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Transfusion risk associated with recent arbovirus outbreaks in French Polynesia

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Vox Sanguinis

Background and objectives French Polynesia, where dengue virus (DENV) has been present for a long time, experienced two successive outbreaks of Zika (ZIKV) and chikungunya viruses (CHIKV) between 2013 and 2015. To avoid the transmission of these viruses by transfusion, nucleic acid testing (NAT) has been in place for DENV since 2013 and for ZIKV and CHIKV during epidemics. The objective was to compare the estimated risk of viraemic blood donation with NAT results and to discuss the impact on the prevention of transfusion-related infectious risk.

Materials and methods The average risks of viraemic blood donation were estimated per year for DENV, and during the epidemic periods for ZIKV and CHIKV, using the Biggerstaff and Petersen model based on the incidence rate, the mean length of viraemia and the frequency of asymptomatic infection. The estimated risks were compared with the number of viraemic blood donations detected by NAT.

Results According to the different assumptions, risks estimates ranged from 11·2 to 53·1/100 000 donations for DENV, 746 to 1924/100 000 for ZIKV and 1083 / 100 000 for CHIKV. When compared to the number of donations collected during the study periods, these estimates match NAT results (5 blood donors reactive for DENV, 42 for ZIKV and 34 for CHIKV).

Conclusion The risks of viraemic blood donation were related to the viral incidence in the general population and concordant with NAT results. These findings suggest that the screening may be optimized by a targeted NAT implementation based on incidence data.

Key words: arbovirus, blood safety, French Polynesia, nucleic acid testing, risk assessment.

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Background

French Polynesia (FP) is an overseas territory located in the South Pacific with 275 918 inhabitants (census 2017) and 118 islands scattered through an area comparable to Europe. The French Polynesia blood bank (FPBB) is the single transfusion independent operator in charge of all the transfusion chain stages, from the blood collection to the blood products delivery.

In this tropical isolated environment, the FPBB has to secure supply for the entire territory with safe blood products and the successive arbovirus waves affecting the FP archipelagos have been a permanent challenge.

Whilst dengue virus (DENV), the most important mosquito-borne virus affecting humans worldwide, has widely spread in tropical and subtropical regions for decades, unexpected new mosquito-borne viral diseases

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have recently emerged to become a major health concern.

During the past decades, FP has experienced a large number of dengue fever epidemics involving the four serotypes [1–3] with seroprevalence studies reporting anti-dengue rates reaching 80% [4,5]. Starting in 2000, outbreaks of DENV in South Pacific Island Countries (SPICs) have been linked to serotype 1 (DENV-1) which caused recurrent epidemics in FP notably in 2001, 2006 and 2013 [1]. In January 2009, after a decade of DENV-1 circulation, a DENV-4 outbreak occurred in FP [2]. The last epidemic involving DENV-3 occurred in 2013, associated with DENV-1 in the same proportion [3]. More recently, the first cases of DENV-2 were reported about 20 years after the previous circulation of this serotype in FP. Most of the DENV clinical cases present a febrile illness, however more severe and sometimes lethal forms including haemorrhagic fevers and shock have been reported.

Whilst DENV was circulating, a large ZIKV outbreak occurred in FP in October 2013 and lasted until May 2014. The attack rate of the ZIKV infection has been estimated from symptomatic cases as between 34 and 46%. Post-epidemic seroprevalence studies showed that 49% of the general population was infected [6–8]. Although 50% of infections remained asymptomatic [8], minor clinical signs were observed for the majority of patients and rare severe forms were described with in particular 42 cases of Guillain–Barré syndrome [9].

ZIKV epidemic was rapidly followed by the circulation of CHIKV which emerged for the first time in FP in October 2014 and was responsible for an outbreak extended to March 2015 [10]. The post-epidemic seroprevalence study showed that 76% of the population had anti-chikungunya antibodies [5] suggesting a high attack rate during the epidemic. Contrary to DENV and ZIKV, CHIKV infection is symptomatic in more than 80% of cases with sudden onset of high fever, headache, back pain, myalgia, severe arthralgia and possibly maculo-papular rash.

