Monitoring International Trends

**posted March 2015**

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 potentially put financial or other pressures on the Australian sector.

A selection of recent matters of interest appears below. Highlights include:

* Scientists in Taiwan have described a cheaper method of collecting immunoglobulin which may enable developing country patients with primary immunodeficiencies to receive regular antibody doses. (Section 1)
* Terumo will start US clinical trials this year to test the effectiveness of its Mirasol process in removing pathogens from blood products. (Section 1)
* Boehringer Ingelheim has filed for approval of idarucizumab in the US, European Union and Canada for patients requiring an antidote to its anticoagulant Pradaxa (dabigatran etexilate). (Section 2)
* **A study has found perioperative blood transfusion was** associated with increased cancer-specific mortality and all-cause mortality for prostate and kidney cancer in a multivariate model. (Section 5)
* The use of hydroxyethyl starch in volume expansion in adult patients has been questioned recently for safety reasons. Now a meta-analysis has examined whether or not HES has any adverse effect in paediatric patients. (Section 5).
* New research found that the high number of blood tests done before and after cardiac surgery can sometimes lead to excessive blood loss, possibly causing anaemia and the need for a blood transfusion. (Section 5)
* Research suggests that patients with atrial fibrillation who are treated with an anticoagulant have an increased risk of thromboembolic events, bleeding complications, and mortality if they have anaemia. (Section 5)
* A study has suggested that a synthetic polymer might help save people from losing too much blood. (Section 5)
* A Canadian-led study compared mortality after 90 days in intensive care patients transfused with either fresh blood (stored for an average of six days) or older blood (stored for an average of 22 days). They reported no difference in mortality or organ dysfunction between the two groups. (Section 5)
* Researchers at Johns Hopkins reported they have successfully corrected a genetic error in stem cells from patients with sickle cell disease, and then used those cells to grow mature red blood cells. (Section 6)
* A study at the University of California has outlined a method that corrects the mutation that causes sickle cell disease and leads to the production of normal red blood cells.
* Researchers have developed a three-dimensional tissue system that can generate functional human platelets. (Section 6)
* Doctors at Royal Melbourne Hospital have been trialling a new method for treating severe stroke. (Section 6)
* Houston Methodist Research Institute scientists found that by loading magnetic nanoparticles with drugs and dressing them in biochemical camouflage they can destroy blood clots very quickly. (Section 6)
* Researchers at the University of North Carolina’s School of Medicine found that the blood platelet protein Rasa3 is critical to the success of the anti-platelet drug Plavix (clopidogrel), used to break up blood clots. .(Section 6)
* Scientists at Sanford-Burnham Medical Research Institute discovered a key role for a protein, dual-specificity phosphatase 3 (DUSP3), in platelet signalling and blood clotting. (Section 6)
* Scientists at the University of Cambridge and Microsoft Research have developed a computer model to simulate development of blood cells and increase understanding of the control mechanisms that operate. (Section 6)
* Dengue and Ross River virus have both been circulating in Queensland. (Section 8)
* The report of the Penrose inquiry into how patients in Scotland were infected through treatment with contaminated blood products was published in Edinburgh. (Section 7)
* In partnership with the Liberian government, the US National Institute of Allergy and Infectious Diseases (NIAID) at the end of February launched a clinical trial to obtain safety and efficacy data on the investigational drug ZMapp as an Ebola treatment. (Section 8)
* Final stage trials of an Ebola vaccine developed by Merck and NewLink Genetics began in Guinea on 7 March. A second vaccine, by GlaxoSmithKline is also being tested. (Section 8)
* Early in March, Saudi Arabia’s total of MERS fatalities passed 400, from a case count of 931. The global total of infections at that time was 1,068. New cases have continued to be reported.
* At Tatura in northern Victoria a dairy cow has died of anthrax[[1]](#footnote-1). The property has been quarantined and stock on the property, and on six adjacent properties, have been vaccinated. (Section 8)
* Queensland has had the second worst salmonella outbreak in its history with 250 conference attendees reportedly taken ill after consuming food at the Brisbane *Convention and Exhibition* Centre. (Section 8)
* The World Health Organization (WHO) announced that the recommended vaccine composition for the 2015-2016 influenza season (northern hemisphere winter) is unchanged from the recommendation for the southern hemisphere in 2015: (Section 8)
  + 1. an A/California/7/2009 (H1N1)pdm09-like virus;
    2. an A/Switzerland/9715293/2013 (H3N2)-like virus; and
    3. a B/Phuket/3073/2013-like virus.
    4. it is recommended that quadrivalent vaccines containing two influenza B viruses contain the above three viruses and a B/Brisbane/60/2008-like virus’

Contents

[1. Products 3](#_Toc415395934)

[Clotting factors 3](#_Toc415395935)

[Sickle Cell treatments 3](#_Toc415395936)

[Immunoglobulin 3](#_Toc415395937)

[Other 4](#_Toc415395938)

[2. Regulatory 4](#_Toc415395939)

[Plasma and recombinant products 4](#_Toc415395940)

[Blood donation, processing, storage and use; blood substitutes 5](#_Toc415395941)

[Devices 5](#_Toc415395942)

[Other 5](#_Toc415395943)

[3. Market structure and company news 5](#_Toc415395944)

[4. Country-specific events 6](#_Toc415395945)

[5. Safety and patient blood management 7](#_Toc415395946)

[Appropriate transfusion 7](#_Toc415395947)

[Preventing and treating iron deficiency 8](#_Toc415395948)

[Other. 9](#_Toc415395949)

[6. Research 9](#_Toc415395950)

[7. Legal actions and enquiries 11](#_Toc415395951)

[8. Infectious diseases 11](#_Toc415395952)

[Mosquito-borne diseases, including dengue, chikungunya, and malaria 12](#_Toc415395953)

[Influenza: strains, spread, prevention and treatment 13](#_Toc415395954)

[Ebola 14](#_Toc415395955)

[MERS-CoV 15](#_Toc415395956)

[Other diseases: occurrence, prevention and treatment 15](#_Toc415395957)

# Products

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

* 1. GlycoMimetics announced the publication[[2]](#footnote-2) of results from a randomized, placebo-controlled Phase II study evaluating the efficacy, safety and pharmacokinetics of rivipansel in sickle cell patients hospitalized with a vaso-occlusive crisis. The company says the study highlighted the potential of rivipansel to improve clinical outcome. Results from the study had already been announced[[3]](#footnote-3) at the December 2013 American Society of Hematology (ASH) Annual Meeting and Exposition.
  2. Thierry Burnouf (who runs the Graduate Institute of Biomedical Materials and Tissue Engineering at Taipei Medical University) and colleagues have described[[4]](#footnote-4) a cheaper method of collecting immunoglobulin G (IgG) which may enable developing country patients with primary immunodeficiencies (PID) to get the regular antibody doses they need. The process requires a centrifuge, disposables such as blood bags and filters, and around 20 plasma donations to produce an economically viable volume of immunoglobulins. The frozen plasma is thawed and centrifuged in its original sterile bag (leftover blood constituents can be used to treat haemophiliac patients). The remaining liquid is mixed with caprylic acid and filtered.
  3. Burnouf says that IgG produced using the method is being trialled for safety in Cairo, in a small group of children affected by PID. He hopes it will be available for wider distribution by early 2016. The authors say this method is “also relevant for preparing hyperimmune IgG from convalescent plasma during infectious outbreaks such as the current Ebola virus episode”. Paul Strengers, president of the International Plasma Fractionation Association, agrees it should be easy to implement the new technique in blood centres in the developing world. “This is a major step forward and a completely new approach in the manufacturing of these important plasma-derived [medicines](http://www.scidev.net/global/health/medicine/),” he says. However, there is a concern from other commentators that since caprylic acid purification of IgG has been patented, there may be serious legal challenges to its widespread use.

