ISBT Science Series
An affiliated publication to Vox Sanguinis

ISBT International Society of Blood Transfusion

ISBT Science Series (2019) **14**, 140–145

CONGRESS REVIEW

5C-S43-01

DOI: 10.1111/voxs.12473

Emerging infectious diseases and blood donation

Bertram Kjerulff & Christian Erikstrup

Department of Clinical Immunology, Aarhus University Hospital, Aarhus, Denmark

Received: 30 August 2018,
revised 17 October 2018,
accepted 25 October 2018,
published online 20 November 2018

Emerging infectious diseases (EIDs) require vigilance from blood banks everywhere. As EIDs spread to new areas and populations, blood banks are forced to re-evaluate safety measures continually. Screening, pathogen inactivation and deferral policies must be balanced against supply, safety and cost-effectiveness. One size does not fit all, and blood banks must adjust to local needs and conditions when considering initiation or halting of screening, pathogen inactivation or deferral procedures to balance between demand/supply, safety and economy.

Key words: blood safety, deferral, emerging infectious diseases, risk assessment, screening, Zika

Introduction

A generally accepted definition of an emerging infectious disease (EID) is a disease likely to increase in incidence because it is caused by a new pathogen or by a known pathogen spreading to new areas [1]. Each year, EIDs are described, several of which could be associated with a risk of transfusion transmission (TT) and compromise blood safety. These EIDs comprise the re-emerging of older diseases due to, for example climate changes, environmental changes or the intensified travelling associated with globalization. The emergence of new drug-resistant pathogen strains may also be considered as EIDs. EIDs pose a risk to blood safety when the EID has an asymptomatic phase and is present in blood, and when the transfused pathogen can establish a symptomatic infection in the recipient [2]. Symptomatic donors would generally not present for donation or be detected in the predonation health screening. To evaluate the risk of TT of the EID, we must know the incidence in the population and the length of the period in which a donor may be infectious but not detectable by screening. This is further complicated because no screening assays are available for many EIDs, and even those that are available may not be implemented in relevant setting. Furthermore, it is useful to know about the risk of infection, asymptomatic period lengths and ratio of symptomatic infections [3]. Blood services are typically risk adverse and often take a precautionary approach with EIDs as one or more characteristics are often not known when a mitigation strategy is planned. The action taken by the blood service comprise either to defer donors who visited areas with transmission, stop donations in the areas, defer donors based on certain behaviour, initiate testing if possible or maybe introduce pathogen inactivation procedures. When data are still sparse, there is a great risk of both under and overreacting. Adhering to the precautionary principle, that is to minimize even theoretical risks, is often a strategy when a disease is not completely understood. In this review, we will describe a few of the EIDs that have or could have implications for blood safety and discuss the considerations regarding when to initiate and halt blood safety measures.

Correspondence: Department of Clinical Immunology, Aarhus University Hospital, Palle Juul-Jensens Boulevard 99, 8200 Aarhus, Denmark
E-mail: bertram.kjerulff@hotmail.com

Why are more pathogens emerging–challenges in the world of today

The increase in EIDs has several explanations, many of which are attributable to human actions. Humans have always travelled but increased traffic has allowed for faster spread of diseases. The increase in traffic encompasses air traffic and consequently reduced travel time. Travellers who would have become sick before arrival may now arrive several days before symptoms occur. Additionally, cargo shipping leads to vector spread as ships provide mobile breeding grounds and transport for mosquitoes and rodents. Together the increase in travelling and shipping may allow spread of arthropods and

establishment of new zoonotic reservoirs [4, 5]. These effects of globalization can be problematic as the spread of vectors both due to introduction into new areas, adaptation to new areas and due to expansion of habitable zones caused by increasing temperatures, and new breeding grounds formed by construction of dams and irrigation systems provide opportunity for disease spread. Large farms allow for zoonotic reservoirs to be near humans providing opportunities for transmission into humans, as has been seen in cases of bird flu spread from markets and farms [6]. As the climate changes, there will also be changes to the habitable zones of disease-carrying mosquitoes, which is a problem when regarding malaria and arboviruses as Zika virus, Ross River virus, Rift Valley fever virus (RVFV), West Nile virus (WNV), Chikungunya virus (CHIKV), yellow fever and dengue fever virus (DENV). Below we will provide some brief background on a few EIDs relevant for transfusion safety.