Characteristics of arboviruses mean that they are a risk for transfusion transmission due to the existence of asymptomatic viraemia and to the high incidence level of cases in the general population during epidemics [11]. Even though it has been reported in a smaller number of cases compared to those from mosquitoes-bite, transmission by blood transfusion has been reported for DENV, West Nile, tick-borne encephalitis, Colorado tick fever, Ross river viruses [11–14] and for ZIKV [15].

To avoid transmission by transfusion, nucleic acid testing (NAT) was introduced for blood donations collected in FP in 2013 for DENV, and in 2014 for ZIKV and CHIKV during the respective outbreaks. The observed proportions of viraemic donations determined by NAT screening for the three viruses were compared to the risks estimated by statistical models as previously described [16–18].

Methods

Estimation of transfusion-associated risk

The mean risk of viraemic blood donation over the course of an outbreak was estimated, according to the Biggerstaff and Petersen model [16,18] as follows:

$$\text{Mean risk} = \left[\frac{(\text{Psympto} \times \text{Vsympto}) + (\text{Pasympto} \times \text{Vasympto})}{\text{duration of the epidemic}}\right] \times \text{Incidence}$$

where Vsympto is the mean length of viraemia in symptomatic donors before symptoms, Vasympto is the mean length of viraemia in asymptomatic donors, and Psympto is the proportion of symptomatic cases, Pasympto is the proportion of asymptomatic cases.

Because the attack rate among blood donors was not available (ZIKV and CHIKV serological testing of blood donors was not carried out, and for DENV it was not possible to distinguish between past and recent infections), the incidence of infection in the overall population was used. It was estimated from syndromic sentinel surveillance data and adjusted on proportion of asymptomatic and no-consulting cases during the study period. The 'no-consulting cases' refer to symptomatic cases who do not consult a doctor and therefore go unreported. The consulting to no-consulting ratios were estimated from data already published [8] or provided by a cross-sectional survey conducted in French Polynesia. The last 2017 FP census (275 000) was used to calculate the incidence rate per 100 000 inhabitants.

Four, one-year periods, from 2014 to 2017, were studied for DENV. Annual incidence was obtained from the surveillance system which gathers syndromic and laboratory-confirmed cases [1]. These figures were increased by consulting/no-consulting ratio and by the proportion of asymptomatic cases. Two rates of asymptomatic cases (50% (low) and 80% (high)) retrieved from seroprevalence surveys [4,5] and two ratios consulting/ no-consulting (1:3 (low) and 1:4 (high)) were used to define two assumptions (low and high). The other parameters were the mean length of viraemia in asymptomatic donors which ranged from 5 days (low assumption) to 9 days (high assumption) [19], and the mean length of viraemia in symptomatic donors prior to the onset of symptoms: 1 day.

The entire epidemic period (from October 2013 to June 2014) was investigated for ZIKV infection. Incident cases

were reported by the surveillance system in FP according to clinically suspected cases definition [6]. The ratio of consulting/no-consulting was 1:3 and 1:4 and the proportion of asymptomatic cases, ranged from 50% to 80%, according to last estimations performed in FP [8]. The length of asymptomatic viraemia was estimated from FP data as the time difference between the collection of ZIKV NAT positive donations and the onset of symptoms collected by post-donation call from all asymptomatic and positive ZIKV NAT donors at the time of donation. The total duration of viraemia ranged between 5 and 8 days with an asymptomatic phase from 2 to 3 days. To establish plausible ranges for risk estimates, the input parameters were assigned upper and lower estimates based on reported values, which define two scenarios named high and low assumptions, respectively. The high one assumed that the mean length of viraemia in asymptomatic donors was of 8 days, the mean length of viraemia in symptomatic donors before symptoms of 3 days, and that 80% infected individuals were asymptomatic and consulting/no-consulting ratio was 1:4. The low assumption was based on a mean length of viraemia in asymptomatic donors of 5 days, a mean length in symptomatic donors before symptom of 2 days, 50% of asymptomatic cases and 1:3 consulting/ no-consulting ratio.

For CHIKV, as the entire epidemic curve was available, we estimated the risk of viraemic blood donation for the different stages of the epidemic: ascending phase, peak, decline phase, epidemic tail. Cases were defined similarly to those used in previous CHIKV outbreaks [20]. We calculated the risk for a single assumption because the feature for this arbovirus was already described [20]. The parameters included in the model were ratio of consulting/no-consulting 1:3, proportion of asymptomatic cases: 15%, and the mean length of viraemia, respectively, 7·5 and 1·5 days in asymptomatic and symptomatic donors before symptoms.

