

Monitoring International Trends

posted March 2019

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.

Some recent matters of interest appear on pages 5 to 20. Highlights are listed below:

Safety and Patient Blood Management (begins page 5)

Appropriate Transfusion

- Researchers have devised a system to measure platelet function within two minutes to inform decisions on whether trauma patients need blood transfusions.
- A recent study found that patients receiving transfusions may be exposed to high levels of aluminium.
- A study in the UK has concluded that: *Extension of the out of temperature rule for red cells to 60 min will potentially not compromise patient safety.*
- Platelet BioGenesis said that it is able to create 100 million platelets with one run of its bioreactor.

Preventing and treating anaemia

- A study suggests that female adolescent blood donors are more likely to have low iron stores and iron deficiency anaemia than adult female blood donors and non-donors, and that this could have a significant negative impact on their developing brains.
- A [new drug application](#) for the oral ferric iron therapy Feraccru is being reviewed by the FDA.
- Two Japanese studies of Akebia's anaemia drug, vadadustat, met their primary endpoints.

Other

- A report says that most healthy people should not be taking low-dose aspirin to prevent heart disease.
- Daxor Corporation has showcased its BVA-100[®] Blood Volume Analyzer.
- Eliquis is the subject of new data showing it's a safer option than warfarin for atrial fibrillation patients who have suffered a heart attack or other serious cardiovascular event, or who have undergone a stent-placing procedure.
- A Danish study in blood donors found that oral iron supplementation was not associated with subsequent short-term risk of infection.

Products and Treatments (begins page 8)

Treating haemophilia

- UniQure said that its gene therapy for haemophilia B had, after 12 weeks, increased the levels of a clotting protein.

Treating beta thalassemia and sickle cell disease

- Doctors have doubled the low amount of total body radiation delivered to patients undergoing bone marrow transplants where donor cells have been only “half-matched”.
- A blood-separation device which has the ability to remove abnormal red blood cells from [sickle cell](#) patients, can efficiently and safely replace these cells with healthy donated red blood cells.
- CRISPR Therapeutics and Vertex Pharmaceuticals announced that one trial patient suffering from beta thalassemia had become the world’s first person treated with CTX001.
- Allogeneic hematopoietic stem cell gene therapy may be an alternative to transplantation for patients with transfusion-dependent thalassemia.

Other products and treatments

- Researchers have suggested a way to detect preeclampsia before it becomes life-threatening.
- Hemoglobin Oxygen Therapeutics announced results from a pilot study of its haemoglobin-based oxygen-carrying solution in which initially rejected donor livers were salvaged for transplantation.
- [Tasso](#) is developing an at-home blood sample collection device.
- Adding ciclosporin to intravenous immunoglobulin treatment may reduce the risk for coronary artery abnormalities in patients with Kawasaki disease.

Regulatory matters (begins page 11)

- Roche’s Hemlibra (emicizumab) is now available in the EU for haemophilia A without inhibitors.
- Takeda announced that the FDA had approved its submission for its plasma manufacturing facility in Stanton Springs, Georgia for the production of Flexbumin.
- Fresenius has FDA breakthrough device designation for its computer-assisted ultrafiltration control software to improve fluid management during haemodialysis.
- The FDA finalized guidance on the nonclinical studies drug makers should conduct when developing products to treat severely debilitating or life-threatening hematologic disorders.
- The FDA released final versions of two guidance documents intended to facilitate the development of regenerative medicines.
- The FDA [approved](#) Novo Nordisk’s long-acting factor VIII replacement therapy ESPEROCT (turoctocog alfa pegol) for adults and children with haemophilia A for routine prophylaxis to reduce the frequency of bleeding episodes, for on-demand treatment and control of bleeding episodes, and for perioperative management of bleeding.

- The FDA has approved Saramas' Early Bird Bleed Monitoring System for endovascular procedures
- Sonavex received clearance from the FDA for a system that delivers data on blood flow following surgery.
- The FDA granted a *de novo* clearance to HemoSonics' point-of-care device for assessing coagulation status.

Company news (begins page 13)

- Spark Therapeutics agreed on a definitive merger with Roche for \$US 114.50 per share.
- CSL announced its interim results for the half year ended 31st December 2018. Sales revenue was up 11 per cent on the previous corresponding period.
- The Octapharma Group reported 2018 sales increased 4.5 per cent compared with 2017.
- Grifols will acquire a 26.2 per cent stake in Shanghai RAAS, a company operating in plasma derivatives.
- With the opening of new biologics facilities in Switzerland Biogen no longer needs its site in Denmark.
- Sunrise Labs and Velico Medical are collaborating to develop the Frontline on-demand plasma system for spray drying human plasma.

Country news (begins page 15)

- In New Zealand, the Health Minister announced the Government was progressing legislation to increase organ donation rates.
- The maternal mortality rate following a caesarean section in Africa may be 50 times higher than that of high-income countries. Severe intraoperative and postoperative bleeding is the most common complication for women in Africa.

Research not included elsewhere (begins page 16)

- Scientists and ethicists from seven nations called for a moratorium on gene-editing experiments designed to alter heritable traits in human babies.
- A study found that brain oxygen supply is different in different regions of the brain of sickle cell disease patients who have anaemia, which may explain the incidence of silent strokes.

Infectious diseases (begins page 16)

Mosquito-borne diseases

- In the Philippines, the country's Food and Drug Administration has cancelled the certificates of product registration of Sanofi's anti dengue vaccine.
- Researchers concluded that political, economic and social unrest in Venezuela, and its consequent ongoing humanitarian crisis, may be facilitating the resurgence of vector-borne diseases, such as malaria, dengue, Zika and Chagas.
- Bharat Biotech International said in March that two of its vaccines against Zika and Chikungunya would be entering Phase II clinical trials.

Influenza

- At the beginning of the northern hemisphere flu season the predominant strain in the US was A H1N1 but by the beginning of March the more severe strain A H3N2 was accounting for almost half of the new cases.

Q fever

- A new study on the national incidence of Q fever found that as many as one in 20 people in some parts of Australia have been exposed to Q fever at some time in their lives. Researchers recommended that rural residents consider vaccination. The study was based on samples of blood from donors at selected blood banks in New South Wales and in Queensland. [Australia has the world's only effective vaccine against Q fever](#), but the study found only 40 per cent of people in groups recommended for vaccination knew about it and only 10 per cent of people in those high-risk groups were vaccinated.

Ebola virus disease

- As at 4 March there had been 900 probable and confirmed cases of Ebola and 565 deaths from the outbreak in the Democratic Republic of Congo.
- The CDC reminded US healthcare facilities to review their processes for managing communicable infections, including Ebola. The Center emphasised that where a patient is infected with or under investigation for Ebola, healthcare facilities should follow the CDC's separate personal protective equipment guidance.

MERS-CoV

- By 5 March there had been 91 new cases of MERS-CoV in Saudi Arabia this year.