### Other

* 1. The Lakewood (US)-based unit of Japanese company Terumo will start US clinical trials this year to test the effectiveness of its Mirasol process in removing pathogens from blood products. The process shines specific wavelengths of ultraviolet light onto bagged blood products — whole blood, plasma or platelets — that have had riboflavin, a vitamin, added to them. The combination of the riboflavin and light changes the nucleic acid in bacteria, viruses, and other biological pathogens, making them incapable of reproducing in the blood. The process also inactivates the white blood cells. The Mirasol technology received its first approvals in Europe seven years ago and Terumo has been selling it in Europe for removing pathogens from blood platelets and plasma. In 2013, the US Department of Defense and Terumo agreed to invest nearly $US30 million over four years to develop Mirasol for whole blood, funding development of the technology and helping win FDA for approval for general use domestically. In 2014 Terumo agreed with Banco de Sangre de Servicios Mutuos in Puerto Rico to start using Mirasol to treat blood platelet products there to combat spread of chikungunya virus and dengue fever. The company applied to the FDA for an exemption permitting that use of Mirasol.
  2. [Apollo Medical Devices](http://www.apollomedicaldevices.com/) of Cleveland, Ohio, has developed technology that provides point-of-care blood analysis with just a single drop of blood, and does so in five minutes. There is no need for venous access or a central laboratory.

# Regulatory

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

### Plasma and recombinant products

* 1. [Octapharma USA](http://cts.businesswire.com/ct/CT?id=smartlink&url=http%3A%2F%2Fwww.octapharmausa.com&esheet=51054080&newsitemid=20150309005120&lan=en-US&anchor=Octapharma+USA&index=1&md5=7024237460200c65686cd3c7bdf2b584) announced the [US Food and Drug Administration (FDA)](http://cts.businesswire.com/ct/CT?id=smartlink&url=http%3A%2F%2Fwww.fda.gov&esheet=51054080&newsitemid=20150309005120&lan=en-US&anchor=U.S.+Food+and+Drug+Administration+%28FDA%29&index=2&md5=dc77c3ae2ef33b5a4fd1fcfc8e489744) has approved revised product labelling for Octaplas [Pooled Plasma (Human), Solvent/Detergent Treated Solution for Intravenous Infusion][[5]](#footnote-5), which increases permitted time between product thawing and patient administration[[6]](#footnote-6). The new labelling also increases the product’s shelf life[[7]](#footnote-7).

### Other

* 1. Boehringer Ingelheim has filed for approval of idarucizumab in the US, European Union and Canada for patients requiring an antidote to its anticoagulant Pradaxa (dabigatran etexilate). Idarucizumab which received breakthrough designation in the US in 2014[[8]](#footnote-8) is a fully humanised antibody fragment designed to reverse the anticoagulant effects of Pradaxa. The submission is a world first for a specific reversal agent to a novel oral anticoagulant. The submissions include interim data from the ongoing Phase III RE-VERSE ADTM study, evaluating idarucizumab in patients treated with Pradaxa who are in need of emergency intervention.
  2. Swedish company Dilaforette has been granted Orphan Drug Designation by the US Food and Drug Administration (FDA) for sevuparin in sickle-cell disease. The company is preparing for a Phase II study.

# 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.*

* 1. Grifols announced its 2014 adjusted net profit of 597.9 million euros ($US 679.57 million), up 32.8 per cent from a year earlier.
  2. Grifols acquired 45 per cent of the equity of Alkahest[[9]](#footnote-9) for $US 37.5 million. Alkahest and Grifols will collaborate to develop plasma-based products for the treatment of cognitive decline in aging and other central nervous system disorders, including Alzheimer's, Huntington’s and Parkinson’s. Grifols will provide a further payment of $US12.5 million and fund the development of plasma-based products, which may be commercialized by Grifols globally. Alkahest will receive milestone payments and royalties on sales of such products by Grifols.
  3. Cerus Corporation announced that Sweden’s Karolinska University Hospital (KUH) had signed a three-year agreement to purchase the Intercept Blood System for platelets. The agreement allows for annual extensions for two further years. KUH is Sweden’s largest platelet supplier and one of the largest University Hospitals in Europe, producing over 10,000 platelet units, or 20 per cent of Sweden’s platelet supply annually.
  4. Cerus Corporation and the Blood Bank of Delmarva (BBD) signed a three-year purchase agreement for the Intercept Blood System for platelets and plasma. BBD provides blood transfusion products and services to Delaware, Cecil County, Maryland, as well as Maryland's and Virginia’s Eastern Shores. BBD supplies around 13,000 platelet and 21,000 plasma units annually.
  5. In recognition of Rare Disease Day, CSL Behring announced it is donating 2 million international units (IUs) of protein therapies to the World Federation of Hemophilia (WFH). The donation supports the WFH’s Global Alliance for Progress (GAP) Program aimed at improving the diagnosis and treatment of bleeding disorders in developing countries. Rare Disease Day, February 28, is coordinated by the European Organization for Rare Diseases (EURORDIS) and by several national alliances and patient organizations around the globe.
  6. Haemonetics Corporation and CSL Plasma announced that CSL Plasma has selected Haemonetics' Next Generation Donor Management System as its future system for managing more than 100 plasma donation centers across the US and Europe.
  7. Baxter International bought German biopharma firm [SuppreMol](http://email.seekingalpha.com:80/track?type=click&mailingid=2345076&messageid=2900&databaseid=&serial=2900O2345076O1425479277869.0.a63e1fee70613697e41d64abc2ca0b67&emailid=2550971&userid=2550971&extra=&&&3000&&&http://www.suppremol.com/overview.html) for $US 225 million. This privately-held firm develops protein therapeutics for autoimmune, inflammatory and allergic diseases.
  8. The US National Institute of Allergy and Infectious Diseases awarded [Inovio Pharmaceuticals](http://www.bizjournals.com/profiles/company/us/pa/blue_bell/inovio_pharmaceuticals_inc/3332519) and its academic collaborators[[10]](#footnote-10), a new five-year, $US 16 million grant to support the continued development of its HIV/AIDS vaccine program.

