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Learning about Zika virus epidemiology and diagnostics from blood donor studies

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Arbovirus transmission risk from blood transfusion relates to the incidence of infection in the blood donor pool and the length of time that the blood of newly infected people remains infectious.[1] Identification of 23 transfusion transmissions during the 2002 West Nile virus outbreak in midwestern USA and models estimating transfusion transmission risk as high as 4.7 per 10 000 donors in certain areas led to the realisation that high infection incidence during mosquito-borne arbovirus outbreaks creates considerable transfusion transmission risk despite viraemia of short duration.[2,3] To mitigate this risk, blood donors have been universally screened with nucleic acid amplification tests (NAATs) for West Nile virus since 2003.[4] Although transfusion transmission of Zika virus has not been documented in the USA, NAAT screening was implemented in 2016 to mitigate risk of transfusion to susceptible populations, including pregnant women, to prevent complications, such as adverse fetal outcomes.[4]

Two studies[5,6] in *The Lancet Infectious Diseases* focus on blood donors identified by NAAT screening for Zika virus during the 2016 Zika virus outbreak in the USA. The study by Phillip C Williamson and colleagues,[5] in which an average of one in 156 Puerto Rican donors tested positive using a highly sensitive NAAT in single-donation testing during the outbreak period, estimated that viral nucleic acid was detectable for a mean of 11.70 days (95% CI 10.06–14.36) and the median time to develop detectable IgM antibodies from initial NAT reactivity was 7.42 days (6.59–8.29). To generate these estimates, Williamson and colleagues adapted previous models that had estimated the duration from donation that West Nile viral RNA remained detectable or to IgM antibody development.[7] By using viral load data of the index donation and Zika virus ramp-up data from macaques, they imputed the actual time that viral RNA was detectable before donation and then analysed follow-up data from donor repeat visits to derive estimates for duration of plasma viraemia and time to IgM seroconversion. Incorporating data on the duration and rates of NAAT positivity, Williamson and colleagues further estimated that 21% of the Puerto Rican population became infected during the outbreak. This proportion was similar to the 25% population

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infection incidence of chikungunya virus estimated from a serosurvey of Puerto Rican blood donors following an outbreak.[8] Both Zika and chikungunya viruses were new to Puerto Rico and were transmitted in an urban mosquito–human–mosquito transmission cycle, with *Aedes aegypti* as the primary vector.

Mars Stone and colleagues[6] prospectively enrolled and studied blood donors identified by NAAT screening in Puerto Rico and the continental USA during the 2016 Zika virus outbreak. Given the cross-reactivity of IgM antibodies to dengue and Zika viruses, which reduces the diagnostic utility of serological assays, extending the duration after infection that definitive diagnosis can be made by NAAT is of considerable benefit. By real-time RT-PCR testing of various sample types during long-term follow-up of positive donors, and using a similar modelling approach to that of Williamson and colleagues, Stone and colleagues estimated that Zika virus RNA was detectable in plasma for a mean duration of 9.9 days (95% CI 8.1–12.0) compared with 73.5 days (39.8–107.5) in whole blood, 14.5 days (10.5–20.3) in urine, and 26.4 days (19.7–38.7) in saliva. However, a major limitation was that Zika virus RNA was not detected by real-time PCR in whole blood from 25% of participants, urine from 57%, and saliva from 62%. The mean time from NAAT-detectable infection to seroreversion of Zika IgM was 237.0 days (95% CI 128.7–459.5). This result has implications for testing of pregnant women, because a positive Zika IgM test result could result from infection before pregnancy. Stone and colleagues also found that 16 (64%) of 25 donors who were positive for Zika virus RNA on NAAT but negative for IgM antibodies at index donation developed at least three of six Zika-associated symptoms. These results suggest that most Zika infections are symptomatic; however, the background incidence of symptoms in uninfected blood donors was not assessed.

These two studies show the unique capability of blood donor studies to ascertain epidemiological and virological data of public health and clinical importance. Data from these studies have informed the diagnostic algorithms used in several large cohort studies of Zika virus infection in pregnant women, including the large National Institutes of Health-funded ZIP study (NCT02856984) and the European Zika Alliance Study. Only NAAT screening of blood donors can identify many people very early in infection, before their immune system mounts an antibody response and they develop symptoms. Identification of such people eliminates potential biases of enrolling only symptomatic people in studies and allows characterisation of the full spectrum of disease, including asymptomatic infections. Measurement of antibodies in viraemic samples pre-seroconversion allows ascertainment of previous arbovirus exposure; subsequent samples obtained during donor follow-up can profile comprehensive virological and immunological outcomes over time. Additionally, around 12.6 million donations are screened each year in the USA.[9] No other source of adult blood samples with similar demographic breadth and number exists. As was shown during West Nile,[7] chikungunya,[8] dengue,[10] and now Zika virus epidemics, studies of blood donors can uniquely contribute to our knowledge of emerging infectious diseases.

References

1. Petersen LR, Busch MP. Transfusion-transmitted arboviruses. Vox Sang 2010; 98: 495–503. [PubMed: 19951309]

2. Pealer LN, Marfin AA, Petersen LR, et al. Transmission of West Nile virus through blood transfusion in the United States in 2002. N Engl J Med 2003; 349: 1236–45. [PubMed: 14500806]

3. Biggerstaff BJ, Petersen LR. Estimated risk of transmission of the West Nile virus through blood transfusion in the US, 2002. Transfusion 2003; 43: 1007–17. [PubMed: 12869104]

4. Busch MP, Bloch EM, Kleinman S. Prevention of transfusion-transmitted infections. Transfusion Med 2019; 133: 1854–64.

5. Williamson PC, Biggerstaff BJ, Simmons G, et al. Evolving viral and serological stages of Zika virus RNA-positive blood donors and estimation of incidence of infection during the 2016 Puerto Rican Zika epidemic: an observational cohort study. Lancet Infect Dis 2020 published online July 13. 10.1016/S1473-3099(19)30706-6.

6. Stone M, Bakkour S, Lanteri MC, et al. Zika virus RNA and IgM persistence in blood compartments and body fluids: a prospective observational study. Lancet Infect Dis 2020; published online July 13. 10.1016/S1473-3099(19)30708-X.

7. Busch MP, Kleinman SH, Tobler LH, et al. Virus and antibody dynamics in acute West Nile virus infection. J Infect Dis 2008; 198: 984–93. [PubMed: 18729783]

8. Simmons G, Bres V, Lu K, et al. High incidence of chikungunya virus and frequency of viremic blood donations during epidemic, Puerto Rico, USA, 2014. Emerg Infect Dis 2016; 22: 1221–28. [PubMed: 27070192]

9. Ellingson KD, Sapiano MRP, Haass KA, et al. Continued decline in blood collection and transfusion in the United States-2015. Transfusion 2017; 57 (suppl 2): 1588–98. [PubMed: 28591469]

10. Busch MP, Sabino EC, Brambilla D, et al. Duration of dengue viremia in blood donors and relationships between donor viremia, infection incidence and clinical case reports during a large epidemic. J Infect Dis 2016; 214: 49–54. [PubMed: 27302934]