disease Control (CDC) reported that in the last week of 2019 influenza B/Victoria viruses were predominant nationally, followed by A (H1N1)pdm09 viruses. WHO said that although influenza B was dominating in the US and Canada, during the last week of December 68.7 per cent of global laboratory specimens were typed as influenza A.

- In early January, China, Poland and India all reported new outbreaks of highly pathogenic avian flu.
- One approach to deal with pandemic threats from A(H5N1) influenza may be to prime the population with an A(H5N1) vaccine and then boost immunity with a dose of the pandemic vaccine as required.

Ebola virus disease (p22)

- Johnson & Johnson filed for European approval for its two-dose experimental vaccine to protect against Ebola.
- The death from Ebola of a woman in the Democratic Republic of Congo has challenged the previously-accepted medical theory that survivors are immune to reinfection.

A new coronavirus first identified in Wuhan, China (2019-nCoV) (p22)

- A new coronavirus caused serious illness in Wuhan, capital of Hubei province. The infection appeared to have some association with a fresh seafood and produce market. A number of countries had initiated screening arriving passengers at airports, but by 31 January there were around one hundred cases in countries other than China. In China itself, 9,262 cases had been confirmed and 213 people had died. The World Health Organisation had declared a global emergency.

MERS-CoV (p25)

- The antiviral drug remdesivir has been shown to lessen lung disease from MERS in mice.

Other diseases (p25)

- A new strain of human immunodeficiency virus (HIV) is the first to be identified in nineteen years.
- Themis Bioscience and the Coalition for Epidemic Preparedness Innovations initiated a Phase I clinical trial with Themis' vaccine candidate against Lassa fever.
- Scientists at The Institute for Molecular Medicine and the University of California at Irvine have developed a preventive vaccine, AV-1980R/A, that targets the pathological Tau protein associated with Alzheimer's disease.
- Researchers have demonstrated that changing the dose of the BCG vaccine, and its route of administration from intradermal to intravenous, significantly enhances the vaccine's ability to protect rhesus macaques from TB.
- Researchers discussed fatalities in Germany from Borna disease virus 1 and recommended more testing for the disease where the virus occurs in the wild.

Detailed Report

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1. Safety and patient blood management

We follow current issues in patient safety and achieving favourable patient outcomes.

Appropriate Transfusion; Bleeding Risk

- A trial has shown that a lower transfusion threshold for pre-term newborns with thrombocytopaenia reduces their risk of death and major bleeds¹.
- Researchers investigating the use of a dopamine bolus as a vasoconstrictor found² that it was correlated with an increase in venous return and reduction in the need for fluid replacement during and after cardiopulmonary bypass in patients undergoing coronary artery bypass grafting.
- Octapharma announced the publication³ of data demonstrating that its fibrinogen concentrate Fibryga is an effective alternative to cryoprecipitate for patients with severe bleeding during cardiac surgery. At the 2019 AABB meeting trial data was reported⁴ demonstrating the equivalence of fibrinogen concentrate to cryoprecipitate for bleeding after cardiac surgery.
- Scientists working on prion detection have demonstrated that their synthetic-molecule-based approach can isolate prion proteins in body fluids sampled from infected animals⁵. This may offer a way of testing blood supplies for prion-related diseases.
- A study⁶ has concluded that patients who restart their blood thinners after a gastrointestinal bleed have a lower risk of dying within the next two years even though they have a higher risk for recurrent gastrointestinal bleeding.
- Researchers found⁷ that for patients undergoing a radical cystectomy “there are no significant differences in short-term or long-term patient outcomes between those who did and did not receive an intraoperative cell salvage transfusion. Cell salvage transfusions with a leukocyte depletion filter are safe and effective methods to reduce

¹ Fustolo-Gunnink S, Fijnvandraat K, van Klaveren D, et al. [Preterm neonates benefit from low prophylactic platelet transfusion threshold despite varying risk of bleeding or death](#) [published online October 24, 2019]. *Blood*. doi:10.1182/blood.2019000899

² Moscarelli M, Condello I, Fattouch K, et al. “Dopamine optimizes venous return during cardiopulmonary bypass and reduces the need for postoperative blood transfusion”, *ASAIO Journal*, 12 November 2019. <https://www.mdlinx.com/journal-summaries/cardiopulmonary-bypass-coronary-artery-bypass-grafting/2019/11/12/7584598/>

³ [Callum J, Farkouh ME, Scales DC, Heddle NM, et al. Effect of fibrinogen concentrate vs cryoprecipitate on blood component transfusion after cardiac surgery: the FIBRES randomized clinical trial. JAMA 2019; doi:10.1001/jama.2019.17312 https://jamanetwork.com/journals/jama/article-abstract/2753529](#)

⁴ [Callum J, Farkouh ME, Scales DC, Heddle NM, et al. Abstract PL1-MN4-32: The FIBRES randomized controlled noninferiority trial of fibrinogen concentrates versus cryoprecipitate in cardiac surgery: subgroup and safety analysis. Presented at AABB Annual Meeting; 2019 Oct 19-22; San Antonio, TX.](#)

⁵ Hornemann, S., Schwarz, P., Rushing, E. J., Connolly, M. D., Zuckermann, R. N., Yam, A. Y., & Aguzzi, A. (2019). “Enhanced detection of prion infectivity from blood by preanalytical enrichment with peptoid-conjugated beads”. *PLOS ONE*, 14(9), e0216013. <https://doi.org/10.1371/journal.pone.0216013>

⁶ Carlos Sostres et al., “Risk of rebleeding, vascular events and death after gastrointestinal bleeding in anticoagulant and/or antiplatelet users” , *Alimentary Pharmacology and Therapeutics*. <https://doi.org/10.1111/apt.15441>

⁷ John M Myrnga et al., “The Safety and Short-term Outcomes of Leukocyte Depleted Autologous Transfusions During Radical Cystectomy”, *Urology Volume 135*, January 2020, Pages 106-110 <https://doi.org/10.1016/j.urology.2019.08.056> and PubMed: <http://www.ncbi.nlm.nih.gov/pubmed/31626857>

the need for allogeneic blood transfusions while controlling for the theoretical risk of metastatic spread.”

- Researchers found⁸ that haemostasis with a balloon urinary catheter is a safe and effective means of preventing postoperative bleeding following vacuum-assisted breast biopsy.
- Researchers undertook a randomized double-blind, placebo-controlled trial comparing intravenous versus combined intravenous and intra-articular tranexamic acid administration in patients undergoing simultaneous bilateral total knee arthroplasty. They found⁹ that adding intra-articular tranexamic acid did not decrease perioperative blood loss compared with placebo. No patients needed allogeneic blood transfusion.
- Researchers used data from the Swedish National Medical Birth Registry (1990–2011), considered 517,874 pregnancies and deliveries¹⁰. Two hundred and seventy-seven women required massive blood transfusion. They found the highest increased risk was for women with abnormal placentation.
- At the 2019 AABB Annual Meeting¹¹ data was reported from a phase I, open-label, multi-centre safety trial of lyophilized platelets¹². Researchers concluded that: “although thrombosome infusion may appear to be safe and feasible, larger studies are needed, and the homeostatic effects of thrombosomes must be examined further.”¹³ The product offers logistical convenience: it is stable at room temperature for up to two or three years, can be quickly rehydrated, and is readily stockpiled and shipped.
- Tranexamic acid has been found to reduce the risk of mortality in patients with traumatic brain injury.¹⁴
- A review of 129 patients has concluded¹⁵ that “the administration of intravenous tranexamic acid can safely and effectively reduce perioperative blood loss and allogeneic blood transfusions in revision surgery for Vancouver type B periprosthetic femoral fractures, without increasing the risk of symptomatic venous thromboembolism”.

⁸ Zhen-qiang Lian et al., “Use of urinary balloon catheter to prevent postoperative bleeding after ultrasound-guided vacuum-assisted breast biopsy”, *The Breast Journal*, <https://doi.org/10.1111/tbj.13484>

⁹ Sachiyuki Tsukada et al., “Intra-articular tranexamic acid as an adjunct to intravenous tranexamic acid for simultaneous bilateral total knee arthroplasty: A randomized double-blind, placebo-controlled trial”, *BMC Musculoskeletal Disorders* (2019) 20:464 <https://doi.org/10.1186/s12891-019-2890-8>

¹⁰ Thurn L, et al. | “Massive blood transfusion in relation to delivery: Incidence, trends and risk factors: A population-based cohort study” *BJOG: An International Journal of Obstetrics and Gynaecology Volume 126, Issue 13* December 2019 Pages 1577-1586 <https://doi.org/10.1111/1471-0528.15952>.