# Country-specific events

*The NBA is interested in relevant safety issues which arise in particular countries, and also instances of good practice. We monitor health issues in countries from which Australia’*s *visitors and immigrants come.*

* 1. The lower House of the US State of Georgia approved a bill that would allow for the limited use of medical marijuana. The House voted 157-2 in favour of the bill, expanding the list of treatable illnesses to include sickle cell anemia, which mostly affects African-Americans. The Georgia Legislative Black Caucus lobbied hard for the change. The bill then allowed for nine illnesses including cancer, seizure disorders and Parkinson’s to be treated with a non-mind altering, oil-based form of marijuana. Bill supporters were concerned the Senate may narrow the bill to cover only seizure disorders. However, the Senate removed only fibromyalgia, and sickle cell remained as an affliction for which doctors may prescribe cannabis oil.
  2. A study[[11]](#footnote-11) in California has found that the top five causes of maternal mortality in the State are cardiovascular disease, preeclampsia or eclampsia, haemorrhage, venous thromboembolism, and amniotic fluid embolism. The study also found that between 41 per cent and 70 per cent of the deaths were probably preventable.
  3. The UK’s National Institute for Health Care and Excellence ([NICE](http://www.fiercepharma.com/tags/nice)) recommended the Bristol-Myers Squibb/Pfizer drug Eliquis for use in patients with deep vein thrombosis (DVT), which can lead to a potentially fatal blood clot in the lungs (pulmonary embolism).
  4. The British embassy in Turkey refused two Iranian haemophiliacs visas when they were hoping to undergo gene therapy at the expense of University College London. Iran has been under tough Western sanctions.
  5. South Korea’s Green Cross has signed a memorandum of understanding with the Guizhou provincial government of China. The company will build a cell therapy facility in the south western Chinese province and produce and distribute cell therapy products in China.

# Safety and patient blood management

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

### Appropriate transfusion

* 1. **A study**[[12]](#footnote-12) **from the Department of Urology, in the University of Minnesota, Minneapolis, has found perioperative blood transfusion (PBT) was** associated with increased cancer-specific mortality (CSM) and all-cause mortality.
  2. A meta-analysis has examined whether or not hydroxyethyl starch (HES) has any adverse effect in paediatric patients[[13]](#footnote-13). Thirteen randomized controlled trials published before January 2014 and involving a total 1,156 paediatric patients were included. Patients all received six per cent low-molecular-weight HES. The study concluded that volume expansion with six per cent HES significantly decreased the platelet count and increased the length of ICU stay, and also might have an adverse effect on renal function. Therefore HES was not recommended for use in paediatric patients without further studies.
  3. Another study also addressed the use of six per cent hydroxyethyl starch (HES) 130/0.4 as an alternative to human albumin (HA) and crystalloids for volume replacement in children undergoing cardiac surgery. In a large propensity-matched analysis[[14]](#footnote-14), researchers assessed efficacy and safety of replacing HA with HES for intra-operative volume therapy in children undergoing cardiac surgery with cardiopulmonary bypass (CPB). From 1832 children reviewed, 1495 were included in the analysis. The study concluded that the use of HES for volume replacement in children during cardiac surgery with CPB is as safe as human albumin. It also found that its use might be associated with less fluid accumulation. The researchers recommended that further large studies be done to assess if the reduction in fluid accumulation could have a significant impact on postoperative morbidity and mortality.
  4. Jacques Lacroix (Sainte-Justine University Hospital Research Center), Dean Ferguson and Alan Tinmouth (both of The Ottawa Hospital), and Paul Hébert (Centre de recherche du centre hospitalier de l'Université de Montréal) led a team of researchers from 64 Canadian and European centres in the Age of Blood Evaluation (ABLE) study. This was a randomized double-blind trial to compare mortality after 90 days in intensive care patients transfused with either fresh blood (stored for an average of six days) or older blood (stored for an average of 22 days)[[15]](#footnote-15). "Current blood bank practice is to provide patients with the oldest blood available. Some doctors, however, feel that fresh blood is better", said Dr. Paul Hébert. "There was no difference in mortality or organ dysfunction between the two groups, which means that fresh blood is not better than older blood", said Dr. Dean Fergusson. "Previous observational and laboratory studies have suggested that fresh blood may be better because of the breakdown of red blood cells and accumulation of toxins during storage. But this definitive clinical trial clearly shows that these changes do not affect the quality of blood", said Dr Alan Tinmouth. Dr Dana Devine, chief medical and scientific officer at Canadian Blood Services naturally welcomed the findings, saying: “The study supports our current inventory management practices for patients receiving transfusions in the [intensive care](http://medicalxpress.com/tags/intensive+care/) setting". The same research team is conducting a similar clinical trial in paediatric [patients](http://medicalxpress.com/tags/patients/).

### Preventing and treating iron deficiency

* 1. New research[[16]](#footnote-16) suggests that the high number of blood tests done before and after cardiac surgery can sometimes lead to excessive blood loss, possibly causing anaemia and the need for a blood transfusion. The study covered close to 1,900 patients who had cardiac surgery at the Cleveland Clinic between January and June 2012. From the time they first met their heart surgeons until they left the hospital, the patients had, on average, 116 blood tests. The total median amount of blood gathered during an entire hospital stay was about 454 millilitres per patient, the researchers found. "We were astonished by the amount of blood taken from our patients for laboratory testing. Total phlebotomy volumes approached 1 to 2 units of red blood cells” study leader Dr Colleen Koch of the Cleveland Clinic said in a journal news release. The highest amounts of blood taken were from patients undergoing the most complex heart surgeries. The greater the number of lab tests and the longer patients stayed in the hospital, the more likely they were to require transfusions. "Prior research shows that patients who receive blood transfusions during heart surgery have more infections after surgery, spend more time on the ventilator, and die more frequently-even after adjusting for how sick they were prior to surgery," Koch said.
  2. Research[[17]](#footnote-17) suggests that patients with atrial fibrillation who are treated with an anticoagulant have an increased risk of thromboembolic events, bleeding complications, and mortality if they have anaemia.

### Other.

* 1. A study[[18]](#footnote-18) has suggested that a synthetic polymer might help save people from losing too much blood. Injected into the circulation of rats, the polymer stopped the animals’ bleeding after their femoral arteries were cut. Suzie Pun, a bioengineer at the University of Washington, and her colleagues derived the polymer (PolySTAT) by combining the material that is used to make contact lenses with a peptide that binds fibrin, a fibrous protein involved in the formation of platelet plugs during blood clotting. “I think this has real power to save people in the battlefield,” she said.
  2. A study[[19]](#footnote-19) has found that while increasing age is not positively associated with risk of complications after implant-based breast reconstruction, it is an independent risk factor for venous thromboembolism.
  3. Patients with cancer are four to seven times more likely than those without cancer to develop venous thrombo-embolism (VTE). The risk for VTE recurrence while on anticoagulant treatment is especially high among cancer patients. **Maria Cristina Vedovati of** the University of Perugia, and colleagues, performed a meta-analysis to compare the safety and efficacy of new direct anti-factor Xa and anti-factor IIa oral anticoagulants vs. standard treatment—low–molecular-weight heparin followed by vitamin K antagonists—in patients with [VTE](http://www.healio.com/hematology-oncology/hematology/news/online/%7Bb06bdb26-3ac4-46d4-b820-1e53b0d8146c%7D/bevacizumab-not-significantly-associated-with-vte-risk-in-patients-with-prostate-cancer) and cancer.[[20]](#footnote-20) They considered six studies—totalling 1,132 patients—two with dabigatran (Pradaxa, Boehringer Ingelheim), two with rivaroxaban (Xarelto, Janssen), one with edoxaban (Savaysa, Daiichi Sankyo) and one with apixaban (Eliquis, Bristol-Myers Squibb). They found patients with cancer were less likely to experience VTE recurrence when treated with direct oral anticoagulants than with conventional treatment; and that major bleeding was lower among those treated with direct oral anticoagulants[[21]](#footnote-21).