NAT

All blood donations were screened over the course of the epidemic in pools of 10. When a pool tested positive, each sample included in the pool was tested individually. Licensed screening tests are used when available: for DENV RealStar® dengue RT-PCR Kit 2.0, (Altona diagnostics, Hamburg, Germany) routinely applied since 15 April 2013, for CHIKV (RealStar® chikungunya RT-PCR Kit 1.0 then 2.0, (Altona diagnostics, Hamburg, Germany) implemented at the epidemic beginning in October 2014 and stopped 1 month after the end of the epidemic declared in April 2015. For ZIKV, as NAT was not available at the time of the emergence in FP, an in-house assay was performed by the Louis Malardé Institute [21]. Systematic NAT testing began 12 weeks after the reporting of the Zika epidemic, on 13 January 2014 and was continued until early May 2014 [22]. Due to the delay in setting up ZIKV NAT, a retrospective screening of blood donations collected between 21 November 2013 and January 2014 was carried out.

Residual risk calculation

As DENV has been systematically screened since April 2013, it was possible to compute the residual transfusion-transmitted risk for the entire 2014–2016 period according to the previous described method [16,17] by using the donor incidence rate multiplied by the window period (WP) before detectable viraemia, and expressed in fractions of a year (divided by 365). The WP was 5 days and the incidence rate in blood donors was estimated from FPBB data (repeat donors who donated at least twice over the 3-year period, 2014–2016). The study period for ZIKV and CHIKV was too short to calculate the risk with this approach.

Results

Estimated risk of viraemic blood donation

For DENV, according to the two assumptions (50% and 80% asymptomatic cases, 1:3 and 1:4 consulting/no-consulting ratio, duration of viraemia 5 and 9 days), the estimated average annual risk of DENV viraemic blood donation was between 11·2 and 93·6/100 000 donations, that is 0·75–6·01 DENV positive blood donations when reported to the donations number per year (Table 1).

For ZIKV the overall risk during the epidemic ranges from 746 (low assumption) to 1924/100 000 (high assumption), that is 33 and 85 ZIKV positive blood donations when reported to the donations number during the epidemic period (Table 2).

For CHIKV, estimates in the different periods of the epidemic show a highest risk during the peak phase: 3080 /100 000 that is 20 positives blood donations, for an average risk over the whole epidemic of 1083/100 000 that is 34 positive blood donations (Table 3).

Results of NAT

Of the 28 180 blood donations tested for DENV RNA between 15 April 2013 and 31 December 2017, five were positive (0·018%).

For ZIKV, including retrospective screening, a total of 1505 donations were tested and 42 donations (2·80 %) were positive, seven of which correspond to donors who reported post-donation symptoms occurring between 3

Table 1 Estimates of the average annual risk of DENV viraemic blood donation according to 2 assumptions low and high, in French Polynesia, 2014–2017

Year	2014	2015	2016	2017
Estimated number of symptomatic cases[a]	2150	1052	2093	819
Low assumption (50% asymptomatic cases, consulting/no-consulting = 1:3, duration of viraemia 5 days)				
Probability of sampling a donor in the asymptomatic viraemia phase[b] (A_l)	0·82%	0·82%	0·82%	0·82%
Incidence/100 000[c] (B_l)	3583	1753	3488	1365
Risk of viraemic blood donation/100 000 [95% CI] $C_l = (A_l x B_l)$	29·5 [29·0–30·0]	14·5 [14·0–15·0]	28·7 [28·1–29·3]	11·2 [10·8–11·5]
Donations number per year (D)	6419	6126	6438	6693
Estimated number of viraemic blood donation per year [95% CI] (C_lxD)/100 000	1·89 [1·85–1·93]	0·88 [0·85–0·91]	1·85 [1·82–1·88]	0·75 [0·72–0·78]
High assumption (80% asymptomatic cases, consulting/no-consulting = 1:4, duration of viraemia 9 days)				
Probability of sampling a donor in the asymptomatic viraemia phase[b] (A_H)	2·03%	2·03%	2·03%	2·03%
Incidence/100 000[c] (B_H)	4619	2260	4496	1759
Risk of viraemic blood donation/ 100 000 [95% CI] $C_H = (A_H x B_H)$	93·6 [92·0–95·3]	45·8 [44·7–47·0]	91·2 [89·5–92·8]	35·7 [34·7–36·7]
Estimated number of viraemic blood donation per year [95% CI] (C_HxD)/100 000	6·01 [5·90–6·12]	2·81 [2·74–2·88]	5·87 [5·77–5·97]	2·39 [2·32–2·46]
DENV NAT positive donations	3	0	2	0