The use of antibiotics and antifungals in agriculture is another cause for EIDs as the pathogens become resistant and hard to treat leading to re-emerging of previously controllable infections, and at the same time, in several countries, there has been little control with prescription of antibiotics for humans while poor adherence to treatment has allowed for more pathogens to become resistant as with the occurrence of treatment-resistant tuberculosis [7] and malaria [8]. Other diseases may re-emerge as a consequence of failure in the healthcare system, and examples are outbreaks of polio and measles in war zones in Syria [9, 10] and cholera in refugee camps [11]. If these diseases are re-emerging, others may also emerge and spread. In recent years, strains of antibiotic resistant *Shigella*, *Salmonella* and *Campylobacter* have emerged and spread with travel [12].

A very important reason for the growing number of EIDs is also the increase in surveillance and indeed a greater focus on EIDs, which leads to the discovery of increases in incidence of known diseases, old diseases in new places or even new diseases [5].

Some current EIDs relevant for blood safety

Flavivirus

Several EIDs have influenced our prescreening and screening of donors in recent years.

As a good example, we can mention WNV. WNV is a flavivirus transmitted by mosquitoes, primarily *Culex* species [13]. The main hosts are birds, and the infection is maintained as an enzootic infection. Several mammals, especially horses, are also infected but represent a dead end for the virus due to low levels of viraemia. WNV was endemic to Southern Europe, Africa, parts of Asia and Australia but not the Americas until an outbreak in New York in 1999 [14]. About 20% of infected individuals develop symptoms such as headache, fever, rash, and only 1/150 experience serious symptoms as encephalitis with significant fatality rate. In the years 1999-2010, there was a cumulative estimate of 3 million infections in the United States [15]. Several cases of TT have been reported, and in the United States alone, 36 cases were reported between 2003 and 2012 with additional reports subsequently [14, 16]. Screening for WNV by nucleic acid test was implemented in the United States in 2003. Since 2004, blood centres in the EU have been obliged to either defer donors for 28 days after travelling to or living in endemic areas or implement blood screening procedures [17].

Zika virus (ZIKV) is also a flavivirus that has caught headlines in recent years. It is transmitted mainly by the mosquito species *Aedes aegypti*. After an incubation period of 3–14 days, about 20% develop symptoms which are often non-specific and similar to those described for WNV [18]. The most serious complication is seen in pregnant women where infection is associated with a risk of microcephaly in the child [19]. Infected individuals, regardless of symptoms or not, are viraemic for a period of about 1 week but may be viraemic for more than 28 days with a proposed threat to blood safety as a consequence [20]. ZIKV was discovered in 1947 but only a few cases were reported before a major epidemic in Yap Island, Federated States of Micronesia, in 2007. Approximately 73% of the population was infected [21], and subsequently, it spreads to French Polynesia and the Americas. While the extent of the epidemic has meant that a high number of viraemic blood donors have been bled, it should be noted that only four potential transfusion-transmitted Zika virus events have been reported [22, 23]. In French Polynesia, retrospective testing of donations for ZIKV showed that no TT infection was detected after the transfusion of 30 blood products with RNA-reactive blood [24].

Zika virus remains in semen for up to 188 [25] days, and several cases of sexually transmitted virus have been reported [26]. The risk of sexual transmission is cause for concern in pregnant women, or women trying to become pregnant, due to risk of microcephaly. Furthermore, the risk of sexual transmission of Zika virus allows for spread outside endemic areas theoretically rendering TT a possibility and it was a contributing factor for the initiation of screening in the United States [27]. The screening programme in the United States was initiated in 2016 by injunction by the Food and Drug Administration (FDA) [28]. Screening was initiated while there were still many unknown factors regarding transmission and spread. Subsequent cost-effectiveness analysis has, however, shown that costs related to universal screening of donations in

the United States are high considering a yield of only nine in 3 932 176 screened donations [29]. Screening has also been used in a few other areas while most areas use a 28-day deferral which is recommended by, for example, the European Centre for Disease Control [30]. Universal ZIKV testing is still performed in the United States.