Other diseases

- A patient in the UK (“the London patient”) has been reported to be experiencing remission from HIV-1 after stem cell transplantation. While scientists say it is too soon to claim this as a “cure”, the treatment is seen as a promising development from the more aggressive treatment given to the first recorded case of remission after stem cell transplantation, the so called “Berlin patient” over a decade ago. A third patient (“the Dusseldorf patient”) is also reported as being in remission.
- A major study in Denmark demonstrated no link between the measles, mumps, and rubella (MMR) vaccine and autism.
- Chagas disease is no longer an endemic disease in Latin America but a global public health threat. Bayer presented the results of the CHICO (Chagas disease In Children treated with NifurtimOx) Phase III clinical trial of nifurtimox in paediatric patients.
- In 2000, the CDC declared that measles had been [eliminated](#) in the US. By mid-March in 2019, 228 individual cases have been reported, compared with 372 during 2018.
- Health officials warned Townsville residents of the dangers of contracting melioidosis as they cleaned up after the floods. The bacterium is soil-borne.
- Tasmania in March reported its first known cases of the mosquito-borne Barmah Forest virus.
- [Space travel](#) caused [herpes](#) viruses to reactivate in more than half of crew aboard Space Shuttle and [International Space Station](#) (ISS), according to a [NASA](#) study.

Table of Contents

1.	SAFETY AND PATIENT BLOOD MANAGEMENT	5
	Appropriate Transfusion _____	5
	Other _____	7
2.	PRODUCTS AND TREATMENTS	8
	Treating haemophilia _____	8
	Treating beta thalassemia and sickle cell disease _____	9
	Other products _____	10
3.	REGULATORY	11
4.	MARKET STRUCTURE AND COMPANY NEWS	13
5.	SPECIFIC COUNTRY EVENTS	15
6.	RESEARCH NOT INCLUDED ELSEWHERE	16
7.	INFECTIOUS DISEASES	16
	Mosquito-borne diseases _____	16
	Influenza _____	16
	Ebola virus disease _____	18
	MERS-CoV _____	19
	Other diseases _____	19

1. Safety and patient blood management

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

Appropriate Transfusion

- Researchers at the University of Washington have devised a system that can measure platelet function within two minutes and inform doctors' decisions on whether trauma patients need blood transfusions¹.
- A recent study² found that patients receiving transfusions may be exposed to high levels of aluminium. The issue is associated with some fluid warming devices which automatically warm blood, blood products and IV solution to 40°C to help prevent hypothermia during transfusions. The aluminium concentration in balanced electrolyte solutions warmed by at least one system was found to exceed dramatically the FDA recommendation³.

¹ See Nathan J Sniadecki et al, in *Nature Communications*, 13 March. [Contractile forces in platelet aggregates under microfluidic shear gradients reflect platelet inhibition and bleeding risk...](#)

² T. Perl et al., "Aluminium release by coated and uncoated fluid-warming devices", *Anaesthesia*. First published: 21 February 2019. <https://doi.org/10.1111/anae.14601> See also an editorial by Charlesworth and van Zundert, *Anaesthesia* 2019; doi: 10.1111/anae.14603

³ <https://www.hippocraticpost.com/medico-legal/aluminium-hazard-in-transfusions/>

- A study in the UK has concluded that: *Extension of the out of temperature rule for red cells to 60 min will potentially not compromise patient safety, although exposures to ambient temperatures should be minimized. Units returned to storage must not be reissued for at least 6 hours and not be exposed to ambient temperatures on more than three occasions*⁴.
- Platelet BioGenesis, in a poster at a Gordon Research Conference in Galveston, Texas, said in March that it is able to create 100 million platelets with one run of its bioreactor⁵. The US Department of Defense has been amongst those funding the company's research. Platelet BioGenesis uses a variety of growth factors to coax stem cells derived from cord blood into megakaryocytes, the cells that create platelets. That is established technology. The more recent achievement has been to create a bioreactor to turn those megakaryocytes into platelets in a sufficiently large scale process. Sven Karlsson, the company's president, says because platelets have such a limited life, being able to produce them close to where they are needed- such as a war zone- has advantages. He said: "You could take the last step of our production process and put it on a hospital ship or a naval vessel, along with a frozen supply of precursor cells".

Preventing and treating anaemia

- A study⁶ led by Johns Hopkins researchers (Eshan Patel⁷ and Aaron Tobian⁸) suggests that female adolescent blood donors are more likely to have low iron stores and iron deficiency anaemia than adult female blood donors and non-donors. The authors suggest this could have a significant negative impact on their developing brains, and they suggest counter-measures.
 - i) Each whole blood donation removes about 200-250 milligrams of iron from the blood donor. Adolescents usually have lower blood volumes, so when donating the same amount of blood, they have a relatively higher proportional loss of haemoglobin during donation than adults. Females are at greater risk of iron deficiency than males due to menstrual blood loss.
 - ii) It is well known that younger age, female sex and increased frequency of blood donation are all associated with lower serum ferritin levels (a surrogate for total body iron levels) in blood donor populations. What Patel and Tobian sought to do was compare the prevalence of iron deficiency and associated anaemia between blood donor and non -donor populations, specifically adolescents.
 - iii) Researchers analysed data from the US National Health and Nutrition Examination Survey, a long-running study assessing both adults and children based on both physical examinations and interviews conducted by the Centers for Disease Control and Prevention (CDC). From 1999 to 2010, this study included collections of blood samples as well as questions about blood donation

⁴ Kate Aplin et al., "Extending the 30-minute rule for red cell units – investigation of the bacterial risk of 60-minute exposures to ambient temperature", *Vox Sangunis*, March 2019.

<https://onlinelibrary.wiley.com/doi/10.1111/vox.12747>

⁵ The company is still doing preclinical work to show the FDA that they can produce platelets that act and behave as they should and that their process meets required standards.

⁶ Eshan U. Patel, et al, "Association of blood donation with iron deficiency among adolescent and adult females in the United States: a nationally representative study". *Transfusion*, 2019; published 18 February 2019. DOI: [10.1111/trf.15179](https://doi.org/10.1111/trf.15179)

⁷ a biostatistician in the Department of Pathology at the Johns Hopkins University School of Medicine

⁸ professor of pathology, medicine, oncology and epidemiology at the Johns Hopkins University School of Medicine and director of transfusion medicine at The Johns Hopkins Hospital.

history in the previous year. Findings highlighted the vulnerability of adolescent blood donors to associated iron deficiency⁹.

- iv) Patel and Tobian noted that some federal policies and regulations were already in place to protect donors in general from iron deficiency, such as haemoglobin screening, a minimum weight to donate and an eight-week interval between donations for repeat whole blood donation. They recommended further protections for adolescent donors—such as oral iron supplementation, increasing the minimum time interval between donations or donating platelets or plasma rather than whole blood.
- Feraccru (Shield Therapeutics) is approved in the European Union for the treatment of iron deficiency in adults. In Switzerland, it is approved for the treatment of iron deficiency anaemia in adults with inflammatory bowel disease. Now a Phase III B trial has compared Feraccru against Ferinject in 242 inflammatory bowel disease patients whose iron deficiency anaemia and haemoglobin measurements are as low as 8.0g/dL. Shield chief medical officer Mark Sampson said: “In a challenging Phase III B clinical study, in which Feraccru has been tested against Ferinject, the standard of care for patients who cannot tolerate or are unwilling to take salt-based oral iron therapies, orally delivered Feraccru has demonstrated it is non-inferior to IV iron therapy in treating iron deficiency anaemia”. A [new drug application](#) for the oral ferric iron therapy is being reviewed in the US by the FDA.
- Akebia Therapeutics announced in March that two pivotal Japanese studies of its anaemia drug, vadadustat, each with active controls, met their primary endpoints by helping people with chronic kidney disease reach mean haemoglobin levels noninferior to Aranesp (darbepoetin alfa). Akebia's commercial partner, Mitsubishi Tanabe Pharma Corporation, will seek Japanese regulatory approval this year.