# Research

*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.*

* 1. Researchers at Johns Hopkins reported[[22]](#footnote-22) they have successfully corrected a genetic error in stem cells from patients with sickle cell disease, and then used those cells to grow mature red blood cells[[23]](#footnote-23).
  2. A study[[24]](#footnote-24) led by Dr Donald Kohn of the UCLA Eli and Edythe Broad Center for Regenerative Medicine and Stem Cell Research has outlined a method[[25]](#footnote-25) that corrects the mutation that causes sickle cell disease and leads to the production of normal red blood cells.
  3. Researchers have developed a three-dimensional tissue system that can generate functional human platelets. The system usesa biomaterial matrix of porous silk to reproduce the complex structure and physiology of human bone marrow. Co-corresponding author Alessandra Balduini from Tufts University said "In this tissue system, we can culture patient-derived megakaryocytes-the bone marrow cells that make platelets-and also endothelial cells, which are found in bone marrow and promote platelet production to design patient-specific drug administration regimes." The system can yield an *in-vitro* tissue system to predict efficacy of new drugs rather than *in vivo* animal models.[[26]](#footnote-26)
  4. Doctors at Royal Melbourne Hospital (and 13 other hospitals in Australia and New Zealand) have been treating the most severe form of stroke by using advanced brain imaging to identify which parts of the brain are salvageable, then using new stent technology to remove the clot, as well as traditional clot-busting medication. The proportion of patients who have not had a disability after their stroke rose from 40 to 70 per cent.[[27]](#footnote-27) The lead investigator, neurologist Dr Bruce Campbell, said: "This is a treatment that applies to patients with the most severe types of strokes, the strokes that are likely to cause disability, people who end up in nursing homes or even dead, and so it is a major advance." Fellow investigator Associate Professor Peter Mitchell said it was a "revolutionary" development that was being welcomed worldwide.
  5. Houston Methodist Research Institute researchers found that by loading magnetic nanoparticles with drugs and dressing them in biochemical camouflage they can destroy blood clots up to 1,000 times faster than a commonly used clot-busting technique[[28]](#footnote-28). Paolo Decuzzi, the study's co-principal investigator, said: "We have designed the nanoparticles so that they trap themselves at the site of the clot, which means they can quickly deliver a burst of the commonly used clot-busting drug tPA where it is most needed."
  6. Researchers at the University of North Carolina’s School of Medicine found that the blood platelet protein Rasa3 is critical to the success of the anti-platelet drug Plavix (clopidogrel), used to break up blood clots[[29]](#footnote-29). Senior author Wolfgang Bergmeier said: "We believe these findings could lead to improved strategies for treatment following a heart attack and a better understanding of why people respond differently to anti-platelet drugs, such as aspirin and Plavix." They also see a possibility that their findings could facilitate the development of an antidote to Plavix, whose anti-platelet effect increases the risk of emergency surgery. An antidote would bypass the need to wait until the kidneys eliminate the drug from circulation.
  7. A team led by Walter J. Koch at Temple University School of Medicine (TUSM) found that a commonly prescribed antidepressant paroxetine (also known as Paxil) restored heart function in mice with heart failure[[30]](#footnote-30). The drug inhibited a specific enzyme. Disease reversal occurred at concentrations of paroxetine similar to those found in the blood of people treated for depression. Dr Koch cautioned that what happens in mice is no guarantee of the same response in humans.
  8. Scientists at Sanford-Burnham Medical Research Institute discovered a key role for a protein, dual-specificity phosphatase 3 (DUSP3), in platelet signalling and blood clotting. They developed a DUSP3 inhibitor that decreases the aggregation of human platelets[[31]](#footnote-31). They hope this will lead to the development of effective drugs for the treatment of blood clotting in heart attacks and ischemic strokes. Co-corresponding author Lutz Tautz, of the Cell Death and Survival Networks Program at Sanford-Burnham, said: “Our findings provide proof-of-principle for a novel and potentially safer DUSP3-based antiplatelet therapy for the treatment of arterial thrombosis.”
  9. Scientists at the University of Cambridge and Microsoft Research have developed a computer model to simulate development of blood cells and increase understanding of the control mechanisms that operate[[32]](#footnote-32). Bertie Gottgens of the Cambridge Institute for Medical Research said: “With this new computer model, we can carry out simulated experiments in seconds that would take many weeks to perform in the laboratory, dramatically speeding up research into blood development and the genetic mutations that cause leukaemia.”
  10. A Chinese study led by Yong Huo of Peking University First Hospital in Beijing reported that folic acid may lower stroke risk in people with high blood pressure[[33]](#footnote-33).

# Legal actions and enquiries

*The NBA is interested in the implications for Australia of any proceedings against companies, governments and professional practitioners in relation to blood and blood products; or of relevant public enquiries.*

* 1. The report of the Penrose inquiry into how patients in Scotland were infected through treatment with contaminated blood products was published in Edinburgh on 25 March. Patient representatives expressed disappointment and anger that the six-year inquiry did not “name and shame” people who could be held responsible for the contaminated treatments provided. It did however suggest that more could have been done to screen for hepatitis C, and that blood donations from prisons, which were once common practice, should have been stopped earlier, because of the higher rates of hepatitis in prison populations. The report’s sole recommendation was that everyone in Scotland who had a blood transfusion before 1991 should be tested for hepatitis. It estimated that nearly 3,000 people in Scotland were known to have been infected with hepatitis C from infected blood and 60 people with HIV.
  2. Speaking in the House of Commons following publication of the report, Prime Minister David Cameron said: “It is difficult to imagine the feelings of unfairness that people must feel at being infected with something like hepatitis C or HIV as a result of a totally unrelated treatment within the NHS and to each and every one of those people I would like to say sorry on behalf of the government for something that should not have happened.” He announced the Government would improve the way that victims are paid compensation and promised £25m next year for the scheme. Scotland’s Health Secretary Shona Robison apologised on behalf of the Scottish NHS and government.
  3. The Haemophilia Society in its initial response said: “Had the UK become self-sufficient in blood products in the 1970s hepatitis C infections may not have had such prevalence in the bleeding disorders community. The Haemophilia Society is therefore shocked and disappointed that Lord Penrose does not recognise from the evidence he has gathered that the UK government through its action and inaction caused the death and devastating long-term illness of so many of our community.”