Usutu virus is another arbovirus in the Flaviviridae family maintaining a zoonotic reservoir in birds. In 2001, it was confirmed in Austria and has since been detected in other places in Europe. It has been found in a German blood donor [31] and is suspected to be more frequent than WNV in some regions [32]. A possible case of TT Usutu fever has been reported in Italy [33]. Like the other mentioned arboviruses, infections are mostly asymptomatic but there have been cases of disease in humans [34]. The relevance of Usutu virus for blood safety is still under investigation.

Japanese encephalitis virus (JEV) is a flavivirus transmitted by mosquitoes of the *Culex* species, and very recently, the first confirmed TT case was reported in Hong Kong [35]. Less than 1% of the infected individuals develop neurological symptoms but the mortality rate in patients with symptoms is as high as 30% and neurological damage in survivors may be permanent [36]. Infection of birds and introduction into new mosquito populations could cause spread of JEV outside Asia. Vaccination is available and along with deferral of donors with a travel history in endemic areas; TT outside endemic areas could hopefully be avoided.

Dengue fever virus is a flavivirus, primarily transmitted by *Aedes* mosquitoes, found in most of the tropics with frequent season-dependent outbreaks. About 75% are asymptomatic, and the symptoms are mild febrile disease but with a risk of more severe dengue shock syndrome or haemorrhage. Cases of transfusion transmission, including cases resulting in disease, have been reported, and a NAT screening option is available although not widely implemented[37, 38].

Other virus families

Borna disease virus (BoDV), of the orthobornavirus genus, is known to cause behavioural changes in mammals, and BoDV antibodies have been found in several patients with mental and neuropsychiatric disorders [39, 40]. Earlier this year, three persons in Germany developed acute encephalitis after receiving organs from an infected donor. Another case was detected simultaneously in a person who did not receive a transplant [41]. The transmission in transplantation calls for caution in BoDV endemic areas as TT may be possible.

In 2007 Chikungunya virus, an alphavirus in the Togaviridae family spread by *Aedes* mosquitoes established itself in Italy, presumably originating from an Indian strain brought to Italy by travel, carrying the A226V mutation allowing for infection of more mosquito species [42, 43]. Screening is not performed for CHIKV, except for platelet donation for a time on Reunion Island [44], and there are no reported cases of TT, although TT is believed to be possible [45]. This could introduce a need for additional screening or travel deferral during the summer months in several European countries if the disease spreads and TTs are reported.

In the past two decades, arboviruses, and flaviviruses in particular, have been in the spotlight when regarding new TT infections and several cases have been reported. It should, however, be noted that arboviruses are most often not easily transmittable by transfusion and the reason for this is unknown. There are other arboviruses that could potentially cause TT but with no reported cases and for which screening is not performed, like Mayaro virus and Rift River Valley virus [46]. These viruses could be candidates for the next outbreak along with Ross River virus, which already has reported TT but where recall and donation restrictions are considered adequate to supersede screening [47].

Hepatitis E virus (HEV) is an orthohepevirus causing inflammation in the liver. In 2014 in the United Kingdom, blood donors were shown to frequently (1/2848) be viraemic with HEV. It was moreover shown to be transfusion transmittable [48]. Even though no morbidity due to TT HEV was found in the study, 18/43 recipients showed signs of infection. In France, the seroprevalence of HEV-specific IgG among 10 569 blood donors was found to be 22% and increasing with age [49].

Hepatitis E virus is an orthohepevirus, in the Hepeviridae family, mostly transmitted to humans through consumption of infected and undercooked foods and contaminated water [49]. Screening is mostly performed by NAT supported by confirmatory testing. In Germany, 1:679 to 1:4252 were found RNA positive, in France, it was 1:2218, and in Denmark, it was 1/2330 [50]. Increases in the number of reported cases and the risk of TT have caused some European countries (United Kingdom, Ireland, the Netherlands) to initiate screening of blood while others are considering it or are evaluating the situation (Germany, France, Switzerland, Greece, Portugal, Italy, Poland, Spain) [51]. In Denmark, it was decided not to screen but the decision is up for re-evaluation this year. Infection is mostly asymptomatic but immunocompromised patients and patients with pre-existing liver disease may develop chronic or fulminant hepatitis. Selective screening of blood for patients in these risk groups has also been considered and performed; however, this involves logistical challenges possibly limiting cost advantage compared to universal

screening. In the Netherlands, the general screening is estimated to have a cost of 310 000 € per avoided chronic case [52].