Other

- A report from the American College of Cardiology and the American Heart Association says that most healthy people should not be taking low-dose aspirin to prevent heart disease. This advice is contrary to previous recommendations. A major trial found that: “Aspirin use in healthy elderly persons did not prolong disability-free survival over a period of 5 years but led to a higher rate of major haemorrhage than placebo”.¹⁰ This ASPREE trial¹¹ concluded: “The use of low-dose aspirin as a primary prevention strategy in older adults resulted in a significantly higher risk of major haemorrhage and did not result in a significantly lower risk of cardiovascular disease than placebo”.¹² The trial found somewhat surprisingly that: “Higher all-cause mortality was observed among apparently healthy older adults who received daily aspirin than among those who received placebo and was attributed

⁹ There were 9,647 female participants 16-49 years old who had provided both samples and blood donor history information. There were 2,419 females aged 16-19 amongst them. The researchers found that about 10.7 percent of the adolescents had donated blood within the previous 12 months, compared with about 6.4 percent of the adults. Mean serum ferritin levels were significantly lower among blood donors than among non-donors in both the adolescent (21.2 vs. 31.4 nanograms per millilitre) and the adult (26.2 vs. 43.7 nanograms per millilitre) populations. The prevalence of iron deficiency anaemia was 9.5 per cent among adolescent donors and 7.9 per cent among adult donors - significantly higher than that of non-donors in both age groups, which was 6.1 percent. As well, 22.6 per cent of adolescent donors and 18.3 per cent of adult donors had absent iron stores.

¹⁰ John J McNeil et al., “Effect of Aspirin on Disability-free Survival in the Healthy Elderly”, [October 18, 2018](#) N Engl J Med 2018; 379:1499-1508 DOI: 0.1056/NEJMoa1800722

¹¹ Involving 19, 114 participants In the US and Australia, and funded by the US National Institute on Aging and others; ASPREE ClinicalTrials.gov number, [NCT01038583](#).)

¹² John J McNeil et al., “Effect of Aspirin on Cardiovascular Events and Bleeding in the Healthy Elderly”, [October 18, 2018](#) N Engl J Med 2018; 379:1509-1518 DOI: 10.1056/NEJMoa1805819

primarily to cancer-related death. In the context of previous studies, this result was unexpected and should be interpreted with caution”.¹³

- Daxor Corporation exhibited at the Annual Meeting of the American College of Cardiology Expo 2019¹⁴. Kathryn Kornafel, Vice- President of Marketing, said the meeting was “an excellent opportunity to generate awareness and educate more hospitals and cardiologists about the significant benefits of direct and objective measurement of intravascular blood volume, red blood cell volume and plasma volume via a simple blood test with the BVA-100[®] Blood Volume Analyzer”. The company said it shared “how use of this unique technology to guide heart failure treatment has been proven to reduce heart failure 30-day mortality by 82 per cent, 30-day readmissions by 56 per cent, and 1-year mortality by 86 per cent in a peer-reviewed study¹⁵”.
- Pfizer and Bristol-Myers Squibb’s next-generation anticoagulant Eliquis is the subject of new data showing it’s a safer option than warfarin for atrial fibrillation patients who have suffered a heart attack or other serious cardiovascular event, or who have undergone a stent-placing procedure. In the Phase IV study, Eliquis showed it carries a [lower risk](#) of bleeding and hospitalisation than warfarin. Data from the AUGUSTUS trial was presented at the American College of Cardiology annual meeting¹⁶. The data demonstrated that adding Eliquis to P2Y12 antiplatelet therapy—such as Sanofi’s Plavix or its generics—with or without aspirin, reduced the number of serious bleeding episodes compared with warfarin combination treatment. In the AUGUSTUS trial’s Eliquis arm, 10.5 per cent of patients had suffered major or clinically relevant bleeding episodes at the six-month mark, compared with 14.7 per cent of patients in the warfarin arm.
- A Danish study in a large cohort of blood donors found that use of oral iron supplementation was not associated with subsequent short-term risk of infection¹⁷.

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

- A population-based study¹⁸ suggests that haemophilia patients who take intermediate-dose preventive medication may experience more of an age-related decline in sports participation, joint status, and physical functioning than those on a high dose.

¹³ John J McNeil et al., “Effect of Aspirin on All-Cause Mortality in the Healthy Elderly”, [October 18, 2018](#) N Engl J Med 2018; 379:1519-1528 DOI: 0.1056/NEJMoa1803955. Dr McNeil is at the Department of Epidemiology and Preventive Medicine, Monash University, Melbourne.

¹⁴ New Orleans, from 16-18 March

¹⁵ published in a Journal of the American College of Cardiology – *JACC: Heart Failure*. John E. Strobeck, Jonathan Feldschuh and Wayne L. Miller, “Heart Failure Outcomes With Volume-Guided Management”, [Volume 6, Issue 11, November 2018](#) DOI: 10.1016/j.jchf.2018.06.017.

¹⁶ New Orleans, from 16-18 March

¹⁷ [https://pure.au.dk/portal/da/publications/oral-iron-supplementation-is-not-associated-with-shortterm-risk-of-infections-results-from-the-danish-blood-donor-study\(5f6434e4-9054-45fa-9ff6-f3a1defeb1e6\).html](https://pure.au.dk/portal/da/publications/oral-iron-supplementation-is-not-associated-with-shortterm-risk-of-infections-results-from-the-danish-blood-donor-study(5f6434e4-9054-45fa-9ff6-f3a1defeb1e6).html)

¹⁸ Olav Versloot et al., “[Sports participation and physical activity in adult Dutch and Swedish patients with severe haemophilia: A comparison between intermediate- and high-dose prophylaxis](#),” *Haemophilia* first published: 28 January 2019 <https://doi.org/10.1111/hae.13683>

- A study¹⁹ in haemophilia A patients reported that [FuseNGo, Pfizer's](#) pre-filled syringe device used for both the treatment and prevention of bleeding, is easy to use and has a range of benefits²⁰.
- Gene therapy company UniQure NV said in February that its treatment for haemophilia B increased the levels of a protein that helps in blood clotting after 12 weeks in a relatively small study. UniQure's treatment aims to reduce bleeding by raising the FIX levels, and no patient suffered bleeding or needed replacement therapy during the trial period. The updated data from a mid-stage study showed that all three patients treated with a single dose of the therapy, AMT-061, showed increased and sustained levels of factor IX (FIX), the company said. FIX activity at 12 weeks increased to 38 percent of normal, which exceeded the threshold levels generally considered enough to eliminate or cut down the risk of bleeding cases, UniQure said. Spark Therapeutics and Pfizer Inc are also developing a gene therapy for treating haemophilia B.