# 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, and the tick-borne babesiosis and Lyme disease).*

### Mosquito-borne diseases, including dengue, chikungunya, and malaria

* 1. Dengue (serotype 1) has once again been circulating in northern Queensland, with Cairns, Innisfail and Tully amongst the areas affected.
  2. On 2 March, Malaysia’s Health Ministry put the death toll from dengue in the first two months of 2015 at 62, with 25,000 cases reported. The death toll for the whole of 2014 was 189, from 100,000 cases.
  3. New research from the University of Oxford and the Wellcome Trust estimates [390 million dengue infections per year worldwide](http://www.examiner.com/article/new-research-estimates-390-million-people-infected-with-dengue-fever-annually)**.**
  4. Researchers in Singapore have identified a powerful antibody known as 5J7 which requires a minute amount to neutralise the [dengue](http://economictimes.indiatimes.com/topic/dengue) virus, DENV-3[[34]](#footnote-34). This new finding[[35]](#footnote-35) gives hope for the development of effective dengue treatments, researchers said. However, while antibody 5J7 has been found to be effective against DENV-3, the remaining serotypes of dengue virus have to be considered.[[36]](#footnote-36)
  5. Scientists have known for some time that people with blood type O are protected from the most severe (and deadly) forms of malaria A. Now a team of at Sweden’s Karolinska Institute has offered an explanation for why only some blood types are vulnerable[[37]](#footnote-37). They demonstrate how the Plasmodium falciparum parasite secretes the protein RIFIN, which makes its way to the surface of an infected person’s blood cells, where it becomes sticky and begins its damage. RIFIN bonds strongly with type A blood cells, but links weakly to type O.
  6. Southern Queensland has been experiencing an outbreak of Ross River fever[[38]](#footnote-38).

### Influenza: strains, spread, prevention and treatment

* 1. The World Health Organization (WHO) announced that the recommended[[39]](#footnote-39) vaccine composition for the 2015-2016 influenza season (northern hemisphere winter)[[40]](#footnote-40) is unchanged from the recommendation for the southern hemisphere in 2015:
     1. an A/California/7/2009 (H1N1)pdm09-like virus;
     2. an A/Switzerland/9715293/2013 (H3N2)-like virus;
     3. a B/Phuket/3073/2013-like virus.
     4. it is recommended that quadrivalent vaccines containing two influenza B viruses contain the above three viruses and a B/Brisbane/60/2008-like virus.
  2. WHO says the highly pathogenic H5N1 avian influenza virus, which has been causing poultry outbreaks in Asia since 2003 and is now endemic in several countries, is the influenza virus of greatest concern for human health[[41]](#footnote-41), although it has now been joined by more recently identified H5N2[[42]](#footnote-42), H5N3, H5N6, and H5N8 strains, all of which are currently circulating in different parts of the world.
  3. Taiwan’s Center for Disease Control issued a travel alert for Sichuan Province in southwest China, after a new human case of H5N1 there was reported on 13 March.
  4. Egypt’s Health Ministry announced on 7 March two women had died from H5N1, bringing to 13 the total number of deaths in the country in 2015[[43]](#footnote-43).
  5. Since December, an outbreak of swine flu in India had killed more than 1,200 people between December and early March. While Indian health officials reported that the strain had not changed from the version of H1N1 that emerged in 2009, a study from the Massachusetts Institute of Technology[[44]](#footnote-44) suggested that the strain has mutated and is more dangerous than previously circulating strains of H1N1.
  6. Mainland China’s health authorities announced on 9 March that 19 new cases of H7N9 avian flu had been confirmed in the five weeks up to 25 February. Three of the patients had died and two remained in a critical condition[[45]](#footnote-45).
  7. Hong Kong had its first death from H7N9 for 2015, a man who had visited a wet market on the mainland.
  8. On 10 March, Hong Kong’s Centre for Food Safety[[46]](#footnote-46) announced that in view of a notification from the US about an [**outbreak of highly pathogenic H5N2 avian influenza in Jasper County, Missouri,**](http://outbreaknewstoday.com/missouri-reports-avian-influenza-at-carthage-area-turkey-farm-60296/) it had banned the import of poultry meat and products (including eggs) from that county[[47]](#footnote-47).
  9. A team of investigators from St. Jude Children's Research Hospital, Stanford University Medical Center, and MacroGenics have developed an antibody which has proved 100 per cent protective against the H5N1virus in ferrets and mice[[48]](#footnote-48). Antibodies target antigens, thus disabling them. However, mutations can render antibodies ineffective. Corresponding author Richard Webby[[49]](#footnote-49) said "Our solution was to make a 'dual-specific' antibody by combining two different antibodies that attach strongly to H5N1 viruses into a single antibody-like molecule". That, he said, should make it much harder for resistance to emerge. The new compound is called FcDART, for Fc (the type of fusion protein) Dual-Affinity ReTargeting molecule. A single, low dose of the compound protected against H5N1 in laboratory models. "This dose could be given one day before infection—for example, to protect healthcare providers—or up to three days after," said Webby.

### Ebola

* 1. Guinea, Liberia and Sierra Leone reported 99 new confirmed Ebola cases in the week to 22 February, down from 128 the previous week. In all, more than 23,500 cases have been reported in the three West African countries, with more than 9,500 deaths. The slowdown in the rate of new infection, while very welcome, has reduced the opportunities for trialling potential treatments and vaccines.
  2. In partnership with the Liberian government, the US National Institute of Allergy and Infectious Diseases (NIAID) at the end of February launched a clinical trial to obtain safety and efficacy data on the investigational drug ZMapp as an Ebola treatment. The study is a randomized controlled trial enrolling adults and children with known Ebola virus infection. ZMapp, developed by Mapp Biopharmaceutical of San Diego, is composed of three different monoclonal antibodies. It is designed to prevent the progression of Ebola virus disease by targeting the main surface protein of the Ebola virus. The antibodies are produced in tobacco plants bioengineered to produce large quantities of these proteins. In nonhuman primates ZMapp demonstrated strong antiviral activity and staved off death as late as five days after infection.
  3. Final stage trials of an Ebola vaccine developed by Merck and NewLink Genetics began in Guinea on 7 March. A second vaccine, by GlaxoSmithKline is also being tested. WHO said its Strategy Advisory Group of Experts (SAGE) will decide in August at the earliest on whether to recommend widespread introduction of an Ebola vaccine. It said the recommendation would depend on results of clinical trials and the epidemic's course. Decisions on whether or not to follow the recommendation would be made by the respective ministries of health of countries individual countries.
  4. Researchers led by immunologist Rafi Ahmed of Emory University in Atlanta, Georgia, found that four Ebola patients treated at Emory between August and October last year mounted strong immune defences against the virus. There is an emerging consensus from the recent outbreak that if patients receive timely care, their bodies have enough time to fight off the infection. “It’s like we’re racing against the virus,” said Anthony Fauci, director of the US National Institute of Allergy and Infectious Diseases in Bethesda, Maryland. “The idea that Ebola causes 90 per cent mortality is under the worst conditions. If you take that same patient and put her in intensive care until her immune system kicks in, you can dramatically diminish the mortality to maybe 20 per cent less”.
  5. A study led by Alexander Khromykh, from the University of Queensland’s School of Chemistry and Molecular Biosciences has found that an experimental Ebola vaccine made using Kunjin virus gave significant protection from Ebola infection in four African green monkeys.