Babesiosis is caused by infection with the *Babesia* parasite, most often *Babesia microtii* [53]. It is usually transmitted through tick bites and causes malaria-like symptoms. The first infection of a human was reported in Croatia in 1957 but it has since been reported around the world, often in areas that also has Lyme disease [54]. TT of babesia is believed to be the most common TT pathogen in the United States, with number of cases possibly as high as 1 per 601 red-blood-cell units [55] though others have found it to be lower (about 1:9000) [56]. It has been argued that donor screening should be initiated, although the cost effectivity should be considered [57]. The FDA recently approved immunoassay and PCR blood donor tests.

Risk assessment in blood donors and when to screen

When considering which diseases to screen for and when several factors should be considered, assessment of TT risk should be performed. One of the first models suggested was the Biggerstaff-Petersen model, developed to estimate TT risk of locally acquired infections [58]. This model estimates risk of collecting an infected blood donation from asymptomatic donors and requires data as number of reported cases, population in the area, duration of viraemia and the ratio of asymptomatic to symptomatic infections.

Collecting the required input data takes time and maybe even several studies to be precise. Unfortunately, risk assessments may not be precise on newly emerged infections with sparse data. The Up-Front Risk Assessment Tool (EUFRAT) is another useful tool released through the ECDC for estimating not only the risk of collecting an infected donation but also the risk of disease transmission including the risk associated with donor travel in areas with ongoing infection. With an estimation of the actual risk of TT, the required steps for securing the blood supply can be considered. Depending on the pathogen, a reliable option for the mitigation of risk can be assessed, for example if cost-efficient methods are available for screening or pathogen inactivation making these viable options compared to deferral through questionnaires.

As an example of the challenges we face with risk assessments, we can reiterate that we are still uncertain on several of the abovementioned viruses' ability to establish clinically relevant TT infections. It is an enigma why TT does not occur more frequently for some of the mosquito-transmitted viral infections. Part of the explanation could be that several of the arboviruses may require mosquito saliva to establish new infections [59]. A transfusion with a high viral load may be less infectious than a single mosquito bite. Another thing which can challenge the consequences of risk assessments is the context: for HEV infection, the risk of food-borne infection may be much greater than to acquire HEV through transfusion. Thus, for HEV, blood screening may only be cost effective if combined with other interventions as screening for HEV or dietary restrictions for immunocompromised patients to avoid exposure.

When choosing an intervention, deferral for travel history is often thought of as a cheap way of risk mitigation in non-endemic areas. However, travel history is a frequent reason for deferral and keeping donors informed of restrictions is important to prevent donors reporting for donation only to be deferred, as on-site deferral makes it less likely for donors to return [60]. Donors who travel frequently may only rarely be eligible for donation, and many donors may be deferred in the time following the main vacation periods. Deferral may be an easily manageable and efficient way to avoid TT of EIDs as returning donors know the questions and thus provide self-selection. However, the cost per prevented infection and gained quality-adjusted life year is very high due to the low specificity of this prescreening [61].

For some pathogens, there are cost-effective and reliable methods for pathogen inactivation using radiation/illumination or chemical treatment of blood products [62]. For some pathogens in some settings, it may be favourable to initiate inactivation instead of screening or deferral, as the same inactivation procedure may work for several pathogens and be a cheaper option than screening, while deferral may also be expensive and cause a considerable drop in available donors [63]. In areas with low infectious pressure, it should, however, be noted that existing studies on the efficacy of pathogen inactivated products compared to untreated products are too small to be conclusive.

Naturally, a certain TT infectious disease cannot be countered by similar interventions everywhere. The most feasible intervention depends on the context. The challenges facing the blood supply differ between high- and low-income countries and between endemic and non-endemic areas, not only because the possible options for screening differ, but also because incidence and prevalence of different diseases vary greatly. The precautionary principle has been widely adapted in high-income countries since the HIV epidemic in the 1980s, but when screening options are limited, infectious pressure is high, or donors are in short supply the risk mitigating strategies must be evaluated accordingly, as some risks may be acceptable to maintain an adequate blood supply. Where screening and deferral might be the favourable strategy

in some countries, others might favour more from pathogen inactivation or vector control strategies.