Treating beta thalassemia and sickle cell disease

- Staff at Johns Hopkins University have followed a new protocol for bone marrow transplants. They doubled the low amount of total body radiation delivered to patients undergoing bone marrow transplants where donor cells have been only "half-matched". This has increased dramatically the rate of engraftment from its previous level of around 50 per cent²¹. Robert Brodsky²² commented: "We're approaching a 90 per cent cure rate for sickle cell and beta thalassemia. Bone marrow transplants are not just for patients with a perfectly matched donor. A half-match is definitely good enough."
- A study reports²³ that the blood-separation device [Spectra Optia](#), which has the ability to remove abnormal red blood cells from [sickle cell](#) patients, can efficiently and safely replace these cells with healthy donated red blood cells. The device uses fewer red blood cell units than regular transfusion where the abnormal red blood cells are not removed.
- In March CRISPR Therapeutics and Vertex Pharmaceuticals announced that one trial patient suffering from beta thalassemia has become the world's first person treated with CTX001. The patient is part of a Phase I/II clinical study of patients with rare and inheritable blood diseases.
- Allogeneic hematopoietic stem cell (HSC) gene therapy may be an alternative to transplantation for patients with transfusion-dependent thalassemia. Intra-bone allogeneic HSC gene therapy after a reduced-toxicity myeloablative conditioning

¹⁹ Giovanni Di Minno et al., , "[Patient satisfaction and acceptability of an on-demand and on-prophylaxis device for factor VIII delivery in patients with hemophilia A.](#)" in [Patient Preference and Adherence](#), Published 31 January 2019 Volume 2019:13 Pages 233—240
DOI <https://doi.org/10.2147/PPA.S175254>

²⁰ Of the eight authors, two said they were employees of Pfizer.

²¹ Kenneth R Cooke et al., "Effect of increased dose of total body irradiation on graft failure associated with HLA-haploidentical transplantation in patients with severe haemoglobinopathies: a prospective clinical trial", *The Lancet Haematology*, 13 March 2019. DOI: [10.1016/S2352-3026\(19\)30031-6](https://doi.org/10.1016/S2352-3026(19)30031-6)

²² professor of medicine and oncology research at the Johns Hopkins University School of Medicine, director of the Division of Hematology, and a member of the Johns Hopkins Kimmel Cancer Center

²³ O Hequet et al., "[Automatic depletion with Spectra Optia allows a safe 16% reduction of red blood cell pack consumption in exchanged sickle cell anemia patients.](#)" [Transfusion](#) first published 12 February 2019 <https://doi.org/10.1111/trf.15188>

regimen may be safe and efficacious in both adult and paediatric patients with transfusion-dependent thalassemia affected by severe mutations²⁴.

- A study suggests [bariatric surgery](#) may help reduce the rates of [vaso-occlusive crises](#) in morbidly obese patients with [sickle cell disease](#) without increasing the risk of mortality or other adverse events²⁵.

Other products and treatments

- [Pluristem Therapeutics Inc.](#) (which is developing placenta-based cell therapy products) announced that the company has fully enrolled the second cohort of six patients in its ongoing Phase I clinical study testing PLX-R18 for the treatment of incomplete hematopoietic recovery following hematopoietic cell transplantation (HCT). The company says results so far show PLX-R18 to be safe and well tolerated, with early indicators of efficacy in improving blood counts. The third and final cohort will have 15 patients. PLX-R18 cell therapy for the treatment of incomplete hematopoietic recovery following HCT has Orphan Drug Designation by the US Food and Drug Administration (FDA).
- Researchers at Tulane University have suggested a way to detect preeclampsia, a dangerous condition that may arise during pregnancy, before it becomes life-threatening²⁶.
- Hemoglobin Oxygen Therapeutics announced results from a pilot study of its haemoglobin-based oxygen-carrying solution, Hemopure²⁷, in which initially rejected donor livers were salvaged for transplantation, according to a press release. The study was conducted in the Netherlands, where 16 [rejected donor livers](#) underwent machine perfusion technology using Hemopure; 10 donor livers were successfully reconditioned and they were all used in patients [undergoing transplantation](#) with 100 per cent survival rates.
- [Tasso](#), a Seattle-based startup, is developing an at-home blood sample collection device²⁸. It announced in early March that it had [raised \\$US 6.1 million](#) from investors. Research and development work on Tasso OnDemand has been supported by \$US 13.1 million of grant funding. Funds have been received from the National Institutes of Health, the Defense Advanced Research Projects Agency and the Defense Threat Reduction Agency.

²⁴ Markt S, Scaramuzza S, Cicalese MP, et al. [Intrabone hematopoietic stem cell gene therapy for adult and pediatric patients affected by transfusion-dependent \$\beta\$ -thalassemia](#) [published online January 21, 2019]. *Nature Medicine*. doi: 10.1038/s41591-018-0301-6

²⁵ The study, "[Impact of Bariatric Surgery on Outcomes of Patients with Sickle Cell Disease: a Nationwide Inpatient Sample Analysis, 2004–2014](#)," was published in [Obesity Surgery](#).

²⁶ Carolyn L Bayer et al., "Spectral Photoacoustic imaging to estimate *in vivo* placental oxygenation during preeclampsia", *Scientific Reports*, published online 24 January 2019.

²⁷ Hemopure is available only in the US through the FDA expanded access program for patients who cannot undergo blood transfusion and have no treatment options remaining. The solution is also under development for other organs prior to transplantation.

²⁸ According to the company, Tasso OnDemand sticks to a patient's upper arm and collects a blood sample in about two minutes. The patient presses a button on the device, which begins drawing blood and depositing it into an attached tube. A set of tiny needles penetrate a couple of millimeters deep into the skin. The device uses proprietary microfluidics technology to suck the blood through the device and into the tube.

- A trial²⁹ has suggested that adding ciclosporin to intravenous immunoglobulin (IVIG) treatment may reduce the risk for coronary artery abnormalities among patients with Kawasaki disease.
- A working group has developed a treatment algorithm for diagnosis and treatment of neonatal thrombocytopenia of suspected or confirmed alloimmune origin³⁰.

3. Regulatory

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

- Grifols has received approval from the FDA for Erytra Eflexis, which is a fully automated, medium-sized analyser for performing pre-transfusion compatibility tests.
- Roche's Hemlibra (emicizumab) is now available for haemophilia A without inhibitors in the EU, following the US and Japan. Earlier approval in Europe was for routine prophylaxis of bleeding episodes in adults and children with severe haemophilia A (congenital factor VIII deficiency, FVIII <1%) without factor VIII inhibitors. The EU Commission has also now approved that Hemlibra can be used with multiple dosing options (once weekly, every two weeks, or every four weeks) for all indicated people with haemophilia A, including those with factor VIII inhibitors.
- Takeda Pharmaceutical Company Limited announced in March that the FDA had approved its submission for its plasma manufacturing facility in Stanton Springs (near Covington, Georgia) for the production of Flexbumin³¹. The facility, previously owned by Shire³², received its first FDA approval to manufacture Gammagard Liquid³³ in June 2018.
- [Precision BioLogic Inc.](#) on 13 March announced FDA 510(k) clearance and the launch of its [CRYOcheck Factor VIII Inhibitor Kit](#) in the US. Approvals had already been given in Canada, the European Union, Australia, and New Zealand, where the kit launched in February.
- Fresenius on 14 March said it had won FDA breakthrough device designation for its computer-assisted ultrafiltration control software intended to improve fluid management during haemodialysis.
- The FDA finalized guidance on the nonclinical studies drug makers should conduct when developing products to treat severely debilitating or life-threatening hematologic disorders³⁴.
- The FDA in late February released final versions of two guidance documents intended to facilitate the development of regenerative medicines³⁵. The FDA confirmed that sponsors can apply for and receive both breakthrough and