[a]Annual cases collected by FP surveillance system based on syndromic cases definition and laboratory-confirmed cases.
[b]Mean length of asymptomatic viraemia (Psympto × Vsympto + Pasympto × Vasympto) divided by the duration of the outbreak (365 days) with *Vsympto* mean length of viraemia in symptomatic donors before symptoms: 1 day, *Vasympto* mean length of viraemia in asymptomatic donors: 5 days low assumption, 9 days high assumption, and *Psympto* proportion of symptomatic cases, *Pasympto* proportion of asymptomatic cases: 50% low assumption, 80% high assumption.
[c]Incidence of symptomatic + asymptomatic + no-consulting cases/100 000 in the general population.

Table 2 Estimates of the average risk of viraemic blood donation during the ZIKV outbreak in French Polynesia (October 2013–June 2014) according to two assumptions

ZIKV	Low assumption	High assumption
Duration of asymptomatic viraemia (days)	5	8
Duration of viraemia before symptoms (symptomatic cases)	2	3
% of asymptomatic cases	50	80
Consulting/no- consulting ratio	1:3	1:4
Estimated number of symptomatic cases[a]	31 342	31 342
Probability of sampling a donor in the asymptomatic viraemia phase[b] (A)	1·43%	2·86%
Incidence/100 000[c] (B)	52 237	67 327
Risk of viraemic blood donation/100 000 [95% CI] C = (A × B)	746 [742–750]	1 924 [1915–1933]
Donations number over the epidemic period (D)	4437	4437
Estimated number of viraemic blood donation during the epidemic [95% CI] (C × D)/100 000	33·1 [32·9–33·3]	85·3 [84·9–85·7]
ZIKV NAT positive donations	44	44

[a]Cases reported according to clinically suspected cases definition used by surveillance system in FP.
[b]Mean length of asymptomatic viraemia (Psympto × Vsympto + Pasympto × Vasympto) divided by the duration of the outbreak (245 days) with *Vsympto* mean length of viraemia in symptomatic donors before symptoms (lane 2), *Vasympto* mean length of viraemia in asymptomatic donors (lane 1), and *Psympto* proportion of symptomatic cases, *Pasympto* proportion of asymptomatic cases (lane 3).
[c]incidence of symptomatic + asymptomatic + no-consulting cases/100 000 in the general population.

and 10 days after the donation. The distribution of weekly positives donations on the epidemic curve is shown in Fig. 1.

For CHIKV, 3433 blood donations were tested during the outbreak. Among the 34 positive donations (0·99%), nine donors were asymptomatic (26%) and 25 declared post-donation symptoms. Six of which spontaneously called back the FPBB to disclose symptoms (17·6%). Figure 2 shows the distribution of positive donations during the different stages of the outbreak.

Table 3 Estimates of the average risk of viraemic blood donation during the CHIKV outbreak, French Polynesia, October 2014–March 2015

	Period 1 10/06/14–11/16/14	Period 2 11/17/14–12/21/14	Period 3 12/22/14–02/22/15	Period 4 02/23/15–03/29/15	Overall Outbreak
Period duration (days)	42	35	63	35	175
Estimated number of symptomatic cases[a]	12 359	38 506	16 549	263	67 677
Probability of sampling a donor in the asymptomatic viraemia phase[b] (A)	5·71%	6·66%	3·81%	6·86%	1·37%
Incidence /100 000[c] (B)	14 419	44 923	19 307	307	78 956
Risk of viraemic blood donation/100 000 [95% CI] C = (A × B)	824 [816–832]	3 080 [3062–3098]	736 [730–742]	21 [19·8–22·5]	1 083 [1078–1087]
Donations number per period (D)	787	657	1115	592	3151
Estimated number of viraemic blood donation per period [95% CI] (C × D)/100 000	6·48 [6·41–6·55]	20·2 [20·1–20·3]	8·20 [8·13–8·27]	0·12 [0·11–0·13]	34·1 [34·0–34·3]
CHIKV NAT positive donations	3	27	4	0	34