### MERS-CoV

* 1. Early in March, Saudi Arabia’s total of MERS fatalities passed 400, from a case count of 931. The global total of infections at that time was 1,068. Germany reported its third imported MERS case, QATAR its eleventh
  2. Abdullah Asiri, undersecretary for preventative health at Saudi Arabia’s health ministry, was reported to have said that around 90 per cent of camels in the Gulf region are carriers of the Middle East Respiratory Syndrome Coronavirus (MERS-CoV), which underlines the urgent need for a vaccine for camels.

### Other diseases: occurrence, prevention and treatment

* 1. Researchers estimate that airport screening for disease will often miss half or more of infected travellers, but can be improved by customizing to pathogens[[50]](#footnote-50). The main barrier to success is dishonest reporting by travellers about their possible exposure.
  2. Afghanistan, one of the three remaining polio endemic countries, has reported it’s first case of wild poliovirus type 1 (WPV1)for 2015. Last year, Afghanistan reported 28 WPV1 cases with many arising from cross-border transmission with Pakistan. So far in 2015 Pakistan has reported nine cases. The third polio endemic country, Nigeria, has not reported a new WPV1 case since last July.
  3. At Tatura in northern Victoria a dairy cow has died of anthrax[[51]](#footnote-51). The property has been quarantined and stock on the property, and on six adjacent properties, have been vaccinated.
  4. Queensland has had the second worst salmonella outbreak in its history with 250 conference attendees reportedly taken ill after consuming food at the Brisbane Convention and Exhibition Centre.
  5. Hong Kong has reported a surge in Hepatitis A since the beginning of 2015. February had the highest monthly total reported since April 2004.
  6. A new vaccine for hepatitis E provides protection from the virus for at least 4.5 years, according to Chinese researchers[[52]](#footnote-52). Hepatitis E is a leading cause of serious liver problems in the developing world.
  7. A team of researchers led by Dr Michael Farzan of the Scripps Research Institute has adopted a new approach to protect against a wide variety of HIV viruses[[53]](#footnote-53). Farzan said “Our compound is the broadest and most potent entry inhibitor described so far…..Unlike antibodies, which fail to neutralize a large fraction of HIV-1 strains, our protein has been effective against all strains tested, raising the possibility it could be part of an effective HIV vaccine alternative.” The team hopes that with further development, this compound could prove a preventative drug and a treatment, although technical and safety issues will need to be addressed before human trials.
  8. Howard Hughes Medical Institute (HHMI) scientists at Albert Einstein College of Medicine say they have created a powerfully effective vaccine against herpes viruses[[54]](#footnote-54). Investigator William Jacobs says: "this might also be a good candidate as a vaccine vector for other mucosal diseases, particularly HIV and tuberculosis." The new vaccine was found to be effective in mice against the common forms of herpes that cause cold sores (HSV-1) and genital ulcers (HSV-2). Both infect the body's nerve cells, where the virus lies dormant until symptoms reappear. Jacobs says: "If our vaccine works in humans as it does in mice, administering it early in life could completely eliminate herpes latency."
  9. Wood rats, western grey squirrels and other small mammals are well recognised as wildlife hosts of the Lyme disease spirochete bacterium in California, but a new study[[55]](#footnote-55) has emphasised the role of birds as reservoirs. The birds identified as significant hosts of Borrelia burgdorferi, such as American robins, dark-eyed juncos and golden-crowned sparrows, are commonly found in suburban environments.
  10. China’s Yisheng Biopharma announced that its new vaccine for the post exposure treatment of rabies was entering human clinical trials.