¹¹ in San Antonio, Texas

¹² Lyophilized human platelets (registered name Thrombosomes) are derived from a pool collected through apheresis, which are heat-sterilized then freeze-dried in a medium which stabilizes their structure until reconstruction.

¹³ Cancelas Perez JA, Ohanian M, Davenport R, Pullarkat V, et al. Abstract PL2-MN4-32: *A phase 1, open-label, multicenter, dose escalation safety trial of lyophilized platelets in bleeding thrombocytopenic patients*. Presented at AABB Annual Meeting; 2019 Oct 19-22; San Antonio, TX. <https://transfusionnews.com/2019/10/24/thrombosomes-lyophilized-platelets-appear-safe-in-phase-1-trial/> See also <https://www.clinicaltrials.gov/ct2/show/NCT03394755>

¹⁴ [The CRASH-3 trial collaborators. Effects of tranexamic acid on death, disability, vascular occlusive events and other morbidities in patients with acute traumatic brain injury \(CRASH-3\): a randomized, placebo-controlled trial. *The Lancet* 2019; 394; 1713-1723.](https://doi.org/10.1016/S0140-6736(19)31111-1) and [Cap AP. CRASH-3: A win for patients with traumatic brain injury. *The Lancet* 2019; 394; 1687-1688.](https://doi.org/10.1016/S0140-6736(19)31111-1)

¹⁵ QR Wang et al., “Intravenous Tranexamic Acid for Reducing Perioperative Blood Loss During Revision Surgery for Vancouver Type B Periprosthetic Femoral Fractures After Total Hip Arthroplasty: A Retrospective Study” *Orthop Surg*. 2019 Dec 29. doi: 10.1111/os.12592. <https://www.ncbi.nlm.nih.gov/pubmed/31884693>

- Researchers analysed the outcomes for over 1100 critically bleeding trauma patients who were managed with a 'major haemorrhage protocol' at the Royal London Hospital Major Trauma Centre between 2008 and 2017¹⁶. The study's lead author, Dr Elaine Cole, from Queen Mary University of London, said: "Changes in transfusion and resuscitation practice for traumatically injured patients that are rooted in research have led to remarkable improvements in survival. Close collaboration between clinical, transfusion and research teams enabled incremental adaptation of the Code Red protocol over time, rapidly implementing new research findings into clinical care." Over the period examined, trauma teams ceased giving clear fluid infusions to patients while they were bleeding, using instead red blood cell transfusions and clotting components derived from blood (plasma, platelets and cryoprecipitate). Patients became able to receive blood before they reached hospital. New devices to diagnose clotting problems at the bedside became available. The overall number of red blood cell transfusions required by each patient fell over the decade, from an average of 12 units in the first 24 hours (2008), to only four units (2017). The number of patients who required a 'massive' transfusion (10 or more units of red blood cells) fell from 68 per cent in 2008 to 33 per cent in 2017. In 2008, 48 per cent of critically bleeding trauma patients died in hospital, down to 27 per cent by 2017. Survivors were also more likely to be discharged to their homes, rather than to other facilities (57 per cent in 2008, 73 per cent in 2017).
- NASA-sponsored research is directed towards discovering if freeze dried blood can be rehydrated in a zero-gravity environment, so that astronauts embarking on years-long trips can receive emergency blood transfusions, not least because cosmic radiation reduces their red blood cell count.
- Simultaneous use of nonsteroidal anti-inflammatories (NSAIDs) and oral anticoagulants (DOACs) could increase the risk for major bleeding, according to [a new post hoc analysis](#) of the ARISTOTLE trial¹⁷.

Other

- Researchers have found that conjoining a healthy mouse and a mouse with Alzheimer's plaques will cause the healthy mouse to begin developing plaques of beta-amyloid protein in its own brain¹⁸. Its brain tissue then begins dying. This raised questions of whether Alzheimer's can be spread through blood transfusions and surgical procedures.
- AstraZeneca presented¹⁹ detailed results from the Phase III OLYMPUS and ROCKIES trials²⁰ showing that roxadustat significantly increased haemoglobin levels in both non-dialysis-dependent and dialysis-dependent patients with anaemia from chronic kidney disease.

¹⁶ Elaine Cole et al., "A Decade of Damage Control Resuscitation: New Transfusion Practice, New Survivors, New Directions", *Annals of Surgery*, 22 October 2019 ahead of print. doi: [10.1097/SLA.0000000000003657](https://doi.org/10.1097/SLA.0000000000003657)

https://journals.lww.com/annalsofsurgery/Abstract/publishahead/A_Decade_of_Damage_Control_Resuscitation_New.94829.aspx, <https://www.sciencedaily.com/releases/2019/11/191112114011.htm>

¹⁷ Frederik Dalgaard et al., "Patients With Atrial Fibrillation Taking Nonsteroidal Anti-Inflammatory Drugs and Oral Anticoagulants in the ARISTOTLE Trial", *Circulation*, vol.141 no 1.

<https://doi.org/10.1161/CIRCULATIONAHA.119.041296> abstract at <https://www.ahajournals.org/doi/10.1161/CIRCULATIONAHA.119.041296>

¹⁸ *Molecular Psychiatry*, DOI: [10.1038/mp.2017.204](https://doi.org/10.1038/mp.2017.204)

¹⁹ at the American Society of Nephrology Kidney Week 2019 in Washington, D.C.

²⁰ The OLYMPUS trial compared roxadustat with placebo; the ROCKIES trial compared roxadustat with epoetin alfa.

- Researchers have reported²¹ that platelet-rich plasma is superior to platelets or plasma for wound healing *in vitro*.
- An international Phase III study²² of rivaroxaban versus standard anticoagulants for venous thromboembolism in children has found similar efficacy and safety in both treatment arms. The study involved almost 500 children, spread over 107 paediatric hospitals in 28 countries. It found recurrent venous thromboembolism in one per cent of children treated for three months with rivaroxaban compared with three per cent with standard anticoagulants.
- A recent study²³ found that early initiation of plasma transfusion during the first 60 minutes of persistent postpartum haemorrhage, compared with no plasma or later plasma, did not lead to adverse maternal outcomes.
- Researchers found²⁴ in a randomized Phase III trial²⁵ that luspatercept²⁶ reduced the severity of anaemia (and hence reduced the transfusion burden) compared with placebo among a specific category of patients²⁷ with lower-risk myelodysplastic syndromes.
- Researchers set out to determine the effect of preoperative anaemia on the prognosis of patients with upper tract urothelial carcinoma (UTUC) following radical nephroureterectomy. They found²⁸ that “preoperative anaemia is an independent risk factor for cancer-specific survival and overall survival. Haemoglobin levels should be considered during patient counselling and in decision-making for further therapy”.
- Sean Pirkle²⁹ and colleagues reviewed bleeding and thrombotic complication rates in elective spine surgery patients³⁰. They suggested that further study is needed to “define the role” of routine deep vein thrombosis (DVT) chemoprophylaxis following this surgery.

²¹ [van der Bijl I, Vlig M, Middelkoop E, and de Korte D. Allogeneic platelet-rich plasma \(PRP\) is superior to platelets or plasma alone in stimulating fibroblast proliferation and migration, angiogenesis, and chemotaxis as relevant processes for wound healing. Transfusion 2019; doi.10.1111/trf.15535](#)

²² Christoph Male, Paul Monagle et al., “Rivaroxaban compared with standard anticoagulants for the treatment of acute venous thromboembolism in children: a randomised, controlled, phase 3 trial”, *The Lancet Haematology*, [VOLUME 7, ISSUE 1](#), PE18-E27, JANUARY 01, 2020 [HTTPS://WWW.THELANCET.COM/JOURNALS/LANHAE/ARTICLE/PIIS2352-3026\(19\)30219-4/FULLTEXT#](https://www.thelancet.com/journals/lanhae/article/piiS2352-3026(19)30219-4/fulltext#)

²³ Dacia D C A Henriquez et al., “Association of Timing of Plasma Transfusion with Adverse Maternal Outcomes in Women With Persistent Postpartum Hemorrhage”, *JAMA Netw Open*. 2019;2(11):e1915628. DOI: [10.1001/jamanetworkopen.2019.15628](https://doi.org/10.1001/jamanetworkopen.2019.15628)

²⁴ Pierre Fenaux et al., “Luspatercept in Patients with Lower-Risk Myelodysplastic Syndromes”, [January 9, 2020](#) *N Engl J Med* 2020; 382:140-151 <https://www.nejm.org/doi/full/10.1056/NEJMoa1908892>

²⁵ Funded by Celgene and Acceleron Pharma; MEDALIST ClinicalTrials.gov number, [NCT02631070](#). EudraCT number, [2015-003454-41](#).