²⁹ Horomichi Hamada et al., "Efficacy of primary treatment with immunoglobulin plus ciclosporin for prevention of coronary artery abnormalities in patients with Kawasaki disease predicted to be at increased risk of non-response to intravenous immunoglobulin (KAICA): a randomised, controlled, open-label, blinded-endpoints, phase 3 trial", in *The Lancet*, VOLUME 393, ISSUE 10176

³⁰ Bertrand G, Blouin L, Boehlen F, et al. [Management of neonatal thrombocytopenia in a context of maternal antiplatelet alloimmunization: expert opinion of the French-speaking working group](#) [published online March 1, 2019]. *Arch Pediatr*. doi: 10.1016/j.arcped.2019.02.006

³¹ FLEXBUMIN 25% [Albumin (Human)], USP, 25% Solution, indicated for hypovolemia, hypoalbuminemia, (burns, Adult Respiratory Distress Syndrome (ARDS), and nephrosis), cardiopulmonary bypass surgery, and haemolytic disease of the newborn (HDN)

³² Takeda completed its acquisition of Shire in early January.

³³ GAMMAGARD LIQUID® [Immune Globulin Infusion (Human)] 10% Solution

³⁴ [Guidance, Federal Register Notice](#)

³⁵ Draft versions of the [Evaluation of Devices Used with Regenerative Medicine Advanced Therapies](#) and [Expedited Programs for Regenerative Medicine Therapies for Serious Conditions](#) were released in November 2017.

regenerative medicine advanced therapy (RMAT) designation for a product³⁶. The FDA reiterated its decision to include gene therapies in the RMAT pathway, stretching the definition that was in the 21st Century Cures Act, which created RMAT. The FDA has gone on to broaden RMAT by defining CAR T therapies as gene therapies. The FDA's final guidance requires qualifying gene therapies to produce a "sustained" effect on cells or tissues³⁷.

- The FDA [approved](#) Novo Nordisk's long-acting factor VIII replacement therapy ESPEROCT (turoctocog alfa pegol) for adults and children with haemophilia A for routine prophylaxis to reduce the frequency of bleeding episodes, for on-demand treatment and control of bleeding episodes, and for perioperative management of bleeding. Novo will wait until 2020 before launching the product in the US due to third-party intellectual property agreements.
- The FDA has approved Saranas' Early Bird Bleed Monitoring System for endovascular procedures. Philippe Génèreux, Saranas' Chief Medical Officer, said in a statement: "Peri-procedural bleeding associated with endovascular procedures has a significant impact on patient safety and adds incremental costs to the healthcare system with longer hospital stays and additional interventional treatment. I firmly believe the Early Bird Bleed Monitoring System will help protect, and in some cases save the lives of, patients undergoing an endovascular procedure by allowing physicians to detect the onset of bleeding early and take appropriate steps to address the bleed before detrimental, irreversible and life-threatening consequences occur"³⁸.
- Johns Hopkins University spinout Sonavex received clearance from the FDA for a system that delivers data on blood flow following surgery³⁹. EchoSure received 510(k) regulatory clearance, which is required to market medical devices in the US. Chief Executive Officer David Narrow called it a "critical milestone" for the Canton-based medical device start-up. In June 2018, Sonavex [received clearance](#) for tiny implants called EchoMark. These ultrasound-detectable devices "mark" a site where surgery was performed, and the system allows for its location and the angle from which it is viewed. The two products can work together to create a solution that does not require expertise in ultrasound to use, according to Sonavex; adding that the data provided by the technology could allow earlier detection of blood clots.
- The FDA granted a *de novo* clearance to HemoSonic's point-of-care device for assessing coagulation status⁴⁰. Quantra QPlus provides timely information on a range of blood properties during cardiac surgeries and other procedures. The new

³⁶ RMAT provides all of the benefits of breakthrough, including early and intensified interactions with senior FDA officials. The threshold for receiving RMAT designation is lower than for breakthrough. RMAT is available to cell therapies and tissue products for which there is preliminary evidence of a potential to address an unmet medical need for a serious or life-threatening condition. Breakthrough designation is contingent on demonstration of the potential to provide a substantial improvement on available therapies.

³⁷ The previous requirement was that gene therapies produce a "durable modification."

³⁸ The system has a vascular access sheath equipped with sensors to monitor potential bleeding during select procedures which use transfemoral access, including transcatheter aortic valve replacement. The sensors detect when the electrical resistance changes across blood vessels, which may indicate blood is pooling outside the vessels. Both audible and visual alerts are issued.

³⁹ EchoSure automates the monitoring of blood flow after vascular surgery, which treats diseases of the arteries and veins. It uses ultrasound imaging and deep learning algorithms to provide both visual and quantitative data, and to detect whether there is a loss of blood flow, indicating compromised blood vessels. An app also allows monitoring from a mobile device.

⁴⁰ The device has a CE mark and is marketed in the European Union.

device will compete with Instrumentation Laboratory's ROTEM and Haemonetics' TEG, which provide similar data employing different mechanisms⁴¹.

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.

- Spark Therapeutics agreed on a definitive merger with Roche for \$US 114.50 per share. Most analysts see the merger as “win-win”. Roche needs Spark for a quick entry to the gene therapy market, while Spark needs Roche’s resources, experience and networks to accelerate its rate of development of gene therapies. Spark has one commercial asset⁴², four programs currently in clinical trials⁴³, and other therapies in development⁴⁴. Spark Therapeutics will maintain its operations in Philadelphia as an independent company within the Roche Group.
- In mid-February CSL Limited announced its interim results for the half year ended 31st December 2018. Sales revenue was up 11 per cent on the previous corresponding period, earnings before interest and tax were up 6 per cent and net profit after tax was up 10 per cent, all on a constant currency basis. CSL reported that the achievement of double-digit profit growth was the result of increased usage of immunoglobulin, sales of specialty products and Seqirus’ portfolio of influenza vaccines. Privigen sales grew 17 per cent and Hizentra sales grew 14 per cent. The company plans on opening 30-35 new plasma collection centres this financial year.
- aTyr Pharma⁴⁵ announced in San Diego that it has entered into a research collaboration and option agreement with CSL Behring⁴⁶, for the development of product candidates derived from up to four tRNA synthetases from aTyr’s preclinical pipeline. Dr Sanjay Shukla, President and Chief Executive Officer of aTyr; said: “We believe the combination of our discovery pipeline and knowledge of tRNA synthetases and CSL Behring’s expertise in drug development will yield innovative

⁴¹ Whereas ROTEM detects changes in clot firmness mechanically. HemoSonics' Quantra applies ultrasound pulses to samples, captures the returning signals and analyses them to characterize changes in the properties of the blood.