When to stop screening

More and more pathogens with potential to cause EIDs are reported, and fortunately, our possibilities for testing or implementing other interventions are increasing as well. However, only very rare examples exist of stopping a universal blood screening test when more detailed evidence of the risk is available. The precautionary principle and the great focus on blood safety since the HIV epidemic in the 1980s have prevented the out phasing of tests. The healthcare systems in most countries are faced with demands of cost reductions, and it is important to evaluate interventions for blood safety and consider their cost-effectiveness as it is for other health-related costs. Therefore, it is important to perform re-evaluations of existing screening and deferral procedures as the EIDs become more thoroughly researched or circumstances change.

Acknowledgements

BE and CE both wrote, revised and approved this manuscript.

Conflict of interests

The authors declare no conflict of interests.

References

1 van Doorn HR: Emerging infectious diseases. *Medicine (Abingdon)* 2014; **42**:60–63
2 Dodd RY: Emerging pathogens and their implications for the blood supply and transfusion transmitted infections. *Br J Haematol* 2012; **159**:135–142
3 Kiely P, Gambhir M, Cheng AC, *et al.*: Emerging infectious diseases and blood safety: modeling the transfusion-transmission risk. *Transfus Med Rev* 2017; **31**:154–164
4 Lounibos LP: Invasions by insect vectors of human disease. *Annu Rev Entomol* 2002; **47**:233–266
5 Lipkin WI: The changing face of pathogen discovery and surveillance. *Nat Rev Microbiol* 2013; **11**:133–141
6 To KK, Tsang AK, Chan JF, *et al.*: Emergence in China of human disease due to avian influenza A(H10N8)–cause for concern? *J Infect* 2014; **68**:205–215
7 Seung KJ, Keshavjee S, Rich ML: Multidrug-resistant tuberculosis and extensively drug-resistant tuberculosis. *Cold Spring Harb Perspect Med* 2015; **5**:a017863
8 Sinha S, Medhi B, Sehgal R: Challenges of drug-resistant malaria. *Parasite* 2014; **21**:61
9 WHO EMRO: Situation Report on the Polio Outbreak in Syria 31 July 2018. http://www.emro.who.int/syr/syria-infocus/situation-reports-on-the-polio-outbreak-in-syria.html [Last accessed 24-08 2018].
10 Ozaras R, Leblebicioglu H, Sunbul M, *et al.*: The Syrian conflict and infectious diseases. *Expert Rev Anti Infect Ther* 2016; **14**:547–555
11 Scobie HM, Phares CR, Wannemuehler KA, *et al.*: Use of oral cholera vaccine and knowledge, attitudes, and practices regarding safe water, sanitation and hygiene in a long-standing Refugee Camp, Thailand, 2012-2014. *PLoS Negl Trop Dis* 2016; **10**:e0005210
12 Schwartz KL, Morris SK: Travel and the spread of drug-resistant bacteria. *Curr Infect Dis Rep* 2018; **20**:29
13 Colpitts TM, Conway MJ, Montgomery RR, *et al.*: West Nile Virus: biology, transmission, and human infection. *Clin Microbiol Rev* 2012; **25**:635–648
14 Dodd RY, Foster GA, Stramer SL: Keeping blood transfusion safe from West Nile Virus: American Red Cross Experience, 2003 to 2012. *Transfus Med Rev* 2015; **29**:153–161
15 Petersen LR, Carson PJ, Biggerstaff BJ, *et al.*: Estimated cumulative incidence of West Nile virus infection in US adults, 1999-2010. *Epidemiol Infect* 2013; **141**:591–595
16 Groves JA, Shafi H, Nomura JH, *et al.*: A probable case of West Nile virus transfusion transmission. *Transfusion* 2017; **57**:850–856
17 Pisani G, Cristiano K, Pupella S, *et al.*: West Nile Virus in Europe and safety of blood transfusion. *Transfus Med Hemother* 2016; **43**:158–167
18 Krow-Lucal ER, Biggerstaff BJ, Staples JE: Estimated incubation period for Zika virus disease. *Emerg Infect Dis* 2017; **23**:841–845
19 Johansson MA, Mier-y-Teran-Romero L, Reefhuis J, *et al.*: Zika and the risk of microcephaly. *N Engl J Med* 2016; **375**: 1–4
20 Mansuy JM, Mengelle C, Pasquier C, *et al.*: Zika virus infection and prolonged Viremia in whole-blood specimens. *Emerg Infect Dis* 2017; **23**:863–865
21 Duffy MR, Chen TH, Hancock WT, *et al.*: Zika virus outbreak on Yap Island, Federated States of Micronesia. *N Engl J Med* 2009; **360**:2536–2543
22 Motta IJ, Spencer BR, Cordeiro da Silva SG, *et al.*: Evidence for transmission of Zika virus by platelet transfusion. *N Engl J Med* 2016; **375**:1101–1103
23 Barjas-Castro ML, Angerami RN, Cunha MS, *et al.*: Probable transfusion-transmitted Zika virus in Brazil. *Transfusion* 2016; **56**:1684–1688
24 Bierlaire D, Mauguin S, Broult J, *et al.*: Zika virus and blood transfusion: the experience of French Polynesia. *Transfusion* 2017; **57**:729–733
25 Nicastri E, Castilletti C, Liuzzi G, *et al.*: Persistent detection of Zika virus RNA in semen for six months after symptom onset in a traveller returning from Haiti to Italy, February 2016. *Euro Surveill*; **21**:21.32.30314
26 Mead PS, Hills SL, Brooks JT: Zika virus as a sexually transmitted pathogen. *Curr Opin Infect Dis* 2018; **31**:39–44
27 Bloch EM, Ness PM, Tobian AAR, *et al.*: Revisiting blood safety practices given emerging data about Zika virus. *N Engl J Med* 2018; **378**:1837–1841