²⁶ [The FDA approved luspatercept](#) (Reblozyl, Acceleron Pharma) in November 2019 for the treatment of anaemia in adults with beta-thalassemia who require regular red blood cell transfusions.

²⁷ patients with ring sideroblasts who had been receiving regular red blood cell transfusions and were intolerant of or refractory to erythropoiesis-stimulating agents.

²⁸ B Guan, M Weng, H Fan, D Peng, D Fang, G Y Xiong, X S Li, L Q Zhou, “Evaluating the impact of preoperative anemia on the prognosis of upper tract urothelial carcinoma following radical nephroureterectomy: A single-center retrospective study of 686 patients”. PubMed <http://www.ncbi.nlm.nih.gov/pubmed/31848504>

²⁹ Department of Orthopaedic Surgery and Rehabilitation Medicine, University of Chicago Medical Center

³⁰ Sean Pirkle et al., “Comparing Bleeding and Thrombotic Rates in Spine Surgery: An Analysis of 119 888 Patients”, *Global Spine Journal*, 26 December 2019 <https://doi.org/10.1177/2192568219896295> <https://journals.sagepub.com/doi/full/10.1177/2192568219896295>

- [CytoSorbents Corporation \(CTSO\)](#) announced the first patient enrolment in the company-sponsored [Ticagrelor CytoSorb Hemoadsorption \(TISORB\) study](#) in the UK. This is a 30-patient, open-label, prospective, multi-centre, single arm clinical trial designed to evaluate the ability of [CytoSorb](#), when used in patients undergoing emergency open heart surgery within 48 hours of their last dose of ticagrelor³¹, to remove ticagrelor and reverse the inhibitory effect of the drug on platelet aggregation. The trial is expected to finish by August 2020.
- Andexxa³² is a recombinant modified human factor Xa molecule designed to reverse the effects of factor Xa inhibitor anticoagulants. Study results reported³³ at the American College of Gastroenterology Annual Meeting showed the drug helped produce high rates of haemostasis in patients with major gastrointestinal bleeding.
- Research has found³⁴ that people with what is called "metabolic syndrome" are vulnerable to recurring blood clots. The term is a catch-all for conditions such as obesity, high blood sugar, high cholesterol and high blood pressure, also risk factors for diabetes and heart disease.

2. Products and treatments

Here the NBA follows the progress in research and clinical trials that may, within a reasonable timeframe, either make new products and treatments available or may lead to new uses or changes in use for existing products.

Treating haemophilia

- On 31 October 2019³⁵, [uniQure N.V.](#) announced the publication of 26-week interim safety and efficacy data from the ongoing Phase IIb clinical trial of etranacogene dezaparvovec³⁶, an investigational gene therapy for hemophilia B³⁷. The company said that "etranacogene dezaparvovec was generally well tolerated, with no clinically significant elevations of liver enzymes or inflammatory markers observed, and no use of corticosteroids related to treatment required". Robert Gut, chief medical officer at uniQure and co-author of the paper, said: "This publication supports the potential of etranacogene dezaparvovec to substantially improve the quality of life for hemophilia B patients through a one-time administration that results in sustained Factor IX activity and may result in a cessation of bleeding episodes. We.....look forward to sharing top-line data from the pivotal Phase III HOPE-B study in 2020."
 - On 14 November 2019 uniQure participated in the World Federation of Hemophilia Global Forum in Montreal. Eileen Sawyer gave an oral presentation on *Interim Results from a Phase 2b trial of Etranacogene Dezaparvovec (AMT-061:AAV5-Padua hFIX variant), an Enhanced Vector for Gene Transfer in Adults with Severe or Moderate-Severe Hemophilia B*.

³¹ Brilinta, from Astra Zeneca

³² andexanet alfa, Portola

³³ Siegal D, et al. Abstract 53. The meeting was held Oct. 25-30, 2019 in San Antonio.

³⁴ Lauren K Stewart and Jeffrey A Kline, "Metabolic syndrome increases risk of venous thromboembolism recurrence after acute deep vein thrombosis", published 9 January 2020, *Blood Adv* (2020) 4 (1): 127–135. <https://doi.org/10.1182/bloodadvances.2019000561>

³⁵ <https://tools.eurolandir.com/tools/Pressreleases/GetPressRelease/?ID=3660864&lang=en-GB&companycode=nl-qure&v=>

³⁶ an investigational [AAV5](#)-based gene therapy containing a patent-protected FIX-Padua variant

³⁷ Annette von Drygalski et al., "Etranacogene dezaparvovec (AMT-061 Phase 2b): normal/near normal FIX activity and bleed cessation in hemophilia B," *Blood Advances* (2019) 3 (21): 3241–3247. <https://doi.org/10.1182/bloodadvances.2019000811>

- ii. Then on 8 December³⁸, in poster presentations at the 61st Annual Meeting of the American Society of Hematology (ASH), uniQure announced updated clinical data on the three patients in the ongoing Phase IIb study. Steven Pipe³⁹, principal investigator in the [HOPE-B clinical trial](#), said: “These updated data show that a single administration of etranacogene dezaparvovec has been well-tolerated now out 52 weeks and has increased FIX activity into the therapeutic range for people living with hemophilia B. These data show a full year of meaningful clinical benefit for all three patients in the study, including durable levels of FIX activity with no bleeds, no requirement for infusions of FIX replacement therapy outside of surgery, and no need for immunosuppression.”
 - iii. uniQure also presented⁴⁰ up to four years of follow-up data on the 10 patients in the Phase I/II trial of AMT-060, the company’s first-generation gene therapy for the treatment of haemophilia B. Patients in that trial, now four years post enrolment, have not seen their Factor IX expression decrease, being at a mean of 7.5 per cent over three and a half years, regarded as mild disease. The patients no longer take factor replacement therapy, and their annualized bleeding rate has fallen to zero. They have not needed immunosuppression via steroids.
- Pfizer also provided updates on its gene therapy for haemophilia B at the American Society of Hematology meeting. Its candidate, which uses the same Padua variant, started its Phase III trial a year and a half ago. Pfizer's [Phase 2 dosing trial](#) of the therapy it licensed from Spark Therapeutics showed that one year after infusion 15 patients achieved an average Factor IX expression of 23 per cent. Twelve of 15 patients experienced no bleeding episodes, yielding an annual bleeding rate of 0.4. Five of the 15 patients reported a total of 20 factor replacement therapy infusions, while two patients were treated with corticosteroids in response to immune-related liver enzyme spikes. Pfizer also reported data from a mouse study of a gene therapy designed to aid blood coagulation by promoting production of thrombin via another antibody.
 - Researchers have conducted direct comparative studies⁴¹ that shed light on the pharmacokinetic differences between extended half-life factor IX products, including the number of injections and overall factor concentrate consumption.
 - Researchers found⁴² that, amongst children with [von Willebrand Disease \(VWD\)](#), boys may be more likely to report bleeding incidents and to use treatment products for the condition than girls.

³⁸ in Orlando, Florida.

<https://tools.eurolandir.com/tools/Pressreleases/GetPressRelease/?ID=3677182&lang=en-GB&companycode=nl-qure&v=>

³⁹ professor of paediatrics and pathology and paediatric medical director of the haemophilia and coagulation disorders program at the University of Michigan [One Year Data from a Phase 2b Trial of AMT-061 \(AAV5-Padua hFIX variant\), an Enhanced Vector for Gene Transfer in Adults with Severe or Moderate-Severe Hemophilia B.](#)

⁴⁰ Also poster presentations at the ASH meeting

⁴¹ Mindy L Simpson et al., “Population Pharmacokinetic Modeling Of On-Demand And Surgical Use Of Nonacog Beta Pegol (N9-GP) And rFIXFc Based Upon The paradigm 7 Comparative Pharmacokinetic Study”, [Journal of Blood Medicine](#) » [Volume 10](#) DOI: <https://doi.org/10.2147/JBM.S217539>

⁴² Abe K, Dupervil B, O’Brien SH, et al. [Higher rates of bleeding and use of treatment products among young boys compared to girls with von Willebrand Disease](#) [published online October 15, 2019]. *Am J Hematol.* doi:10.1002/ajh.25656

- A report⁴³ on the results of a 10-year gene therapy study in dogs has rekindled past concerns that, by using a virus to insert therapeutic genes into the human genome, scientists may inadvertently be triggering cancer in the treated cells.
- In a multiyear follow up of AAV5 -hFVIII-SQ gene therapy⁴⁴ for haemophilia A, researchers discovered⁴⁵ that the therapy had resulted in “sustained and clinically relevant benefit, as measured by a substantial reduction in annualized rates of bleeding events and complete cessation of prophylactic factor VIII use in all participants who had taken 4×10^{13} vg per kilogram or 6×10^{13} vg per kilogram of the gene therapy”.

