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# Medical importance of Sindbis virus in south-west Germany

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In 1965, Sindbis virus (SINV) was demonstrated to circulate in Europe and epidemics were first noticed in Fennoscandia in the early 1980s.<sup>1</sup> Arthritis, rash and fever are the main symptoms during the acute phase of human SINV infection.<sup>2</sup> Characteristically, in 50% of the patients joint symptoms last for more than 12 months.<sup>2</sup> The main vectors for SINV are ornithophilic mosquitoes of the genera *Culex* and *Culiseta* and the main hosts are tetraonid and migratory birds, which might be responsible for the distribution of the virus.<sup>2</sup> In 2009, SINV was isolated from *Culex* and *Anopheles* mosquitoes that were exclusively trapped within the city center of Weinheim, south-west Germany.<sup>3</sup> Therefore, we initiated this study to investigate the medical importance of SINV in an area with high SINV infection rates in mosquitoes.

From January 2010 to February 2011, 355 blood samples from patients in Germany (Fig. 1A) with clinical suspected acute SINV infections were collected. RNA extraction and SINV real-time reverse transcription (RT)-PCR were performed with serum or plasma samples.<sup>3</sup> Serum samples were investigated for the presence of SINV-specific-IgM and -IgG antibodies using an in-house indirect IFA based on SINV-infected Vero E6 cells.<sup>4</sup> Precise information about the clinical symptoms of each patient was recorded in a questionnaire. In addition, 3389 serum samples from healthy blood donors from Germany (Fig. 1B) were analyzed for the presence of SINV-specific-IgG antibodies with a commercial and an in-house SINV indirect IFA according to the manufacturer's protocol (Euroimmun, Lübeck, Germany) and to Tappe et al., respectively. Positive tested serum samples were further investigated using IFAs counterstained with SINV murine monoclonal antibody E1K1 to demonstrate the specific reactivity pattern of the positive tested samples. In addition, serological cross-reactivity was investigated with Chikungunya virus (CHIKV) and Venezuelan equine encephalitis virus (VEEV) IFAs according to the manufacturer's protocol (Euroimmun) and to Tappe et al., respectively.

All samples from patients in Germany (Fig. 1A) with clinically suspected acute SINV infections were tested negative for SINV-specific-IgM and -IgG antibodies and SINV RNA. However, some caution might be raised on the possibility that acute SINV infections may, by unknown reasons, vary in time despite the presence of SINV in mosquitoes from Germany. According to the questionnaire, 73% of

the patients suffered from joint pains in the knee or the shoulder and other frequent reported symptoms were tiredness, fever, muscle pain and headache. Only 15% of the patients reported an itching rash.

Four serum samples originating from different healthy blood donors (Fig. 1 B) were tested positive for SINV-specific-IgG antibodies with a titer of 1:100, which is near to the cut-off titer of 1:10 demonstrating past infection. Serological cross-reactivity with CHIKV and VEEV was not observed in the IFA. In addition, the fluorescence pattern obtained with the positive tested samples was identical with the pattern obtained with the murine SINV monoclonal antibody E1K1, thus demonstrating the specificity of the positive results obtained with the SINV IFA. The blood donors of the positive samples lived close to (Hirschberg, Bietigheim-Bissingen and Östringen) and or even within the city of Weinheim (Fig. 1B). The SINV-IgG-seroprevalence in the investigated blood donors was found to be 0.1%.

In conclusion, only four out of 3389 investigated blood donor samples were tested positive for SINV-specific-IgG antibodies and all samples from 355 patients with clinically suspected acute SINV infections were tested negative for SINV-specific antibodies or SINV RNA, thus demonstrating the low medical importance of SINV in south-west Germany.

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### ***Conflict of interest***

The authors do not have commercial or other associations that might pose a conflict of interest (e.g., pharmaceutical stock ownership or consultancy)

### ***Ethical approval***

None.

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## Tables and Figures

**Figure 1.** Origin (according to administrative districts) of blood samples from patients ( $n = 355$ ) in Germany with clinically suspected acute SINV infections (A) and origin (according to ZIP districts) of serum samples from healthy blood donors ( $n = 3389$ ) in Germany (B). The red dot represents the city of Weinheim where SINV was isolated from *Culex* and *Anopheles* mosquitoes in 2009.