1. [↑](#footnote-ref-1)
2. Study results were pre-published online by *Blood*, the journal of the American Society of Hematology. The article was entitled “Randomized Phase 2 Study of GMI-1070 in SCD: Reduction In Time To Resolution Of Vaso-Occlusive Crisis and Decreased Opioid Use”. [↑](#footnote-ref-2)
3. in two oral presentations and one poster presentation [↑](#footnote-ref-3)
4. Magdy El-Ekiaby, Mariángela Vargas, Makram Sayed, George Gorgy, Hadi Goubran, Mirjana Radosevic, Thierry Burnouf “Minipool Caprylic Acid Fractionation of Plasma Using Disposable Equipment: A Practical Method to Enhance Immunoglobulin Supply in Developing Countries”, *PLOS Neglected Tropical Diseases,*Published: February 26, 2015, DOI: 10.1371/journal.pntd.0003501 [↑](#footnote-ref-4)
5. Octaplas is made from plasma frozen within eight hours of collection in order to preserve labile coagulation factors. It undergoes multiple manufacturing steps, including plasma pooling, cell filtration and solvent detergent treatment. These steps are claimed to “minimize pathogen transmission and reduce the risk of adverse events such as transfusion related acute lung injury (TRALI), and allergic reactions.” [↑](#footnote-ref-5)
6. Octaplas can now be used within 24 hours if refrigerated (between 1°C and 6°C) or within 8 hours if stored at room temperature (between 20°C and 25°C). Previous product information had directed that thawed product should be used within 12 hours if stored between 2°C and 4°C or within three hours if stored between 20°C and 25°C. [↑](#footnote-ref-6)
7. Octaplas can now be stored frozen, ≤-18°C, for three years from the date of manufacture rather than two. [↑](#footnote-ref-7)
8. after Phase I studies showed that the agent induced “immediate, complete and sustained reversal of dabigatran-induced anticoagulation in healthy humans” [↑](#footnote-ref-8)
9. Alkahest was founded in 2014 by scientists who demonstrated at Stanford University that factors in the blood of young animals were able to restore mental capabilities in old animals. In their study published online May 4, 2014 in *Nature Medicine* they characterized important molecular, neuroanatomical and neurophysiological changes in the brains of old mice that shared the blood of young mice. [↑](#footnote-ref-9)
10. Researchers at the University of Pennsylvania, Emory University, Duke University and the University of Massachusetts. The collaborators also work with VGXi, a contract DNA plasmid manufacturer based in Texas, and Waisman Biomanufacturing, a contract protein manufacturer in Wisconsin. [↑](#footnote-ref-10)
11. Elliott K. Main, from California Maternal Quality Care Collaborative, Stanford University, Palo Alto, and the Department of Obstetrics and Gynecology, California Pacific Medical Center, San Francisco, and colleagues reporte on the study in the April 2015 issue of *Obstetrics & Gynecology*. [↑](#footnote-ref-11)
12. Soubra A, Zabell JR, Adejoro O, Konety BR, “Effect of Perioperative Blood Transfusion on Mortality for Major Urologic Malignancies” [*Clin Genitourin Cancer.*](http://www.ncbi.nlm.nih.gov/pubmed/25600760) 2014 Dec 18. pii: S1558-7673(14)00266-3. doi: 10.1016/j.clgc.2014.12.006. [**PubMed Abstract**](http://www.ncbi.nlm.nih.gov/pubmed/25600760) **PMID:** 25600760 [↑](#footnote-ref-12)
13. **Lixia Li**†, **Yongyang Li**†, **Xiaoxing Xu**, **Bo Xu**4, **Rongrong Ren**4, **Yan Liu**, **Jian Zhang** and **Bin He, “**Safety evaluation on low-molecular-weight hydroxyethyl starch for volume expansion therapy in pediatric patients: a meta-analysis of randomized controlled trials”, *Critical Care* 2015, 19:79 doi:10.1186/s13054-015-0815-y [↑](#footnote-ref-13)
14. Philippe Van der Linden, Melanie Dumoulin, Celine Van Lerberghe, Cristel Sanchez, Torres Ariane Willems, David Faraoni, “Efficacy and safety of 6% hydroxyethyl starches 130/0.4 (Voluven® ) for perioperative volume replacement in children undergoing cardiac surgery: a propensity-matched analysis”, *Critical Care* 2015, 19:87 Published on 17 March 2015. [↑](#footnote-ref-14)
15. A total of 2,430 adults participated in the study, including 1,211 patients in the fresh blood group and 1,219 in the older blood group. In the fresh blood group, 423 patients died within 90 days post-transfusion, compared with 398 patients who died in the group that received older blood. [↑](#footnote-ref-15)
16. published in the 2 March issue of *The Annals of Thoracic Surgery*. [↑](#footnote-ref-16)
17. [Westenbrink BD](http://www.ncbi.nlm.nih.gov/pubmed/?term=Westenbrink%20BD%5BAuthor%5D&cauthor=true&cauthor_uid=25683276), [Alings M](http://www.ncbi.nlm.nih.gov/pubmed/?term=Alings%20M%5BAuthor%5D&cauthor=true&cauthor_uid=25683276), [Connolly SJ](http://www.ncbi.nlm.nih.gov/pubmed/?term=Connolly%20SJ%5BAuthor%5D&cauthor=true&cauthor_uid=25683276), [Eikelboom J](http://www.ncbi.nlm.nih.gov/pubmed/?term=Eikelboom%20J%5BAuthor%5D&cauthor=true&cauthor_uid=25683276), [Ezekowitz MD](http://www.ncbi.nlm.nih.gov/pubmed/?term=Ezekowitz%20MD%5BAuthor%5D&cauthor=true&cauthor_uid=25683276), [Oldgren J](http://www.ncbi.nlm.nih.gov/pubmed/?term=Oldgren%20J%5BAuthor%5D&cauthor=true&cauthor_uid=25683276), [Yang S](http://www.ncbi.nlm.nih.gov/pubmed/?term=Yang%20S%5BAuthor%5D&cauthor=true&cauthor_uid=25683276), [Pongue J](http://www.ncbi.nlm.nih.gov/pubmed/?term=Pongue%20J%5BAuthor%5D&cauthor=true&cauthor_uid=25683276), [Yusuf S](http://www.ncbi.nlm.nih.gov/pubmed/?term=Yusuf%20S%5BAuthor%5D&cauthor=true&cauthor_uid=25683276), [Wallentin L](http://www.ncbi.nlm.nih.gov/pubmed/?term=Wallentin%20L%5BAuthor%5D&cauthor=true&cauthor_uid=25683276), [van Gilst WH](http://www.ncbi.nlm.nih.gov/pubmed/?term=van%20Gilst%20WH%5BAuthor%5D&cauthor=true&cauthor_uid=25683276), “Anemia predicts thromboembolic events, bleeding complications and mortality in patients with atrial fibrillation: Insights form the RE-LY trial”, [*J Thromb Haemost*.](http://www.ncbi.nlm.nih.gov/pubmed/25683276) 2015 Feb 13. doi: 10.1111/jth.12874. [Epub ahead of print] [↑](#footnote-ref-17)
18. [Leslie W. Chan](http://stm.sciencemag.org/search?author1=Leslie+W.+Chan&sortspec=date&submit=Submit), [Xu Wang](http://stm.sciencemag.org/search?author1=Xu+Wang&sortspec=date&submit=Submit), [Hua Wei](http://stm.sciencemag.org/search?author1=Hua+Wei&sortspec=date&submit=Submit), [Lilo D. Pozzo](http://stm.sciencemag.org/search?author1=Lilo+D.+Pozzo&sortspec=date&submit=Submit), [Nathan J. White](http://stm.sciencemag.org/search?author1=Nathan+J.+White&sortspec=date&submit=Submit), and [Suzie H. Pun](http://stm.sciencemag.org/search?author1=Suzie+H.+Pun&sortspec=date&submit=Submit)[,](http://stm.sciencemag.org/content/7/277/277ra29#corresp-1),“A synthetic fibrin cross-linking polymer for modulating clot properties and inducing hemostasis” [Science Translational Medicine](http://stm.sciencemag.org/content/7/277/277ra29). 4 March 2015: Vol. 7, Issue 277, p. 277ra29 *Sci. Transl. Med*. DOI: 10.1126/scitranslmed.3010383 [↑](#footnote-ref-18)
19. [Butz DR, et al. *Plast Reconstr Surg.* 2015;doi:10.1097/PRS.0000000000000988.](http://journals.lww.com/plasreconsurg/Fulltext/2015/02000/Advanced_Age_Is_a_Predictor_of_30_Day.6.aspx) [↑](#footnote-ref-19)
20. [Vedovati MC, et al.CHEST 2015; doi:10.1378/chest.14-0402.](http://journal.publications.chestnet.org/article.aspx?articleid=1905082) [↑](#footnote-ref-20)
21. The researchers acknowledged several limitations of their study; they also variously acknowledged personal fees from Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, Daiichi-Sankyo and Sanofi, as well as speaking fees from Bayer and Boehringer Ingelheim. [↑](#footnote-ref-21)
22. In the journal Stem Cells. Authors included Linzhao Cheng (Edythe Harris Lucas and Clara Lucas Lynn Professor of Hematology and a member of the Institute for Cell Engineering) [↑](#footnote-ref-22)
23. The results appear in an upcoming issue of the journal *Stem Cells*. Authors Linzhao Cheng. [↑](#footnote-ref-23)
24. Published March 2 in the journal *Blood* [↑](#footnote-ref-24)
25. The technique used specially engineered enzymes, zinc-finger nucleases, to replace the mutated genetic code with a corrected version that repairs the beta-globin mutation. Researchers say the method holds the potential to permanently treat the disease if a higher level of correction is achieved. [↑](#footnote-ref-25)
26. The findings were published online in the journal *Blood* [↑](#footnote-ref-26)
27. The study was published in the *New England Journal of Medicine.* [↑](#footnote-ref-27)
28. # Eszter Voros, Minjung Cho, Maricela Ramirez, Anna Lisa Palange, Enrica De Rosa, Jaehong Key, Zsolt Garami, Alan B. Lumsden and Paolo Decuzzi. “TPA Immobilization on Iron Oxide Nanocubes and Localized Magnetic Hyperthermia Accelerate Blood Clot Lysis”, *Advanced Functional Materials,* Article first published online: 11 Feb 2015. DOI: 10.1002/adfm.20140435