Treating beta thalassemia and sickle cell disease

- Nova Laboratories launched its new liquid formulation of hydroxycarbamide for sickle cell disease. Xromi was granted a license by the European Medicines Agency (EMA) in July 2019. Solid dosage forms of the drug have been used in the treatment of sickle cell disease since the 1990s⁴⁶, but the new formulation makes administering the drug to young children easier.
- Researchers report⁴⁷ that iron chelation therapy with a combination of deferasirox and deferoxamine may improve bone mass in patients with transfusion-dependent beta thalassemia at the same time as it reduces serum ferritin levels.

Treating other conditions

- At the annual congress of the European Society of Cell and Gene Therapy⁴⁸ Rocket Pharmaceuticals reported long-term follow-up data from the Phase I/II study of RP-L102, its gene therapy for Fanconi anemia⁴⁹. Rocket said it represented the first evidence of long-term improvement.
- A meta-analysis suggests⁵⁰ Iron chelation therapy may reduce mortality and leukaemia transformation risk among patients with [myelodysplastic syndrome \(MDS\)](#).
- Apellis Pharmaceuticals in early January announced that results from its Phase III Pegasus study were positive. This trial is evaluating Pegcetacoplan (APL-2) in adults suffering from paroxysmal nocturnal haemoglobinuria (PNH).
- Akari Therapeutics reported positive interim data from its Phase III paroxysmal nocturnal haemoglobinuria (PNH) CAPSTONE study in complement inhibitor naïve,

⁴³ on December 9, 2019, at the American Society of Hematology (ASH) meeting in Orlando. See <https://www.news-medical.net/news/20200108/Dog-study-suggests-that-AAV-in-gene-therapy-could-induce-cancer.aspx> or <https://www.sciencemag.org/news/2020/01/virus-used-gene-therapies-may-pose-cancer-risk-dog-study-hints>

⁴⁴ Funds by BioMarin Pharmaceutical; ClinicalTrials.gov number, EudraCT number, [2014-003880-38](#).

⁴⁵ K John Pasi, “Multiyear Follow-up of AAV5-hFVIII-SQ Gene Therapy for Hemophilia A” *N Engl J Med* 2020; 382:29-40, 2 January 2020 DOI: 10.1056/NEJMoa1908490 <https://www.nejm.org/doi/full/10.1056/NEJMoa1908490>

⁴⁶ The drug is used to increase foetal haemoglobin to prevent red blood cells sickling and therefore to reduce vaso-occlusive complications.

⁴⁷ Bordbar M, Haghpanah S, Zekavat OR, Saki F, Bazrafshan A, Bozorgi H. [Effect of different iron chelation regimens on bone mass in transfusion-dependent thalassemia patients](#). *Expert Rev Hematol.* 2019;12:997-1003

⁴⁸ In Barcelona

⁴⁹ <https://www.businesswire.com/news/home/20191024005460/en/Rocket-Pharmaceuticals-Presents-Evidence-Long-Term-Improvement-Stabilization>

⁵⁰ Liu H, Yang N, Meng S, Zhang Y, Zhang H, Zhang W. [Iron chelation therapy for myelodysplastic syndrome: a systematic review and meta-analysis](#) [published online November 11, 2019]. *Clin Exp Med.* doi:10.1007/s10238-019-00592-5

transfusion-dependent PNH patients. All patients treated with nomacopan achieved the primary endpoint of transfusion independence.

- [Thrombocytopenia](#) in pregnancy is a complication for clinicians, with the need to identify whether thrombocytopenia is associated with a life-threatening disorder and to evaluate the risk of foetal thrombocytopenia, which carries the risk of abnormal bleeding in the newborn, or even before birth. A recent paper⁵¹ suggests a general approach to the diagnosis and management of thrombocytopenia in pregnancy.
- US research⁵² found that initial treatment with low-dose aspirin and intravenous immunoglobulin is not associated with an increased risk for recurrent fever relative to high-dose aspirin in children with Kawasaki disease.
- Protagonist Therapeutics initiated a Phase II study of its hepcidin mimetic PTG-300 in patients with hereditary haemochromatosis⁵³.

3. Regulatory

The NBA monitors overseas regulatory decisions on products, processes or procedures which are or may be of relevance to its responsibilities.

- [BioCryst Pharmaceuticals](#) submitted a [new drug application](#) (NDA) to the US Food and Drug Administration (FDA) for [berotralstat \(BCX7353\)](#), a once daily, oral (capsule) treatment to prevent attacks (swelling) in patients with [hereditary angioedema](#) (HAE)⁵⁴.
- The FDA approved Celgene and Acceleron's Reblozyl (luspaterecept-aamt) for the treatment of anaemia in adult patients with beta thalassemia who require regular red blood cell (RBC) transfusions. The product is not indicated for use as a substitute for RBC transfusions in patients who require immediate correction of anaemia. It is an erythroid maturation agent, which regulates late-stage red blood cell maturation to help patients reduce their RBC transfusion burden.
- The FDA awarded Fresenius Medical Care a breakthrough device designation for a new haemodialysis system designed to prevent blood clots in the patient. The device incorporates an anti-thrombogenic polymer (Endexo⁵⁵), added during the manufacturing of dialyzers and blood flow lines.
- The FDA awarded rare paediatric disease designation to ARU-1801 (Aruvant), Roivant Sciences' gene therapy for sickle cell disease and beta-thalassemia. The possible one-time treatment aims to increase functioning red blood cells by inserting a modified foetal haemoglobin gene into the patient's CD34-positive haematopoietic stem cells through a lentiviral vector.
- In India Pharmazz submitted an application for Marketing Authorization of centhaquine to the Central Drugs Standard Control Organization (CDSCO), Director General of Health Services, Ministry of Health and Family Welfare for the treatment of patients with hypovolemic shock and excessive blood loss. The company also

⁵¹ Pishko AM, Levine LD, Cines DB. [Thrombocytopenia in pregnancy: diagnosis and approach to management](#) [published online November 6, 2019]. *Blood Rev.* doi:10.1016/j.blre.2019.100638

⁵² Brooks Platt, James B Wood et al., "Comparison of Risk of Recrudescence Fever in Children With Kawasaki Disease Treated With Intravenous Immunoglobulin and Low-Dose vs High-Dose Aspirin", 3 January 2020, [JAMA Netw Open 2020; 3: e1918565](#)

⁵³ Hereditary haemochromatosis is a blood disorder caused by a deficiency of hepcidin hormone. This leads to excessive iron accumulation in body tissues. Standard treatment is regular phlebotomy (removal of blood) to prevent restrictive cardiomyopathy, diastolic dysfunction, heart failure, cirrhosis, and an increased risk for hepatocellular carcinoma. <http://www.protagonist-inc.com>.

⁵⁴ For clinical trials see the double-blind, placebo-controlled Phase III trial, called [APeX-2 \(NCT03485911\)](#), and the open-label Phase II/III trial [APeX-S \(NCT03472040\)](#).

⁵⁵ Endexo consists of "surface-modifying macromolecules" to block platelets and proteins from sticking to and coating solid surfaces

arranged a pre-IND (Investigational New Drug) meeting with the US Food and Drug Administration. Centhaquine is designed to increase cardiac output and decrease vascular resistance, assisting in resuscitation.

- On 23 December 2019 FibroGen announced the submission of a New Drug Application (NDA) to the FDA for roxadustat for the treatment of anaemia of chronic kidney disease in both non-dialysis-dependent and dialysis-dependent patients⁵⁶.
- Also on 23 December 2019, Biomarin announced the submission of a Biologics License Application (BLA) to the FDA for its investigational AAV gene therapy, valoctocogene roxaparovec, for adults with haemophilia A. This is the first marketing application submission in the US for gene therapy for any form of haemophilia.
- Samsung Bioepis Co., Ltd. and AffaMed Therapeutics announced that the China National Medical Products Administration (NMPA) has approved the Clinical Trial Application (CTA) for SB12, also referred to as AMT904 in China – a biosimilar candidate referencing Soliris (eculizumab). The CTA approval permits initiation of a Phase III clinical study at Chinese sites. The drug is designed to treat paroxysmal nocturnal haemoglobinuria.

4. Market structure and company news

The NBA's business intelligence follows company profitability, business forecasts, capital raisings or returns, mergers and takeovers, arrangements for joint research and/or development, contracts for supply of manufacturing inputs, and marketing agreements. Companies considered include suppliers, potential suppliers and developers of products which may be of interest.