[a]Cases reported according to clinically suspected cases definition used by surveillance system in FP.
[b]Mean length of asymptomatic viraemia (Psympto × Vsympto + Pasympto × Vasympto) divided by the length of the period (lane 1). *Vsympto* mean length of viraemia in symptomatic donors before symptoms: 1·5 days, *Vasympto* mean length of viraemia in asymptomatic donors: 7·5 days, and *Psympto* proportion of symptomatic cases, *Pasympto* proportion of asymptomatic cases (15%).
[c]incidence of symptomatic + asymptomatic + no-consulting cases/100 000 in the general population.

Dengue residual risk

The incidence rate of DENV among blood donors, estimated from FPBB data for the period 2014–2016 is 2·82 (95% CI: 0·35–5·29) per 10 000 person- years. On the basis of a 5-days window period, the residual risk was estimated at one for 260 000 donations (0–1/138 000 donations) for the 2014–2016 period.

Discussion

Nucleic acid testing results obtained in French Polynesian blood donors for the three arbovirus infections investigated in this study, DENV, ZIKV and CHIKV, validate the risks of viraemic donations estimated during the last outbreaks.

For DENV, over the 2014–2017 period, transfusion estimated risk (from 0·75 to 6·01 viraemic donations per year) was consistent with NAT yield (0–3 cases observed each year). This is in line with the low circulation level of the DENV during the studied period.

For ZIKV, the estimated number of contaminated donations during the epidemic period (October 2013 to April 2014) ranged from 33 to 85 whilst NAT yield accounted for 44 cases.

For CHIKV, the number of contaminated donations estimated during the outbreak matched the observed NAT results (n = 34) even though some variations according to the different stages of the epidemic have been identified but without any statistically significant difference (data not shown). The computed risk (3080 [95% CI: 3062–3098] contaminated donations in 100 000) was twice as high as that the risk during the epidemic peak in the Reunion Island in 2005–2006 (1500/100 000 donations). As the parameters used to estimate the risk, and the lengths of study periods in Reunion Island and FP are close, respectively, 35 and 42 days, this difference may be explained by the higher infection incidence rate in FP: 44 923 /100 000, versus 26 275/100 000 in the Reunion Island at the same phase of the outbreak [20].

However, the risk model has some limitations due to uncertainties regarding the parameters and assumptions used for estimates. For example, whilst the asymptomatic viraemia duration has been previously established for DENV and CHIKV, little is known about ZIKV, which has led us to use several assumptions based either on the rare published data or on our own estimate based on the delay between the time of collection of ZIKV NAT positive donations and the onset of symptoms collected through post-donation phone call. To include the characterization of uncertainty in the viraemia duration parameter into the uncertainty statements for the risk estimates, Biggerstaff and Petersen proposed a statistical resampling

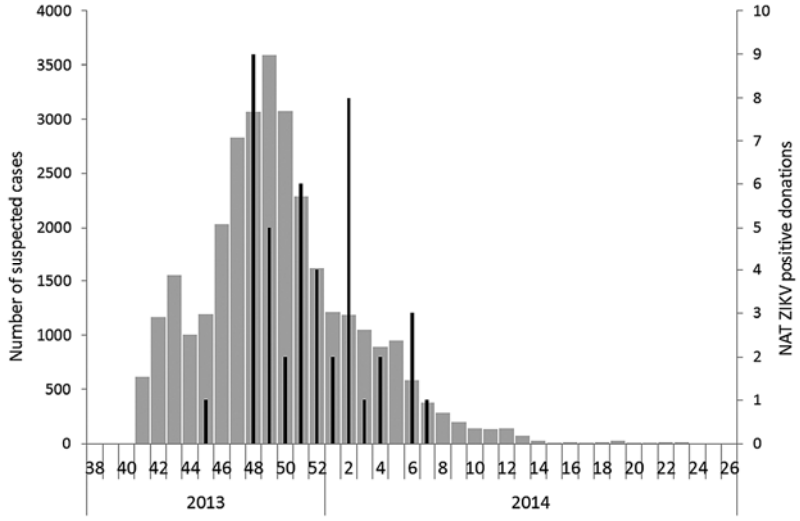

Fig. 1 Epidemic curve of weekly suspected ZIKV cases and distribution of weekly NAT positive donations (narrow black bars). French Polynesia, October 2013–June 2014.