    [↑](#footnote-ref-28)
29. see the *Journal of Clinical Investigation* [↑](#footnote-ref-29)
30. The findings were published in the March 4 issue of the journal Science Translational Medicine. [↑](#footnote-ref-30)
31. reported recently in the journal *Circulation* [↑](#footnote-ref-31)
32. The research was published in the journal [*Nature Biotechnology*](http://www.nature.com/nbt/journal/vaop/ncurrent/full/nbt.3154.html). [↑](#footnote-ref-32)
33. The research team tracked outcomes for more than 20,000 adults in China with high blood pressure who had not suffered a heart attack or stroke. Participants were randomly assigned to take a daily pill with folic acid and the high blood pressure drug enalapril (brand name Vasotec) or a pill with enalapril alone. Over a median treatment period of 4.5 years, first strokes occurred in 2.7 percent of those in the enalapril/folic acid group and 3.4 percent of those in the enalapril group Patients taking enalapril/folic acid also had a lower risk of ischemic stroke (2.2 percent versus 2.8 percent), specifically. Ischemic strokes are strokes caused by a blockage, and comprise about by far the largest proportion all strokes. Adding folic acid was also associated with a reduction in heart-related death, heart attack and stroke (3.1 percent versus 3.9 percent). The study was published 15 March in the *Journal of the American Medical Association* and was presented simultaneously at a meeting of the American College of Cardiology in San Diego. [↑](#footnote-ref-33)
34. Researchers examined the virus-antibody complex structure at very high magnification and showed that each arm of the antibody is surprisingly effective in grabbing three surface proteins on the surface of the virus at the same time. The sites on the virus where the antibody was bound were critical for the virus to invade cells. "This kind of binding with the virus has never been observed and it explains why the antibody itself is so highly potent," said Associate Professor [Shee Mei Lok](http://economictimes.indiatimes.com/topic/Shee-Mei-Lok) from [Duke-NUS Graduate Medical School Singapore](http://economictimes.indiatimes.com/topic/Duke-NUS-Graduate-Medical-School-Singapore) (Duke-NUS). "The movement of virus surface proteins is highly essential for invading cells-you can think of antibody 5J7 locking the virus surface proteins, thus strapping the virus," said Lok, senior author of the study. Lok said the compound will first be tested in mouse models, and then researchers hope to move to clinical trials. [↑](#footnote-ref-34)
35. The study was published in the journal *Nature Communications* [↑](#footnote-ref-35)
36. When a patient is infected by one serotype this stimulates the production of a variety of antibodies that kills that serotype, and that patient will have life-time immunity towards that particular serotype. However, in this process, the patient will become susceptible to developing a more severe form of the disease if they are infected with another serotype. [↑](#footnote-ref-36)
37. Goel S, Palmkvist M, Moll K, et al. “RIFINs are Adhesins Implicated in Severe Plasmodium falciparum Malaria”. Nature Medicine. 2015. [↑](#footnote-ref-37)
38. Inner city Brisbane has had its worst outbreak in twenty years. The virus is transmitted from animals such as wallabies and possums to humans by mosquitoes that breed in salt marshes, rivers and domestic containers. A vaccine for the virus has been developed but the designer, Queensland virologist Professor John Aaskov, said governments and suppliers were reluctant to take it up because of cost. [↑](#footnote-ref-38)
39. As in previous years, national or regional authorities approve the composition and formulation of vaccines used in each country. National public health authorities are responsible for making recommendations regarding the use of the vaccine. [↑](#footnote-ref-39)
40. WHO noted that in the northern hemisphere flu season just ending the Americas, Asia and Europe had reported high levels of circulating flu viruses and low levels of protection from vaccines that did not match the relevant strains. [↑](#footnote-ref-40)
41. WHO reported that from 2003 until October 2014 there were 686 human cases testing positive for H5N1 globally, of which 393 were fatal. [↑](#footnote-ref-41)
42. Found this year in poultry and wild birds in Washington State, Oregon, Idaho, and British Columbia, and now confirmed in a turkey flock in Minnesota. The U.S. Animal and Plant Health Inspection Service (APHIS) is paying particular attention to what is termed the Mississippi flyway, a flight path for migratory birds running up from the Gulf of Mexico through the US Midwest into Ontario, Manitoba and Saskatchewan, Canada’s northern territories, northwestern Quebec and the Alberta and British Columbia. [↑](#footnote-ref-42)
43. 38 bird flu cases had been diagnosed in 2015, significantly in poor rural areas, where villagers raise poultry on the rooftops of their homes to supplement their diet. [↑](#footnote-ref-43)
44. Published in the 11 March issue of Cell Host & Microbe, senior author Ram Sasisekharan, the Alfred H. Caspary Professor of Biological Engineering at MIT. [↑](#footnote-ref-44)
45. Total confirmed cases globally since March 2013 was 638, 618 in mainland China, 13 in Hong Kong, 4 in Taiwan, 2 in Canada and 1 in Malaysia. [↑](#footnote-ref-45)
46. of the Food and Environmental Hygiene Department [↑](#footnote-ref-46)
47. About 267 000 tonnes of chilled and frozen poultry meat and about 530 million poultry eggs were exported to Hong Kong from the US in 2014. [↑](#footnote-ref-47)
48. The research is published ahead of print February 11, in the *Journal of Virology*. [↑](#footnote-ref-48)
49. a Member in the Infectious Diseases Department at St. Jude Children's Research Hospital, Memphis, and Director of the World Health Organization (WHO) Collaborating Center for Studies on the Ecology of Influenza Viruses in Lower Animals and Birds. [↑](#footnote-ref-49)
50. Katelyn Gostic, Adam Kucharski, Jamie Lloyd-Smith. Effectiveness of traveller screening for emerging pathogens is shaped by epidemiology and natural history of infection. eLife. DOI: 10.7554/eLife.05564 [↑](#footnote-ref-50)
51. Anthrax lives in the soil. It is rare in Australia, but most recent cases have occurred in the dairy farms in Victoria’s Goulburn Valley. In 2007, 34 cattle died of anthrax at Tatura and Stanhope. A mass vaccination program of 32,000 cattle was undertaken. [↑](#footnote-ref-51)
52. See Ning-Shao Xia (professor, department of biology, Xiamen University, China); John Ward (director, division of viral hepatitis, US Centers for Disease Control and Prevention); March 5, 2015, *New England Journal of Medicine* [↑](#footnote-ref-52)
53. Gardner MR, Kattenhorn LM, Kondur HR, von Schaewen M, Dorfman T, Chiang JJ, Haworth KG, Decker JM, Alpert MD, Bailey CC, Neale ES, Fellinger CH, Joshi VR, Fuchs SP, Martinez-Navio JM, Quinlan BD, Yao AY, Mouquet H, Gorman J, Zhang B, Poignard P, Nussenzweig MC, Burton DR, Kwong PD, Piatak M, Lifson JD, Gao G, Desrosiers RC, Evans DT, Hahn BH, Ploss A, Cannon PM, Seaman MS, Farzan M, “[AAV-expressed eCD4-Ig provides durable protection from multiple SHIV challenges”](http://www.ncbi.nlm.nih.gov/pubmed/25707797). Nature. 2015 Mar 5;519(7541):87-91. doi: 10.1038/nature14264. Epub 2015 Feb 18. PMID: 25707797. [↑](#footnote-ref-53)
54. Findings were reported on March 10, 2015, in the journal *eLife*. [↑](#footnote-ref-54)
55. published 25 February in the journal PLOS ON, lead author Erica Newman, a UC Berkeley Ph.D. student in the Energy and Resources Group and the Department of Environmental Science, Policy and Management at the University of California at Berkeley. [↑](#footnote-ref-55)