28 FDA: FDA advises testing for Zika virus in all donated blood and blood components in the US. 2016. https://www.fda.gov/newsevents/newsroom/pressannouncements/ucm518218.htm [Last accessed 30-08 2018]

29 Saa P, Proctor M, Foster G, *et al.*: Investigational testing for Zika virus among U.S Blood donors. *N Engl J Med* 2018; **378**:1778–1788

30 ECDC: Zika virus and safety of substances of human origin: a guide for preparedness activities in Europe - first update. 2017. https://ecdc.europa.eu/en/publications-data/zika-virus-and-safety-substances-human-origin-guide-preparedness-activities-0 [Last accessed 30-08 2018]

31 Cadar D, Maier P, Muller S, *et al.*: Blood donor screening for West Nile virus (WNV) revealed acute Usutu virus (USUV) infection, Germany, September 2016. *Euro Surveill* 2017; **22**:30501

32 .Grottola A, Marcacci M, Tagliazucchi S, *et al.*: Usutu virus infections in humans: a retrospective analysis in the municipality of Modena, Italy. *Clin Microbiol Infect* 2017; **23**:33–37

33 Cavrini F, Gaibani P, Longo G, *et al.*: Usutu virus infection in a patient who underwent orthotropic liver transplantation, Italy, August-September 2009. *Euro Surveill* 2009; **14**:19448

34 Gaibani P, Rossini G: An overview of Usutu virus. *Microbes Infect.* 2017; **19**:382–387

35 Cheng VCC, Sridhar S, Wong SC, *et al.*: Japanese encephalitis virus transmitted via blood transfusion, Hong Kong, China. *Emer Infect Dis*. 2018; **24**: 49–57

36 WHO: Japanese Encephalitis. WHO.int, 2015. http://www.who.int/news-room/fact-sheets/detail/japanese-encephalitis) [Last accessed 24/08 2018]

37 Pozzetto B, Memmi M, Garraud O: Is transfusion-transmitted dengue fever a potential public health threat? *World J Virol* 2015; **4**:113–123

38 Levi JE: Dengue virus and blood transfusion. *J Infect Dis* 2016; **213**:689–690

39 Richt JA, Pfeuffer I, Christ M, *et al.*: Borna disease virus infection in animals and humans. *Emerg Infect Dis* 1997; **3**:343–352

40 Zaliunaite V, Steibliene V, Bode L, *et al.*: Primary psychosis and Borna disease virus infection in Lithuania: a case control study. *BMC Psychiatry* 2016; **16**:369

41 ECDC: Acute encephalitis associated with infection with Borna disease virus 1, Germany. ecdc.europa.eu, ECDC, 2018. https://ecdc.europa.eu/sites/portal/files/documents/09-03-2018-RRA-Borna%20disease%20virus-Germany.pdf [Last accessed 24-08 2018]