⁴² In 2017 Spark Therapeutics was the first company to receive FDA market approval for a gene therapy for a genetic disease. LUXTURNA[®] (voretigene neparvovec-rzyl), is a one-treatment product for the treatment of patients with confirmed biallelic *RPE65* mutation-associated retinal dystrophy. In 2018 the European Commission granted marketing authorisation for LUXTURNA.

⁴³ Spark’s lead clinical asset is SPK-8011, a gene therapy for haemophilia A, which is expected to start Phase III trials this year. Spark has SPK-8016 in a Phase I/II trial aimed at the haemophilia A inhibitor population. SPK-9001 is an investigational gene therapy for haemophilia B in Phase III and SPK-7001 for choroideremia in Phase I/II.

⁴⁴ Spark is also developing SPK-3006 for Pompe disease and SPK-1001 for CLN2 disease (a form of Batten disease) which are expected to be ready for clinical development in 2019, and it has preclinical programmes for Huntington's disease and Stargardt disease.

⁴⁵ For information about aTyr see <http://www.atyrpharma.com>.

⁴⁶ CSL Behring will fund all research and development activities related to the development of the applicable product candidates for the duration of the collaboration. CSL Behring will pay a total of up to \$US 4.25 million per synthetase program (\$US 17 million if all four synthetase programs advance) in option fees based on achievement of research milestones and CSL Behring's interest in continuing. CSL Behring will have an option to negotiate licenses for worldwide rights to each Investigational New Drug candidate arising from the collaboration. Specific license terms will be negotiated during an exclusivity period following the exercise of each program option.

immunological therapies, and we look forward to a long and mutually beneficial partnership.”

- In mid-March, the Octapharma Group reported strong results for 2018. Group sales increased 4.5 per cent compared with 2017 (on a constant currency basis, the growth rate was 6.6 per cent). The company said all products performed well. It highlighted the year-on-year growth of its immunoglobulin product portfolio, as well as its recombinant factor VIII, Nuwiq, and its new fibrinogen concentrate, Fibryga.
- Grifols announced in March that it will acquire a 26.2 per cent stake in Shanghai RAAS, a company operating in the plasma derivatives sector. This will be a strategic alliance to manufacture, market, and develop plasma products and transfusion diagnostic solutions in China. Grifols will acquire its stake in exchange for 45 per cent of the economic rights and 40 per cent of the voting rights in its US subsidiary, Grifols Diagnostic Solutions⁴⁷. Grifols will become the second-largest shareholder in Shanghai RAAS, which will become Grifols' exclusive distributor of plasma-derived products and transfusion diagnostic solutions in China and will use Grifols' NAT to screen plasma donations throughout its 41 plasma collection centres. Grifols will have three members on Shanghai RAAS's board of directors, and it will appoint quality and manufacturing officers to guarantee compliance with a quality assurance agreement. Depending on regulatory approvals, the transaction is expected to close in the second half of 2019.
- [Arix Bioscience PLC](#) has invested US \$15 million in Imara, a company developing treatments for sickle cell disease. This gives it a 10 per cent stake in the company. The treatment, known as IMR-687, has successfully completed a Phase I study in healthy volunteers and is currently in a global Phase II A study using adult sickle cell patients.
- With the opening of new biologics facilities in Switzerland Biogen no longer needs its older operational site in Denmark⁴⁸. Fujifilm, which has been building a biologics contract business⁴⁹, will pay Biogen up to \$US 890 million in cash for the facilities in Hillerød. It will take on the 800 employees. It will also supply Biogen with some products manufactured there, including multiple sclerosis drug Tysabri. The Hillerød biologics production facility has assembly, labelling and packing capabilities, quality control laboratories and warehouses. Fujifilm expects the deal to be completed by August.
- [Sunrise Labs](#)⁵⁰ and [Velico Medical](#)⁵¹ are collaborating to develop the Frontline on-demand plasma system for spray drying human plasma. The companies say this allows blood centres to spray dry plasma for transfusion instead of freezing it, extending its availability. Frontline ODP works by rehydrating with sterile water at the point-of-care in less than five minutes. Through the agreement, Sunrise Labs will design the Frontline ODP spray drain instrument and build and test prototypes. Both

⁴⁷ The price tag of the transaction to Grifols is about \$US 1.9 billion. It requires no external financing to fund the transaction.

⁴⁸ Biogen CEO Michel Vounatsos [said](#) in a statement that with the biologics plant the company has in Research Triangle Park, North Carolina, and the \$1 billion biologics facility it is building in Solothurn, Switzerland, the company decided it could do without the Denmark site. The new facility is expected to come online in 2020. Separately, Biogen has a joint venture with Samsung BioLogics that makes biosimilars.

⁴⁹ Nine months ago, Fujifilm paid about \$US 800 million for two cell culture media units from Japan's JXTG Holdings. In January, it said it would invest about \$US 90 million to expand its biologics plant in Morrisville, North Carolina, and build a new facility in Madison, Wisconsin, to ramp up induced pluripotent stem cell technologies for its pipeline of regenerative drugs and to manufacture iPS cells for others. It also has operations at College Station, Texas.

⁵⁰ Of Bedford, New Hampshire

⁵¹ Of Beverly, Massachusetts

Velico and Sunrise Labs will test the system to make sure it meets clinical and regulatory requirements.

5. Specific country events

- Facebook rolled out its blood donation feature in India in 2017, and the following year expanded to Pakistan, Brazil and Bangladesh. It expects to introduce the program to the US in 2019. The technology allows Facebook users to sign up as blood donors and then notifies them when blood banks in their area are in need.
- On 14 March it was reported that President Trump's budget proposals for 2020 include seeking a budget cut for the National Institutes of Health (for the third year in a row) and seeking an increase in funds for the FDA.
- FDA Commissioner Scott Gottlieb announced his resignation in March. Ned Sharpless, then Director of the National Cancer Institute, was announced as the FDA's acting Chief.
- In the UK, Essex and Herts Air Ambulance is now carrying blood supplies on its helicopters and in its rapid response vehicles. Until 20 March, patients who had suffered blood loss were given saline, which neither carries oxygen nor assists with clotting. Now packed red blood cells of blood group O negative, and plasma, are carried.
- In New Zealand, Health Minister Dr David Clark announced the Government is progressing legislation to increase organ donation rates. The Organ Donors and Related Matters Bill introduced to Parliament in March enables the New Zealand Blood Service to add the role of a national organ donation service to its responsibilities. The Bill also extends, in certain situations, the financial compensation for qualifying donors while they recuperate. The Minister said: "This Bill is the first step in the process towards creating a new national organ donation agency which will establish a clinical governance framework and a consistent approach to supporting best practice across the sector. As such, it will help deliver on the Government's priority to improve the wellbeing of New Zealanders. The Ministry will continue to work closely with the New Zealand Blood Service and Auckland District Health Board, which currently supports Organ Donation New Zealand. A key focus is on ensuring that the dedicated service Organ Donation New Zealand staff provide is not disrupted, and their expertise is retained".
- The maternal mortality rate following a caesarean section in Africa may be 50 times higher than that of high-income countries, according to an observational study of more than 3,500 mothers from 22 African countries⁵². Severe intraoperative and postoperative bleeding was the most common complication for women in Africa. Professor Bruce M Biccard, University of Cape Town, who led the study said that amongst matters which should be targeted are consideration of a lower threshold for the use of drugs used to treat post-partum haemorrhage, especially where availability of blood is low; and improvement of access to blood and blood products with long shelf lives. "Paradoxically, while many countries are aiming to reduce the caesarean delivery rate, increasing the rate of caesarean delivery remains a priority in Africa. Improving access to surgery might allow patients to present earlier and prevent complications and deaths but it is vital that this improvement occurs in parallel with programmes aimed at improving patient safety during caesarean delivery," says Professor Biccard.