- CSL Behring has partnered with US-based SAB Biotherapeutics to investigate the possibility of, and the potential for, new therapies to treat autoimmune, infectious and idiopathic diseases⁵⁷ by leveraging SAB's technology platform. This platform can, through advanced genetic engineering, naturally and quickly produce large amounts of human antibodies without using human donors. CSL's Dr Andrew Nash⁵⁸ described it as "an interesting and novel platform for the production of human immunoglobulins". SAB CEO and co-founder Eddie J Sullivan said: "We believe combining our unique human antibody development and production capabilities with CSL Behring's established immunoglobulin franchise and vast expertise in biopharmaceutical development will broaden therapeutic possibilities".
- The FDA recently finalized a guidance letter concerning platelet storage. Cerus' INTERCEPT system could be the new standard-of-care for platelet transfusion safety in the US. By 31 March 2021 every one of the 2.6 million platelet units collected annually must comply with the FDA's new standard.
- [Sangamo Therapeutics](#) has handed over the development of [SB-525](#), a gene therapy for haemophilia A, to Pfizer, which will now take the therapy into Phase III clinical trials⁵⁹.

⁵⁶ A Phase III study has shown roxadustat effective in haemodialysis patients regardless of prior treatment with erythropoiesis-stimulating agents. See Akizawa T, Ueno M, Shiga T, Reusch M. [Oral roxadustat three times weekly in ESA-naïve and ESA-converted patients with anemia of chronic kidney disease on hemodialysis: Results from two phase 3 studies](#) [published online December 31, 2019]. *The Apher Dial.* doi:10.1111/1744-9987.13468

⁵⁷ conditions of unknown cause which arise suddenly

⁵⁸ Senior Vice President, Research

⁵⁹ SB-525 was originally developed by Sangamo Therapeutics in [collaboration with Pfizer](#), with Sangamo leading a Phase I/II trial ([NCT03061201](#)) for safety and efficacy. It has now transferred the investigational new drug application (IND) ahead of schedule and has received a \$US 25 million milestone payment from Pfizer, which will lead clinical development. The Phase III trial is being

- [Global Blood Therapeutics \(GBT\)](#) and [Syros Pharmaceuticals](#) have agreed to collaborate to discover, develop, and market new therapies for sickle cell disease (SCD) and beta thalassemia. Syros will be responsible for identifying new therapeutic targets and the discovery of drugs that stimulate the production of [foetal hemoglobin](#), using its [gene control platform](#). GBT then has the option of an exclusive, global licence to develop, manufacture and market the drugs which result.
- [Generation Bio](#) announced the closing of a \$US 110 million Series C financing. Funds will advance two lead liver-targeted gene therapy programs for haemophilia A and phenylketonuria (PKU) into IND⁶⁰-enabling studies and clinical development.

5. Specific country events

- Paediatrician Dr Hamish Graham of the Murdoch Children's Research Institute worked with colleagues in Nigeria to record the blood oxygen levels of more than 23,000 children admitted to 12 medium-sized hospitals. They found⁶¹ “that one in four newborns and one in 10 children in hospital had low blood oxygen, and these children were eight times more likely to die than those with normal blood oxygen.”
- Researchers have shown⁶² that patient blood management (PBM) guidelines introduced by Australia’s National Blood Authority in 2012 have reduced blood transfusions in cardiac surgery without any adverse impact on patient outcomes.
- The tick-borne parasite *Babesia venatorum* has been found in sheep in the north east of Scotland.
- US researchers found⁶³ their computer modelling showed there may be a significant number of patients with symptomatic, undiagnosed Von Willebrand disease (VWD) or other mucocutaneous bleeding disorder in the commercially insured population. They suggested that “enhanced awareness of VWD symptoms and their impact, and of screening and testing procedures, may improve the diagnosis of VWD and reduce disease burden”.
- In the US, red blood cell transfusions have decreased over the past decade, but the demand for platelet transfusions has increased. Researchers have analysed⁶⁴ data from 2013 to 2016 from twelve hospitals involved in the Recipient and Donor Epidemiology Study III (REDS-III). Over 60 per cent of all platelets transfused were apheresis-derived, and 93 per cent were leukoreduced. Patients with leukemia, myelodysplastic syndrome, or lymphoma accounted for 46 per cent of platelets transfused.
- The Alliance for Regenerative Medicine (ARM), an international advocacy organization representing the cell and gene therapy and broader regenerative medicine sector, on 10 January announced in Washington DC the release of a

launched after [Promising results](#) of the open-label Phase I/II Alta trial ([NCT03061201](#)) were [presented](#) at the [61stAnnual Meeting of the American Society of Hematology](#) in December.

⁶⁰ Investigational New Drug

⁶¹ Hamish Graham, et al., “[Hypoxaemia in hospitalised children and neonates: A prospective cohort study in Nigerian secondary-level hospitals](#),” *EClinicalMedicine*. DOI: [10.1016/j.eclinm.2019.10.009](#)

⁶² Adam H Irving et al., “Impact of patient blood management guidelines on blood transfusions and patient outcomes during cardiac surgery”, *The Journal of Thoracic and Cardiovascular Surgery*, [https://doi.org/10.1016/j.jtcvs.2019.08.102](#) First published online 7 October 2019

⁶³ Robert F Sidonio Jr, Ayesha Zia, Dana Fallaize, “Potential Undiagnosed VWD Or Other Mucocutaneous Bleeding Disorder Cases Estimated From Private Medical Insurance Claims”, *Journal of Blood Medicine*, 6 January 2020 Volume 2020:11 Pages 1—11, DOI [https://doi.org/10.2147/JBM.S224683](#)

[https://www.dovepress.com/journal-of-blood-medicine-journal](#)

⁶⁴ [Gottschall J, Wu Y, Triulzi D, Kleinman S, et al. The epidemiology of platelet transfusions: an analysis of platelet use at 12 US hospitals. Transfusion 2019](#)

report, *A Transformative Therapy Value Model for Rare Blood Diseases*. The report argues that cell and gene therapies have the potential to deliver cost savings to health systems⁶⁵.

- Studies⁶⁶ from the University of Toronto and the Hospital for Sick Children are suggestive of a need for Canadians to undertake more screening for iron deficiency in early childhood. The studies follow on from the researchers' earlier work that showed screening with a ferritin blood test can detect iron deficiency earlier than the more standard haemoglobin test, which reveals a deficiency only when it has progressed to anaemia.
- A James Cook University (JCU) study has found 60 per cent of Indigenous children are affected by anaemia in remote Far North Queensland communities. The study found 46 per cent of babies who suffered early childhood anaemia under-performed in national standards for measuring development⁶⁷, compared with 23 per cent of those who had not. JCU senior lecturer Dympna Leonard said the findings could help explain poor education outcomes among Indigenous children, and that Indigenous communities should be consulted about solutions to address iron deficiency in infants. "The World Health Organisation recommends that food is fortified with a special multi-micronutrient preparation that is added to the baby's food," she said. "Where they've done those interventions it's been very effective at preventing the early childhood anaemia".

6. Research not included elsewhere

A wide range of scientific research has some potential to affect the use of blood and blood products. However, research projects have time horizons which vary from "useful tomorrow" to "at least ten years away". Likelihood of success of particular projects varies, and even research which achieves its desired scientific outcomes may not lead to scaled-up production, clinical trials, regulatory approval and market development.

- US researchers found⁶⁸ that adolescents with heavy menstrual bleeding appear to have a high prevalence of bleeding disorders.
- Researchers from the Keck School of Medicine⁶⁹, University of Southern California, Los Angeles, have also reported that the incidence of von Willebrand disease in adolescent girls with heavy menstrual bleeding (HMB) is high and that treatment for the condition may need to be, or to include, haemostatic medications. They recommend a multidisciplinary approach to distinguish etiology so treatment can be appropriate, and the patient can avoid anaemia, blood transfusions and hospitalization⁷⁰.

⁶⁵ <https://www.biospace.com/article/releases/new-report-demonstrates-potential-for-cell-and-gene-therapies-to-provide-cost-savings/>

⁶⁶ Patricia C Parkin et al., "Association between Serum Ferritin and Cognitive Function in Early Childhood", *The Journal of Pediatrics*, DOI: <https://doi.org/10.1016/j.jpeds.2019.09.051> and Sarah Carsley et al., "Iron deficiency screening for children at 18 months: a cost-utility analysis", *CMAJ Open*, 3 December 2019, vol.7 no 4 E689-E698 doi: 10.9778/cmajo.20190084 <http://cmajopen.ca/content/7/4/E689.full>

⁶⁷ The study relied on results from the Australian Early Development Census (AEDC), a national measure of child development.