42 Angelini R, Finarelli AC, Angelini P, *et al.*: Chikungunya in north-eastern Italy: a summing up of the outbreak. *Euro Surveill* 2007; **12**:E071122

43 Tsetsarkin KA, Vanlandingham DL, McGee CE, *et al.*: A single mutation in chikungunya virus affects vector specificity and epidemic potential. *PLoS Pathog* 2007; **3**:e201

44 Brouard C, Bernillon P, Quatresous I, *et al.*: Estimated risk of Chikungunya viremic blood donation during an epidemic on Reunion Island in the Indian Ocean, 2005 to 2007. *Transfusion* 2008; **48**:1333–1341

45 Chiu CY, Bres V, Yu G, *et al.*: Genomic assays for identification of Chikungunya virus in blood donors, Puerto Rico, 2014. *Emerg Infect Dis* 2015; **21**:1409–1413

46 Esposito DLA, Fonseca B: Will Mayaro virus be responsible for the next outbreak of an arthropod-borne virus in Brazil? *Braz J Infect Dis*. 2017; **21**:540–544

47 Faddy HM, Tran TV, Hoad VC, *et al.*: Ross River virus in Australian blood donors: possible implications for blood transfusion safety. *Transfusion* 2018; **58**:485–492

48 Hewitt PE, Ijaz S, Brailsford SR, *et al.*: Hepatitis E virus in blood components: a prevalence and transmission study in southeast England. *Lancet* 2014; **384**:1766–1773

49 Mansuy JM, Gallian P, Dimeglio C, *et al.*: A nationwide survey of hepatitis E viral infection in French blood donors. *Hepatology (Baltimore, MD)* 2016; **63**:1145–1154

50 Harritshoj LH, Holm DK, Saekmose SG, *et al.*: Low transfusion transmission of hepatitis E among 25,637 single-donation, nucleic acid-tested blood donors. *Transfusion* 2016; **56**:2225–2232

51 Domanovic D, Tedder R, Blumel J, *et al.*: Hepatitis E and blood donation safety in selected European countries: a shift to screening? *Euro Surveill* 2017; **22**:30514

52 de Vos AS, Janssen MP, Zaaijer HL, *et al.*: Cost-effectiveness of the screening of blood donations for hepatitis E virus in the Netherlands. *Transfusion* 2017; **57**:258–266

53 CDC CfDCaP: Babesiosis CDC.gov, 2014. https://www.cdc.gov/parasites/babesiosis/epi.html [Last accessed 29-08 2018]

54 Vannier E, Gewurz BE, Krause PJ: Human babesiosis. *Infect Dis Clin North Am* 2008; **22**:469–488

55 Gerber MA, Shapiro ED, Krause PJ, *et al.*: The risk of acquiring Lyme disease or babesiosis from a blood transfusion. *J Infect Dis* 1994; **170**:231–234

56 Asad S, Sweeney J, Mermel LA: Transfusion-transmitted babesiosis in Rhode Island. *Transfusion* 2009; **49**:2564–2573

57 Levin AE, Krause PJ: Transfusion-transmitted babesiosis: is it time to screen the blood supply? *Curr Opin Hematol* 2016; **23**:573–580

58 Biggerstaff BJ, Petersen LR: Estimated risk of transmission of the West Nile virus through blood transfusion in the US, 2002. *Transfusion* 2003; **43**:1007–1017

59 Pingen M, Bryden SR, Pondeville E, *et al.*: Host inflammatory response to mosquito bites enhances the severity of Arbovirus infection. *Immunity* 2016; **44**:1455–1469

60 Wevers A, Wigboldus DH, de Kort WL, *et al.*: Characteristics of donors who do or do not return to give blood and barriers to their return. *Blood Transfus* 2014; **12**(Suppl 1):s37–s43

61 de Kort W, van den Burg P, Geerligs H, *et al.*: Cost-effectiveness of questionnaires in preventing transfusion-transmitted infections. *Transfusion* 2014; **54**:879–888

62 Seltsam A: Pathogen inactivation of cellular blood products-an additional safety layer in transfusion medicine. *Front Med (Lausanne)* 2017; **4**:219

63 McCullough J, Goldfinger D, Gorlin J, *et al.*: Cost implications of implementation of pathogen-inactivated platelets. *Transfusion* 2015; **55**:2312–2320