⁵² published in *The Lancet Global Health* journal.

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.

- In March, scientists and ethicists from seven nations called for a moratorium on gene-editing experiments designed to alter heritable traits in human babies⁵³.
- A study⁵⁴ reports that women with sickle cell disease may find that the number of eggs left in their ovaries may decline earlier than occurs in women without the disease.
- A study⁵⁵ found that brain oxygen supply is different in different regions of the brain of sickle cell disease patients who have anaemia, which may explain the incidence of silent strokes.
- Icefish are the only vertebrates that lack haemoglobin. They also maintain liquid blood in below-freezing temperatures. Their adaptations to their environment are discussed in a recent paper [published](#) in *Nature*⁵⁶.

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

- In the Philippines, the country’s Food and Drug Administration has cancelled the certificates of product registration of Sanofi’s anti dengue vaccine⁵⁷.
- In the US, the FDA’s advisers in March backed Dengvaxia only in people aged at least 9 but under 17, who have laboratory confirmation of previous dengue infection,

⁵³ Researchers have been simultaneously excited and concerned by the powerful genetic engineering technique CRISPR, which can potentially prevent congenital diseases but also could lead to permanent changes in the human species and create a market for enhanced, augmented offspring, or “designer babies.”

⁵⁴ Julia Kopeika et al., “[Ovarian reserve in women with sickle cell disease](#),” was published in the journal *PLOS ONE*. February 22, 2019 <https://doi.org/10.1371/journal.pone.0213024>

⁵⁵ Yaqiong Chai. Et al., [White matter has impaired resting oxygen delivery in sickle cell patients](#),” *American Journal of Hematology*. First published: 29 January 2019 <https://doi.org/10.1002/ajh.25423>

⁵⁶ Bo-Mi Kim, “Antarctic blackfin icefish genome reveals adaptations to extreme environments”, *Nature Ecology & Evolution* volume 3, pages469–478 (2019) |

⁵⁷ [Food and Drug Administration has permanently canceled the certificates of product registration of the anti-dengue vaccine Dengvaxia.](#)

and who live in an area where the disease is endemic. Dengvaxia recently gained European approval. Takeda has disclosed its candidate met its efficacy endpoint in a large Phase III trial.

- Co-Diagnostics announced that its new Logix Smart ZDC (Zika, Dengue and Chikungunya) test meets the essential requirements of the European Community's In-Vitro Diagnostic Medical Device Directive, allowing immediate export and sales of the product to markets that accept a CE mark.
- At the University of Bath's Department of Electronic and Electrical Engineering Dr Paulo Rocha is developing a low-cost integrative sensing tool for early identification of dengue virus, using a platform containing electrical sensors to study the behaviour of infected human cells.
- Researchers concluded that political, economic and social unrest in Venezuela, and its consequent ongoing humanitarian crisis, may be facilitating the resurgence of vector-borne diseases, such as malaria, dengue, Zika and Chagas⁵⁸.
- Vaccine maker Bharat Biotech International said in March that two of its vaccines against Zika and Chikungunya would be entering Phase II clinical trials, where they will be tested on humans for safety and efficacy.

Influenza

- The World Health Organization in March launched a strategy to protect the global population against the threat of influenza, warning that new pandemics are "inevitable"⁵⁹. WHO's strategy, for 2019 through 2030, aims to prevent seasonal influenza, and control the virus's spread from animals to humans. The new strategy calls for every country to strengthen routine health programmes and to develop tailor-made influenza programmes that emphasise disease surveillance, response, prevention, control, and preparedness. WHO recommended annual flu vaccines and also called for the development of more effective and more accessible vaccines and antiviral treatments.
- At the beginning of the northern hemisphere flu season the predominant strain in the US was A H1N1 but by the beginning of March the more severe strain A H3N2 was accounting for almost half of the new cases.
- WHO in March released its recommendations for the composition of northern hemisphere flu vaccines for the 2019–2020 season. No changes are recommended for the influenza B virus components. The recommendation for the A(H1N1) virus component has been changed. The A/Michigan/45/2015 (H1N1) pdm09-like virus included in the 2018–2019 vaccine composition is replaced by an A/Brisbane/02/2018 (H1N1) pdm09-like virus from the subclade 6B.1A, which is now predominant globally. The recommendations are as listed below, with the first three of these strains for inclusion in trivalent influenza vaccines, and the last as a recommended additional strain for inclusion in quadrivalent influenza vaccines:
 - an A/Brisbane/02/2018 (H1N1) pdm09-like virus
 - an A/Kansas/14/2017 (H3Ns)-like virus
 - a B/Colorado/06/2017-like virus (B/Victoria/2/87 lineage)
 - a B/Phuket/3073/2013-like virus (B/Yamagata/16/88 lineage).

⁵⁸ Grillet ME, Hernández-Villena JV, Llewellyn MS, et al. [Venezuela's humanitarian crisis, resurgence of vector-borne diseases, and implications for spillover in the region](#) [published on February 21, 2019]. *Lancet Infect Dis*. doi: 10.1016/s1473-3099(18)30757-6

⁵⁹ The Spanish flu pandemic occurred in 1918. Subsequent pandemics have occurred in 1957, 1968 and 2009.

Q fever

- Mid-March brought a much-discussed report on the Australian Broadcasting Commission's *Landline* that a new study⁶⁰ on the incidence of Q fever⁶¹ had found that as many as one in 20 people in some parts of Australia have been exposed to Q fever at some time in their lives⁶². The study had found the risk higher in regional areas and researchers recommended that rural residents consider vaccination.
- The study was based on 2,740 samples of blood from donors at blood banks (Australian Red Cross Blood Service) in the Hunter New England region of New South Wales, Toowoomba in Queensland and metropolitan Sydney and Brisbane. Associate Professor Heather Gidding, from the University of Sydney, said 3.6 per cent of the blood sampled overall had antibodies to the bacteria which causes Q fever, showing the donor had been exposed to the disease.
- [Australia has the world's only effective vaccine against Q fever](#)⁶³, but the study found only 40 per cent of people in groups recommended for vaccination knew about it and only 10 per cent of people in those high-risk groups were vaccinated. A report in August 2018 described a nationwide Q fever vaccine shortage, with people on long waiting lists and/or travelling hours for vaccination.
- Q fever is difficult to diagnose, so annual cases recorded probably underestimate the extent of human infection. In the 1990s there were around 500 to 800 cases reported each year⁶⁴. A national Q fever management program begun in 2001 and provided subsidised vaccination to at-risk people including abattoir workers, beef cattle farmers and families of those working on farms. Q fever cases decreased during the program and after it came to an end in 2006, with a historic low of 314 cases in 2009. From 2010, Q fever cases have gradually increased with 558 cases reported in 2016. Each year, the highest numbers of people diagnosed are from [Queensland and NSW](#).