⁶⁸ Zia A, Jain S, Kouides P, et al. [Bleeding disorders in adolescents with heavy menstrual bleeding in a multicentre prospective US cohort](#) *Haematologica*. doi:10.3324/haematol.2019.225656

⁶⁹ University of Southern California, Los Angeles

⁷⁰ Claudia Borzutsky and Julie Jaffray "Diagnosis and Management of Heavy Menstrual Bleeding and Bleeding Disorders in Adolescents", *JAMA Pediatr*. Published online December 30, 2019. doi:10.1001/jamapediatrics.2019. <https://jamanetwork.com/journals/jamapediatrics/article-abstract/2757556>

- Retired haematologist [Dr. Carol Kasper](#) has a continuing interest in her specialisation⁷¹, including the issues faced by women who carry a haemophilia mutation. A decade ago, she reported that research on her files had identified 277 potential female carriers for every 100 diagnosed males (their mothers, aunts, sisters, and daughters). Testing found that there were approximately 156 true female carriers⁷². In a recent interview⁷³ she said she believes that women genetically connected to men with haemophilia should have their factor levels tested, and also ascertain their carrier status through genetic testing. She commented: “When analyzing the subset of women who are carriers of haemophilia, one can predict the average factor level will be about 50 per cent.” Where the line should be drawn for a diagnosis of haemophilia remains a debate. The [World Federation of Hemophilia](#) says any person, male or female, with levels under 40 percent should receive a haemophilia diagnosis. Kasper found that in the women she tested, one in five carriers had factor levels below 30 percent, a mild hemophilia diagnosis. In some families, factor levels can be lower in women than in men. Kasper believes giving women a formal haemophilia diagnosis is important, so that they and their healthcare professionals understand their bleeding risk, and they are able to ensure any surgical procedures are carried out in a suitable context. She says they should be connected with a haemophilia treatment centre and should wear a medical alert tag.
- New research suggests that children's immune systems may be less capable of fighting off new infectious diseases after a measles virus infection due to "immune amnesia".⁷⁴
- Researchers at Harvard's Wyss Institute have developed a technique to deliver chemotherapy to the lungs using red blood cells⁷⁵.
- A study⁷⁶ based on Sweden's medical birth register has found that women who are haemophilia B carriers have more than three times the risk of bleeding following childbirth than non-carriers. Researchers did not establish a difference in the risk of postpartum bleeding between haemophilia A carriers and non-carriers. Nor did they uncover a difference in the risk of complications (such as preeclampsia, preterm birth, or low birth weight) between haemophilia carriers and non-carriers.
- Researchers reported⁷⁷ that real-time peer auditing reduced the rate of central-line-associated bloodstream infections, or CLABSIs, by 12 per cent at a hospital in North Carolina.

⁷¹ she has a lifetime achievement award from the Hemostasis and Thrombosis Research Society and two career achievement awards from the National Hemophilia Foundation.

⁷² Carol K Kasper and J C Lin, “How many carriers are there?”, letter to the editor, *Haemophilia*, 24 August 2010. <https://onlinelibrary.wiley.com/doi/10.1111/j.1365-2516.2010.02210.x>

⁷³ Reported 7 January 2020 <https://hemophilianewstoday.com/2020/01/07/carol-kasper-diagnosing-women-hemophilia-research-pioneer/>

⁷⁴ Velislava N Petrova et al., “Incomplete genetic reconstitution of B cell pools contributes to prolonged immunosuppression after measles”, *Science Immunology* : Vol. 4, Issue 41, eaay6125 DOI: 10.1126/sciimmunol.aay6125 <https://immunology.sciencemag.org/content/4/41/eaay6125>

⁷⁵ Zongmin Zhao et al., [Erythrocyte leveraged chemotherapy \(ELeCt\): Nanoparticle assembly on erythrocyte surface to combat lung metastasis](#) *Science Advances*: 13 Vol. 5, no. 11, eaax9250 DOI: 10.1126/sciadv.aax9250

⁷⁶ Anna Olsson et al., “[Maternal and neonatal outcomes in carriers of haemophilia A and B: A Swedish Medical Birth Register study](#),” in the journal *Haemophilia*. 19 November 2019 <https://doi.org/10.1111/hae.13884>

⁷⁷ “The little things matter- How peer audits contribute to CLABSI prevention”.

[DiBiase LM, et al. Infect Control Hosp Epidemiol. 2019;doi:10.1017/ice.2019.341.](#)

- Researchers report⁷⁸ that time spent in space has a dose-response relationship with acute and chronic reductions in haemoglobin, or “[space anaemia](#)”.
- An international research team reported⁷⁹ that the ThromboGenomics high-throughput sequencing test may validate recently discovered genetic variants associated with [rare bleeding, thrombotic, or platelet disorders \(BTPDs\)](#) in a large cohort of index patients. They said that the ThromboGenomics test may allow for “more precise prognostication and management of disease and, with cascade testing, better informed counselling of patients and their close relatives.”
- A study⁸⁰ found that among a geriatric population hospitalized for femoral neck fracture surgery, preoperative hypoalbuminaemia was a predictor of postoperative pneumonia, followed by other independent risk factors: chronic obstructive pulmonary disease, prior stroke, and the time interval between injury and surgery. The study suggested that patients who undergo femoral neck fracture surgery and have preoperative hypoalbuminaemia should be closely monitored and receive particular perioperative attention.
- Researchers have evaluated the therapeutic potential of a protein therapy called recombinant human platelet-derived growth factor-AB (rhPDGF-AB) to improve recovery after a heart attack. They tested the new treatment in a porcine model of heart attack, and they reported their results to be promising⁸¹.

7. Infectious diseases

The NBA takes an interest in infectious diseases because: the presence of disease in individual donors (e.g. influenza), or potential disease resulting from travel (e.g. malaria) means a donor must be deferred; temporary disease burden within a community (e.g. dengue in North Queensland) may limit blood collection in the community for a time; and some people may not be permitted to donate at all (e.g. people who lived in the UK for a period critical in the history of vCJD). Blood donations are tested for a number of diseases (e.g. HIV and Hepatitis B), but there are also emerging infectious diseases for which it may become necessary to test in the future (e.g. Chagas disease, Zika virus and the tick-borne babesiosis and Lyme disease).

Mosquito-borne diseases

- Researchers⁸² have used drones to spray rice fields in Zanzibar with a thin, non-toxic film⁸³. They say preventing pupae and larvae from attaching themselves to the surface of the water should have an impact on the transmission of malaria.

⁷⁸ Trudel G, Shafer J, Laneville O, Ramsay T. [Characterizing the effect of exposure to microgravity on anemia, more space is worse](#) [published online December 9, 2019]. *Am J Hematol*. doi:10.1002/ajh.25699

⁷⁹ Downes K, Megy K, Duarte D, et al. [Diagnostic high-throughput sequencing of 2396 patients with bleeding, thrombotic, and platelet disorders](#) [published online December 5, 2019]. *Blood*. doi:10.1182/blood.2018891192

⁸⁰ Yakang Wang, Xiaoli Li, Yahong Ji, Hua Tian, Xiaofang Liang² Na Li, Junning Wang, “Preoperative Serum Albumin Level As A Predictor Of Postoperative Pneumonia After Femoral Neck Fracture Surgery In A Geriatric Population”, [Clinical Interventions in Aging » Volume 14 Pages 2007—2016](#) DOI <https://doi.org/10.2147/CIA.S231736>

⁸¹ James Chong et al., “Platelet-derived growth factor-AB improves scar mechanics and vascularity after myocardial infarction”, *Science Translational Medicine*. 01 Jan 2020: Vol. 12, Issue 524, eaay2140 DOI: 10.1126/scitranslmed.aay2140 <https://stm.sciencemag.org/content/12/524/eaay2140>

⁸² led by Bart Knols from Radboud University in The Netherlands

⁸³ The silicone-based liquid, Aquatain AMF, is made by Australian company Aquatain Products Pty Ltd. The liquid is highly permeable to gases so does not prevent the water from being oxygenated.

- Scientists from the Pasteur Institute and CNRS (French National Center for Scientific Research) report⁸⁴ that they have identified molecules that can inhibit DNA methylation and kill even the most resistant of the malaria parasites, *Plasmodium falciparum*.
- Takeda's tetravalent vaccine against the dengue virus, TAK-003, was found in a Phase III trial to be effective and appeared safe among healthy children and adolescents⁸⁵. Takeda has opened a new plant in Singen, Germany, which will manufacture the vaccine.
- The American Society of Tropical Medicine and Hygiene Annual Meeting was told⁸⁶ that cases of dengue declined significantly in areas of Australia, Brazil, Indonesia and Vietnam where lab-grown mosquitos carrying *Wolbachia* were released.
- French vaccine manufacturer Valneva SE announced that an End of Phase II meeting has been scheduled with the FDA on February 24, 2020, for its single-shot chikungunya vaccine candidate, [VLA1553](#). Valneva will present its plan for Phase III clinical studies and licensure. The company reported final [Phase 1 results](#) in November 2019 confirming the vaccine's immunogenicity and safety profile.