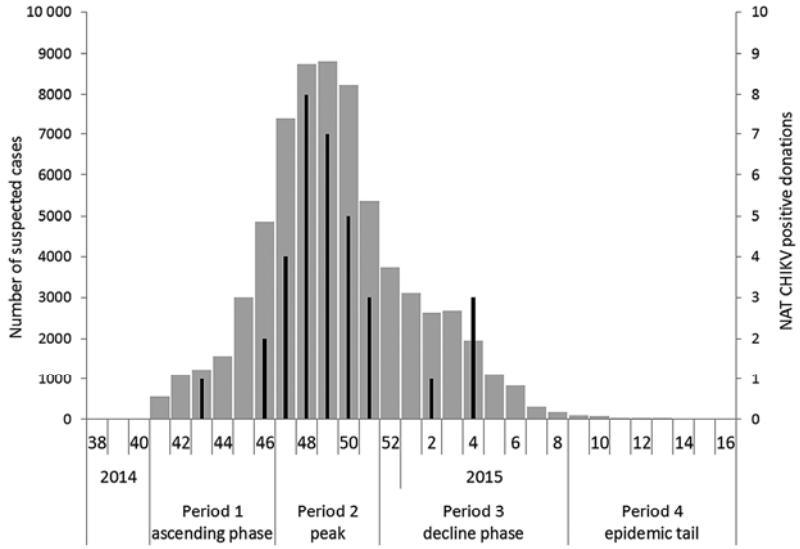

Fig. 2 Epidemic curve of weekly suspected CHIKV cases and distribution of weekly NAT positive donations (narrow black bars). French Polynesia, October 2014–March 2015.

method, simulating viraemia times for each case [18]. The results of this method are in good agreement with those of the derived formula used in our study to estimate the average risk of viral blood donation during an outbreak [16,18], which has led us to use the simplest approach.

Another limitation relates to the proportion of asymptomatic cases which is well known for CHIKV (15%) but more variable for DENV (between 20% and 80% according to reports) and for ZIKV (from 50%, as recently published from outbreaks in FP and Martinique Island to 80% during a previous ZIKV outbreak in Yap Island) [7,8].

Incidence rates were retrieved from syndromic surveillance done by sentinel network performed in the general population. Their extrapolation from general population to blood donors assumes that the risk of infection is the same in both populations. This assumption seems reasonable for arbovirus diseases since there are no specific selection criteria for asymptomatic donors [16]. Nevertheless, we have used incidence rate observed in the overall population and not in the 18–65 age class (not available) corresponding to the blood donor population although seroprevalence studies showed that the incidence of arbovirus infections varies with age [4,5].

Furthermore, incidence rates have been adjusted by taking into account the proportion of asymptomatic cases and the ratio of consulting/no-consulting in order to not underestimate the risk. Conversely, febrile infections not caused by these infections would have overestimated the risk even though the positive predictive value of a clinical case definition strongly increases when the incidence is high [20].

Finally, a geographic bias could have affected our results since donations are almost exclusively collected in the Tahiti Island and not in all FP archipelagos population which was included in the national surveillance.

Despite these weaknesses, our estimates can be considered as a reliable approach to assess the transfusion risk, given that they were confirmed by NAT results.

The effectiveness of first-line donor preventive measures through the pre-donation interview, clinical examination and encouragement of donors to give post-donation information is hampered in the case of arbovirus infections by the high number of asymptomatic infections. In our study only seven (16·7%) and six (17·6%) post-donation calls were recorded among donors whose NAT was positive for ZIKV and CHIKV, respectively. Therefore, these measures are complemented by NAT screening, which makes possible the detection of viral RNA in donors in the absence or before the onset of clinical symptoms and also detect infection prior to the serology. For example, DENV NAT is positive 5 days before IgM test and NAT was reported as significantly more sensitive and specific than NS1 antigen testing [23].