⁶⁰ Heather F Gidding et al., Seroprevalence of Q fever among metropolitan and non-metropolitan blood donors in New South Wales and Queensland, 2014–2015, *Med J Aust* 2019; 210 (7): 309-315. || doi: 10.5694/mja2.13004 Published online: 11 March 2019
<https://www.mja.com.au/journal/2019/210/7/seroprevalence-q-fever-among-metropolitan-and-non-metropolitan-blood-donors-new>

⁶¹ [Q fever is caused by the highly-infectious bacterium *Coxiella burnetii*](#), which infects wild and domestic animals and their ticks. Cattle, sheep and goats are considered the main carriers in Australia, which has one of the highest rates of Q fever worldwide. The Q fever bacteria is [resistant to dehydration and UV radiation](#). With inhalation of contaminated dust a common route of infection drought conditions can increase risk. Abattoir workers, farmers, shearers, veterinarians, stock transport drivers are known to be at risk. In the acute phase of the disease, symptoms include fever and severe headaches, muscle pain and weakness, but some patients continue to suffer serious symptoms long-term, such as heart valve failure, bone infections, seizures and chronic fatigue. The disease is occasionally fatal.

⁶² The one in 20 figure refers to the Toowoomba region in Queensland, with the figure in metropolitan Sydney being one in 36. The researchers found people who had resided in a rural area for at least three months at some time during their life were at a significantly higher risk, even if they had no direct contact with livestock.

⁶³ The [Q-VAX® vaccine](#) has been in use since 1989. It has an [estimated success rate of 83–100%](#). People who have already been exposed to the bacteria are discouraged from having the vaccination, as they can develop a reaction to it. Previous exposure is determined by both a skin and a blood test. This process takes one to two weeks before the vaccine can be administered, and it takes a further two weeks after vaccination to develop protection. This delay and the cost of vaccination are both seen as barriers to widespread use. People aged under 15 years are also [advised against](#) the vaccine.

⁶⁴ The [National Notifiable Diseases Surveillance System](#) gives further details.

Ebola virus disease

- As at 4 March there had been 900 probable and confirmed cases of Ebola and 565 deaths from the outbreak in the Democratic Republic of Congo⁶⁵.
- Returning from a trip to the Democratic Republic of Congo, the Director of the US Centers for Disease Control and Prevention (CDC) warned that the Ebola epidemic in the Congo could last another year.
- The CDC reminded⁶⁶ US healthcare facilities to review their processes for managing communicable infections, including Ebola. The Center emphasised that where a patient is infected with or under investigation for Ebola, healthcare facilities should follow the CDC's separate personal protective equipment guidance.

MERS-CoV

- By 5 March there had been 91 new cases of MERS-CoV in Saudi Arabia this year, including 52 from Wadi ad-Dawasir, where cases were linked to both healthcare and camel exposure. Oman had reported two MERS clusters

Other diseases

- A patient in the UK (“the London patient”) has been reported to be experiencing remission from HIV-1 after stem cell transplantation. While scientists say it is too soon to claim this as a “cure”, the treatment is seen as a promising development from the more aggressive treatment given to the first recorded case of remission after stem cell transplantation, the so called “Berlin patient” over a decade ago. A third patient (“the Dusseldorf patient”) is also reported as being in remission⁶⁷.
- Researchers reported⁶⁸ at the Conference on Retroviruses and Opportunistic Infections that the HIV rate in southern African communities has fallen by 30 percent as a result of house-to-house voluntary testing and treatment.
- A major study⁶⁹ in Denmark demonstrated no link between the measles, mumps, and rubella (MMR) vaccine and autism.

⁶⁵ <https://www.who.int/ebola/situation-reports/drc-2018/en/>

⁶⁶ <https://content.govdelivery.com/accounts/USCDC/bulletins/2336709>

⁶⁷ Anthony Fauci, director of the National Institute of Allergy and Infectious Diseases at NIH commented: “This cure is an exceedingly risky procedure, and while developing it into a safe and scalable treatment is a laudable goal, we must focus on using the tools we already have to end the HIV/AIDS epidemic. ... The importance of the [bone marrow stem cell] transplants for the Berlin and London patients is not the potential for widespread use; it is most valuable as a road map for further research. ... [A] more immediate issue is the gap in providing proven, lifesaving anti-HIV drugs to people who need them. ... [I]f we could identify almost all people with HIV infection and get them on therapy, as well as provide PrEP to a high percentage of people at risk, we could end the HIV/AIDS epidemic. The Berlin and London patients give important insights for HIV researchers, and a cure for HIV is an aspiration we continue to pursue. But the end of the epidemic — the reduction of new HIV infections and HIV-related deaths to very low levels — is within our reach even without a cure. It is our ethical duty to use the tools we have already to stop this disease. Because that would be a real breakthrough”.

⁶⁸ Helen Ayles et al., “HIV Testing and ART Coverage Before a UTT Intervention: Findings in HPTN071(PopART)”, Abstract 982. <http://www.croiconference.org/sessions/hiv-testing-and-art-coverage-utt-intervention-findings-hptn071popart>

⁶⁹ The study appeared in the *Annals of Internal Medicine*. <https://annals.org/aim/article-abstract/2727726/measles-mumps-rubella-vaccination-autism-nationwide-cohort-study> with patient summary at <https://annals.org/aim/fullarticle/2727209/mmr-vaccine-associated-risk-autism> and editorial at <https://annals.org/aim/article-abstract/2727208/further-evidence-mmr-vaccine-safety-scientific-communications-considerations>

- On 14 March at a conference in Barcelona Bayer presented the results of the CHICO (Chagas disease In Children treated with NifurtimOx) Phase III clinical trial of nifurtimox in paediatric patients. Bayer said the trial results demonstrated safety and efficacy of the new formulation. Chagas disease is no longer an endemic disease in Latin America but a global public health threat. The control of the disease by screening programs, access to treatment and vector control are all important measures in chasing the goal of eliminating the disease.
- In 2000, the CDC declared that measles had been [eliminated](#) in the US. By mid-March in 2019, 228 individual cases have been reported⁷⁰, compared with 372 during 2018.
- Nigeria's Lassa fever outbreak peaked at the end of January.
- Health officials warned Townsville residents of the dangers of contracting melioidosis as they cleaned up after the floods⁷¹. The bacterium is soil-borne.
- Tasmania in March reported its first known cases of the mosquito-borne Barmah Forest virus⁷².
- [Space travel](#) caused [herpes](#) viruses to reactivate in more than half of crew aboard Space Shuttle and [International Space Station](#) (ISS), according to a [NASA](#) study. Virus reactivation rates increase with [spaceflight](#) duration, and could present a significant health risk on future missions.

⁷⁰ By mid-March there were confirmed measles cases in California, Colorado, Connecticut, Georgia, Illinois, Kentucky, New Hampshire, New Jersey, New York State, Oregon, Texas, and Washington State.

⁷¹ <https://www.health.qld.gov.au/cdcg/index/melioidosis>

⁷² A summary of Barmah Forest virus epidemiology in Australia and the disease it produces can be found at <http://promedmail.org/post/20130417.1653395>. The virus was first isolated from mosquitoes in the Barmah Forest, Northern Victoria, in 1974.