Influenza

- Scientists have identified antibodies that protect against multiple strains of the influenza virus by targeting the surface protein neuraminidase⁸⁷.
- BiondVax Pharmaceuticals announced the completion of enrolment and randomization of 12,463 participants in the pivotal, clinical efficacy, Phase III trial of the M-001 universal influenza vaccine candidate. Results are expected by the end of 2020.
- The US Centers for Disease Control (CDC) reported that there had been 800 deaths from influenza in the last week of 2019. At that time, nationally, influenza B/Victoria viruses were predominant, followed by A (H1N1)pdm09 viruses. "A(H3N2) and B/Yamagata viruses are circulating at very low levels," the CDC said, noting that influenza B viruses do not usually predominate so early in the season. The CDC commented: "Almost all (>99 per cent) of the influenza viruses tested this season are susceptible to the four FDA-approved influenza antiviral medications recommended for use in the US."
- WHO said that although influenza B was dominating in the US and Canada, during the last week of December 68.7 per cent of global laboratory specimens were typed as influenza A. 71.1 per cent were H3N2, 28.9 per cent were 2009 H1N1.
- In early January, China, Poland and India all reported new outbreaks of highly pathogenic avian flu⁸⁸, respectively H5N6 in wild swans, H5N8 on poultry farms and H5N1 in poultry.

⁸⁴ Flore Nardella et al., "DNA Methylation Bisubstrate Inhibitors Are Fast-Acting Drugs Active against Artemisinin-Resistant *Plasmodium falciparum* Parasites", *ACS Central Science*. 27 November 2019 <https://pubs.acs.org/doi/10.1021/acscentsci.9b00874>

⁸⁵ Shibadas Biswal et al., "Efficacy of a Tetravalent Dengue Vaccine in Healthy Children and Adolescents", *New England Journal of Medicine*. N Engl J Med 2019; 381:2009-2019, DOI: 10.1056/NEJMoa1903869

⁸⁶ Anders K, et al. "Growing evidence that the World Mosquito Program's *Wolbachia* method reduces dengue transmission". ASTMH 68th Annual Meeting; Nov. 20-24, 2019; National Harbor, Maryland.

⁸⁷ Daniel Stadlbauer, Ian A. Wilson, Ali H. Ellebedy, Florian Krammer et al., "Broadly protective human antibodies that target the active site of influenza virus neuraminidase". *Science*, 2019; 366 (6464): 499 DOI: [10.1126/science.aay0678](https://doi.org/10.1126/science.aay0678) also reported at <https://www.sciencedaily.com/releases/2019/10/191025094024.htm>

⁸⁸ Jan 8 AFD [post](#), Jan 7 OIE report on [H5N8 in Poland and](#) Jan 8 OIE report on [H5N1 in India](#)

- A study has suggested that one approach to deal with pandemic threats from A(H5N1) influenza may be to prime the population with an A(H5N1) vaccine and then boost immunity with a dose of the pandemic vaccine as required. The Phase II/ III study was conducted by the Institute of Vaccines and Medical Biologicals (IVAC) in Vietnam⁸⁹.

Ebola virus disease

- Johnson & Johnson filed for European approval for its two-dose experimental vaccine to protect against Ebola. Merck's single dose Ebola vaccine was approved in Europe in October, and in the US in December.
- The death from Ebola of a woman in the Democratic Republic of Congo has challenged the previously-accepted medical theory that survivors are immune to reinfection.

New coronavirus first identified in Wuhan, China

- Between 12 December and 5 January, 59 cases of a viral pneumonia of unknown cause were identified in persons associated with the City of Wuhan, capital of Hubei province, China. Seven were in a critical condition at 5 January. Some of the patients worked at a fresh seafood and produce market⁹⁰. Authorities said that 163 people who had had contact with those infected were under medical observation. Symptoms were mainly fever, with a few patients having difficulty in breathing and some chest radiographs showing invasive lesions on both lungs. Authorities said there were no clear indications of human-to-human transmission, and that no healthcare workers had become infected.
- Authorities were isolating patients, tracing close contacts, cleaning up the market⁹¹, and searching for the cause and for additional cases.
- WHO, which was notified of the outbreak on 31 December, said on 5 January it was continuing to monitor the mysterious lung infection. Wuhan health authorities said that pathogen studies had ruled out more common respiratory diseases, including influenza, avian flu and adenovirus. They said they had also ruled out Severe Acute Respiratory Syndrome (SARS) and Middle East respiratory syndrome (MERS). Patients were being treated under quarantine. The seafood market had by then been closed and sanitized amidst concerns about a possible jump of an unknown animal virus to humans. Commentators were recalling Severe Acute Respiratory Syndrome, or SARS, which about 17 years ago infected more than 8,000 people around the world and killed almost 800⁹². WHO said it was believed to have originated in the southern Chinese province of Guangdong. Virologists globally have been speculating whether the current culprit is a SARS-like "coronavirus"⁹³.

⁸⁹ Tran Nhu Duong, "A Phase 2/3 double blinded, randomized, placebo-controlled study in healthy adult participants in Vietnam to examine the safety and immunogenicity of an inactivated whole virion, alum adjuvanted, A(H5N1) influenza vaccine (IVACFLU-A/H5N1)", *Vaccine*, online 4 December 2019. <https://doi.org/10.1016/j.vaccine.2019.11.059>
<https://www.sciencedirect.com/science/article/pii/S0264410X19316019>

⁹⁰ the South China Seafood City food market, which was reported to be also selling birds, pheasants, marmots, snakes and organs of rabbits and other wildlife

⁹¹ Which was reportedly closed on 1 January for environmental sanitation and disinfection.

⁹² Including 349 people in mainland China and another 299 in Hong Kong in 2003.

⁹³ During the SARS outbreak, WHO requested a global network of 11 laboratories to find its cause. It was a month before a new coronavirus was confirmed as the culprit. The SARS coronavirus is thought to have originated in bats, but civet cats — eaten as a delicacy in southern China — were its route to humans. Scientists hope new technology will make the search quicker this time.

- On 5 January WHO said it was against imposing any travel or trade restrictions on China.
- Hong Kong's Hospital Authority announced on 5 January that 15 patients in Hong Kong were being treated for symptoms including fever and respiratory infection after recent visits to Wuhan; doctors and hospitals had been instructed to report cases of fever in anyone who had been to Wuhan in the previous 14 days, whether or not they had visited any of the city's live markets or seafood markets. Hong Kong's health chief, Sophia Chan, warned Hong Kong residents against visiting wet markets and eating wild game in mainland China.
- Some Asian airports⁹⁴ were screening travellers arriving from Wuhan. China's busiest travel season occurs round the Lunar New Year holiday, 25 January.
- On 11 January, the Center for Infectious Disease Research and Policy (CIDRAP) at the University of Minnesota reported that China had released the genetic sequence of the new coronavirus (2019-nCoV)⁹⁵ responsible for the outbreak. The first death from the disease had been reported. Michael T. Osterholm, Director of CIDRAP, said "the main focus now turns toward identifying the animal species that transmitted nCoV to humans and determining whether exposure to those animals poses a threat of outbreaks in other areas"⁹⁶. Andrew Rambaut, professor of molecular evolution at the University of Edinburgh⁹⁷, said that 2019-nCoV is 89 per cent similar to SARS-related bat coronavirus in the *Sarbecovirus* group of betacoronaviruses. "But that doesn't mean it comes from bats. MERS-CoV is 88 per cent identical to the nearest known bat virus, and MERS is endemic in camels."
- On 22 January, the AABB's Transfusion Transmitted Diseases Committee wrote: "No data on the presence of viral nucleic acid or infectious virus in blood have been reported to date for this coronavirus strain. AABB's Transfusion Transmitted Diseases Committee is monitoring developments continuously and members have been in contact with both FDA and CDC to assess any need for interventions to protect the safety of the blood supply as our information expands, given the potential similarities of this virus to SARS (Grant PR and Chan PKS. Detection of SARS Coronavirus in Plasma by Real-Time RT-PCR. N Engl J Med. 2003. 349:2468-69) and MERS-CoV (the Mideast Respiratory Syndrome Coronavirus). A rapid risk assessment from the European Centers for Disease Control recommends a brief travel deferral for blood donors returning from Wuhan, China as has been done previously in the settings of SARS and MERS-CoV."⁹⁸
- By 23 January the Chinese government had five cities in lockdown, including Wuhan. Some events in Beijing had been cancelled. At that stage 634 confirmed cases in China were acknowledged with 95 patients "critical". Eighteen had died, with one death in a city other than Wuhan. Cases had been confirmed elsewhere, including in the US, Taiwan, South Korea, Thailand, Japan, Hong Kong, Vietnam and Singapore.