However, NAT implementation for arboviruses requires the availability of a specific molecular biology assay. ZIKV outbreak in FP has shown that a delayed implementation of NAT screening allows contaminated donations to enter the transfusion chain [22]. Conversely, during the CHIKV epidemic, the early introduction of the specific NAT made it possible to rule out 34 donations from infected donors.

Surprisingly, NAT has detected only five DENV positive donations since its introduction in blood screening in FP in 2013, accounting for a rate of 0·018% which is 30 times lower than what was reported in Brazil in 2012 [19]. Mini pool NAT impairs the sensitivity of the screening and hence could have underestimated the number of positive donations [11,24] as it was reported that the DENV RNA loads in blood donors are not very high (median 2·3–3·5 log copies/ml) [19]. However, in contrast to Brazil, which was experiencing an epidemic during the study period, the circulation of DENV in FP over the past four years was low as suggested by the high prevalence (80%) of anti-DENV antibodies in the FP adult population explaining the low NAT yield [4,5]. The residual risk estimated for the 2014–2016 period is 1 in 260 000 donations, that is only one DENV contaminated donation for approximately 40 years of FPBB activity, suggesting that DENV NAT implementation in FP may not be a cost-effective measure.

The dynamics of ZIKV and CHIKV outbreaks were similar with the same transmission potential when spreading in the same territories [25]. The time distribution of the weekly number of contaminated blood donations during ZIKV and CHIKV outbreaks shows a correlation with the incidence of the disease in the overall population (Figs 1 and 2). The first positive donations appeared in the ascending phase of the curve for cumulative observed incident cases of 5500 for ZIKV, 2900 for CHIKV, that is incidence rates of 2045 and 1080 cases/100 000, respectively.

To date, no cases of transfusion-related arbovirus infection have been seen in FP whilst 26 patients have been transfused with blood products contaminated with ZIKV [22]. The absence of reported recipient contamination despite long-standing arbovirus circulation in FP is probably related to the immunization of a large part of the adult population as observed for DENV [4,5] and also, to the well-documented efficacy of Intercept™ mitigation used for platelets and plasma against arboviruses [26]. In addition, the efficiency of arboviruses transmission by blood transfusion is not yet well established and probably depends on individual factors and the minimum infectious dose that is currently unknown.

Several studies highlight the best cost effectiveness of a targeted implementation of the arbovirus NAT according to the epidemiological situation versus a mass donor screening [11,24]. This option has been successfully applied in FP during ZIKV and CHIKV outbreaks. It could be applied to dengue fever and to any other arbovirus according to the results of the estimate of the risk of transfusion-associated arbovirus transmission in FP, by recommending an incidence threshold in the general population above which the arbovirus-specific NAT would be added to the donation testing. For DENV, which is routinely screened, it would then switch from 10 minipool NAT to individual unit testing as applied for West Nile virus in the US or recently recommended by the FDA for ZIKV [11,27].

Conclusion

Arboviruses represent an actual transfusion transmission risk in FP. Dengue fever has been present for a long time, and ZIKV and CHIKV have recently emerged, both with a potential risk of transfusion-associated transmission.

The use of models to estimate transfusion risk is an appropriate approach provided that parameters such as incidence, viraemia duration and proportion of

asymptomatic cases can be accurately estimated. To date, the screening of blood donations by NAT in FP introduced either as permanent screening for endemic infections such as DENV, or targeted during outbreaks for ZIKV and CHIKV, has a key role in the prevention of transfusion-related infectious risk. Our results suggest that NAT screening only becomes effective above a certain rate of incidence of arbovirus diseases in the overall population. In the current circulation of arboviruses in FP, NAT strategy should be optimized according to the surveillance data of infectious diseases in the general population and triggered above an incidence threshold during epidemic periods that should be determined. Even though non-specific measures such as pathogen reduction technologies contribute to improve the blood safety regarding arbovirus, it will however be necessary to wait for the extension of their use to whole blood or packed red blood cells as an universal response to the infectious safety of blood products.

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