⁹⁴ In Thailand, Singapore and the Philippines

⁹⁵ Chinese scientists submitted the gene sequencing data for posting on Virological.org, a site designed to assist with research and public health. The post was reportedly communicated by Edward Holmes, of the University of Sydney, acting for a group led by Yong-Zhen Zhang, of Fudan University in Shanghai.

⁹⁶ <http://www.cidrap.umn.edu/news-perspective/2020/01/china-releases-genetic-data-new-coronavirus-now-deadly>

⁹⁷ and administrator of Virological.org

⁹⁸ The Joint United Kingdom (UK) Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee defines this as Must not donate if

a) Less than 21 days from a donor's return from a Coronavirus risk area (SARS, MERS, nCoV); or
 b) Less than 21 days from the last contact with a person with Coronavirus infection (SARS, MERS, nCoV); or
 c) Less than three months since recovery from Coronavirus infection (SARS, MERS, nCoV).

An emergency committee convened by the World Health Organization [decided not to declare a global health emergency](#) — but planned to meet again within 10 days.

- Also on 23 January, Cerus emphasised that coronavirus inactivation (MERS) in human platelet concentrates by its Intercept Blood System had been reported in *Transfusion Medicine*⁹⁹.
- By 25 January, three cases of 2019-nCoV had been confirmed in NSW and one in Victoria. Other cases were under investigation. The Coalition for Epidemic Preparedness Innovation, or CEPI, had engaged a number of research groups to work on a vaccine, including one at the University of Queensland.
- Australia awoke on 28 January to read estimates of confirmed cases in China had reached around 3000 with the death toll at 81. At least 44 cases had been confirmed outside China. The US was in the process of testing 73 people. France expected to repatriate up to a few hundred of its citizens living in the Wuhan area, with evacuees then to spend 14 days in quarantine. Japan was also planning to evacuate its nationals from Hubei province, as was the US. In Shanghai, the government had decreed businesses would not return to work till 10 February. Hong Kong, which had eight confirmed cases, had said schools would be closed till 17 February. Mongolia had closed its border with China, closed schools till 2 March, and banned public events. Chinese officials had warned [the virus was able to spread during its incubation period](#), believed to be between one and 14 days. Australia confirmed its fifth case, as did the US. By our evening news bulletins we were hearing there had been 4,515 confirmed cases in China, with 106 deaths. *Transfusion News* on 28 January said the medical community had a number of unanswered questions, including transfusion-transmissibility.
- By 29 January the official case count was 6,000 with 132 deaths, but a shortage of test kits meant the real number might be much higher. China had agreed to permit involvement of some international health experts (co-ordinated by WHO) to assist with research and containment. Thailand had reported 14 cases; Hong Kong eight; Japan, seven; the US, Taiwan, Australia and Macau five each; Singapore, South Korea and Malaysia four each; France three; Canada and Vietnam two each; and Nepal, Cambodia and Germany each have one. There had at that stage been no deaths outside China. The US had expanded its airport screening to twenty locations. Person to person transmission was being reported¹⁰⁰. Hong Kong had said it would suspend high-speed and other train services to and from the mainland, decreed a 50 percent reduction in the number of flights — and banned some tourism visas. Employees from Hong Kong's Hospital Authority were planning to strike, demanding wearing a mask in public be made mandatory and banning any overseas visitors who entered via the mainland. Tibet had temporarily closed all tourist sites. Shanghai and Beijing had suspended long distance bus services. Britain said it was working on plans to evacuate its nationals from Wuhan. The head of WHO, having met with President Xi Jinping in Beijing, said he was confident in China's ability to contain the new coronavirus.
- Also on 29 January the Australian government announced that QANTAS would evacuate Australians to Christmas Island, for a fourteen-day quarantine period. 600 Australians had registered, with priority to be given to infants and the elderly. The

⁹⁹ Hashem AM, Hassan AM, Tolah AM, Alsaadi MA, Abunada Q, Damanhoury GA, El-Kafrawy SA, Picard-Maureau M, Azhar EI, Hindawi SI. Amotosalen and ultraviolet A light efficiently inactivate MERS-coronavirus in human platelet concentrates. *Transfus Med* 2019 (<https://onlinelibrary.wiley.com/doi/abs/10.1111/tme.12638>)

¹⁰⁰ For instance a Japanese bus driver who had driven two tour groups from Wuhan earlier in the month, a man from Bavaria who had been in contact with a Chinese visitor, a person in Vietnam who had a relative who had visited China, and a man in Taiwan whose wife returned from working in China.

New Zealand government was participating in planning and discussions as there were about 50 New Zealanders in Wuhan seeking evacuation.

- Scientists at Melbourne's Peter Doherty Institute for Infection and Immunity have re-created the coronavirus 2019-nCoV. This should enable development of a test to identify people who might be infected before they display any symptoms, and hopefully fast track vaccine development¹⁰¹. The virus was grown from a sample from an infected patient. The virus will be shared globally with other labs via WHO.
- By the morning of 31 January Australia had confirmed its ninth novel coronavirus case. China said its death toll had reached 213, confirmed cases had risen to 9,262. The World Health Organization had declared a global emergency.

MERS-CoV

- Timothy Sheahan¹⁰² and colleagues showed that the antiviral drug remdesivir lessened lung disease from MERS in mice¹⁰³. He says developing drugs to treat coronaviruses is an important priority for public health and hopes to study the effects of remdesivir on the new Wuhan strain. The drug has been trialled in people with Ebola, and lessened the severity of their illness, though not as much as two other therapies.

Other diseases

- A research group at Abbott has discovered a new strain of human immunodeficiency virus (HIV)—the first to be identified in 19 years¹⁰⁴.
- [Themis Bioscience](#) and CEPI – the Coalition for Epidemic Preparedness Innovations – announced the initiation in healthy volunteers of a Phase I clinical trial with Themis' vaccine candidate against Lassa fever.
- Scientists at The Institute for Molecular Medicine (IMM) and the University of California at Irvine have developed a preventive vaccine, AV-1980R/A, that targets the pathological Tau protein associated with Alzheimer's disease¹⁰⁵. The commercial partner in the collaboration is Capo Therapeutics.
- Researchers from the US National Institute of Allergy and Infectious Diseases (NIAID) and their colleagues have demonstrated¹⁰⁶ that changing the dose of the BCG vaccine, and its route of administration from intradermal to intravenous, significantly enhances the vaccine's ability to protect rhesus macaques from TB infection following exposure to *Mycobacterium tuberculosis* (*Mtb*).

¹⁰¹ It will enable researchers to test any vaccine against a lab-grown version of the virus

¹⁰² an assistant professor of epidemiology at UNC's Gillings School of Global Public Health

¹⁰³ Timothy P Sheahan et al., "Comparative therapeutic efficacy of remdesivir and combination lopinavir, ritonavir, and interferon beta against MERS-CoV", [Nature Communications](#) volume 11, Article number: 222 (2020) <https://www.nature.com/articles/s41467-019-13940-6>

¹⁰⁴ Julie Yamaguchi, Mary Rodgers et al., "Complete genome sequence of CG-0018a-01 establishes HIV-1 subtype L", [JAIDS Journal of Acquired Immune Deficiency Syndromes: November 06, 2019 - Volume Publish Ahead of Print - Issue - p](#) doi: 10.1097/QAI.0000000000002246

¹⁰⁵ Armine Hovakimyan et al., "A MultiTEP platform-based epitope vaccine targeting the phosphatase activating domain (PAD) of tau: therapeutic efficacy in PS19 mice", [Scientific Reports](#) 9, Article Number 15455 (2019) <https://doi.org/10.1038/s41598-019-51809-2>. <https://www.nature.com/articles/s41598-019-51809-2>

¹⁰⁶ PA Darrach et al., "Prevention of tuberculosis in macaques after intravenous BCG immunization". [Nature](#) 1 January 2020. <https://www.nature.com/articles/s41586-019-1817-8>

- Researchers discussed¹⁰⁷ eight fatalities in Germany from Borna disease virus 1 (BoDV-1) and recommended more extensive testing for the disease¹⁰⁸ where the virus occurs in the wild¹⁰⁹.

¹⁰⁷ Hans Helmut Niller et al., [Jan 7 Lancet Infect Dis study](#) and Tomoyuki Honda, [Jan 7 Lancet Infect Dis commentary](#)

¹⁰⁸ in patients with unknown and rapidly evolving central or peripheral nervous system disorders

¹⁰⁹ The natural reservoir for the virus is the white-toothed shrew, found in southern Germany, Austria, Switzerland, and Liechtenstein.