

# TBE in Japan

Kentaro Yoshii

## E-CDC risk status: affected, possibly endemic

(this information will also go to the TBE global map down to county level, last edited: date 02.02.2024, data from 2023)

### History and current situation

In Japan the Japanese encephalitis virus (JEV), one of mosquito-borne flaviviruses, has been widely endemic on the main and on the southern islands with more than 1,000 Japanese encephalitis (JE) cases reported annually in the late 1960s.<sup>1</sup> In contrast, until 1993, no TBE case had ever been reported and it was considered that there was no endemic focus of TBEV.

In 1993, a case of viral encephalitis in Hokuto city, in the southern part of Hokkaido, was diagnosed as TBE.<sup>2</sup> The patient had suffered from fever, headache, and neurological symptoms such as seizures. Hemagglutination inhibition (HI) test against JEV showed significant increase in HI antibodies. However, 2-mercaptoethanol-sensitive HI antibodies were not detected, and it was unlikely that JEV infection occurred in Hokkaido, where JEV was not endemic. Furthermore, blood-sucking vector mosquitoes were not active at the end of autumn in the area. Further serological analysis was conducted against other flaviviruses. IgM-ELISA and neutralization tests revealed very low antibody titer against JEV while high titers of antibodies were detected by neutralization test against TBEV.

Because the patient was a dairy farmer with no history of overseas travel, it was concluded that she had been infected with TBEV by a tick in her living area in Hokkaido. Epizootiological surveys were conducted in Hokkaido, antibodies against TBEV were detected in dogs, horses, racoons, deer and wild rodents in the wide areas of Hokkaido.<sup>3-12</sup> TBEV was isolated from dogs, wild rodents and from *Ixodes ovatus* ticks, which are the predominant ticks in the area. Sequence and phylogenetic analysis classified the TBEV isolates as Far-Eastern subtype. Besides, antibodies against TBEV were detected in deer and wild rodents in the Tochigi, the Shimane and the Nagasaki prefectures, and antibodies against the TBEV-serocomplex were also detected in wild boars in wide areas of Japan (the Yamaguchi, Wakayama, Hyogo, Oita, Gifu, Toyama and Chiba prefecture), indicating wide distribution of TBEV all over Japan.<sup>4,11,13,14</sup>

Ever since the first confirmed TBE case in 1993, only four additional cases of TBE were reported from Japan, the last one in 2018, although endemic foci of TBEV were detected in various parts of the country, not only in Hokkaido. It is possible that TBE patients are missed in Japan. One major

problem is the low awareness for the disease in Japan, even among physicians. Another problem is that commercial tests for diagnostic confirmation of TBEV-infections are not available due to low awareness and due to the restrictions to handle TBEV in high biosafety level laboratories (BSL 3) only. In Japan, no TBE vaccine is licensed, and it is an urgent medical need to conduct a serological survey among residents in TBEV-endemic areas and to establish preventive measures for residents as well as for travelers to Europe and Russia.

**Table 1: TBE in Japan**

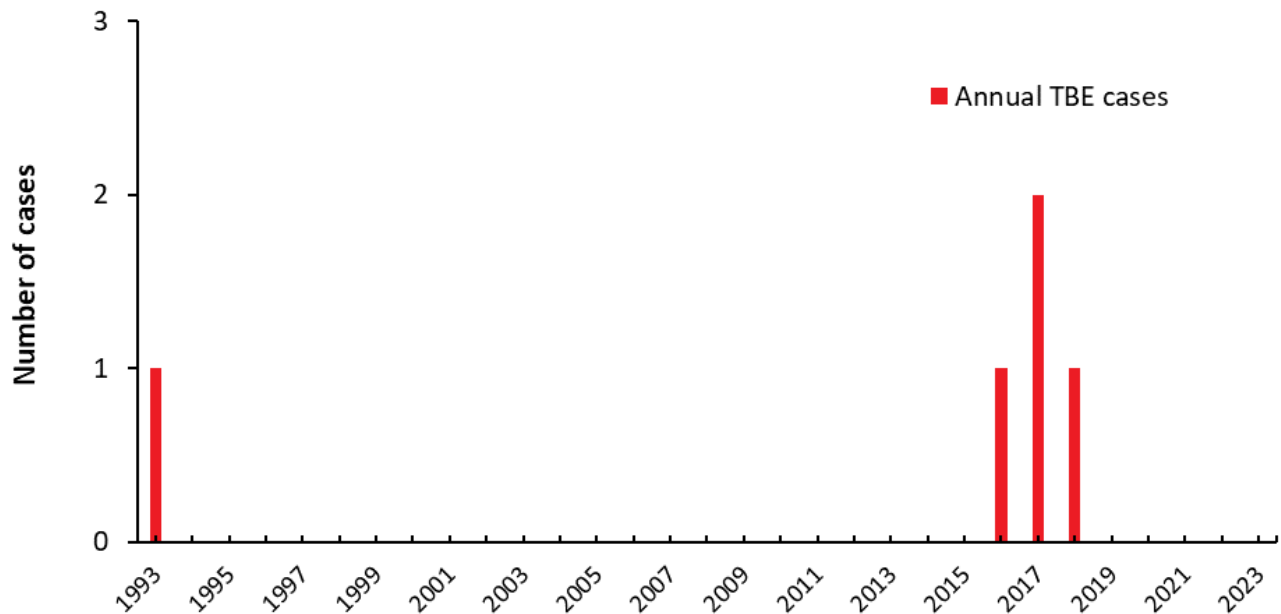
<b>Viral subtypes isolated</b>	Far-Eastern subtype <sup>5-9,12</sup>
<b>Reservoir animals</b>	Wild rodents <sup>5,9,11</sup>
<b>Percentage infected ticks</b>	<i>I. ovatus</i> (0.05%–0.33%) <sup>7,8</sup>
<b>Dairy product transmission</b>	Not reported
<b>Case definition used by authorities</b>	Isolation of TBEV or detection of TBEV genomic ribonucleic acid by RT-PCR from blood or cerebrospinal fluid; detection of IgM antibodies against TBEV from blood or cerebrospinal fluid; detection of significant increase in neutralizing antibodies against TBEV in paired serum.  Based on the Infectious Diseases Control Law
<b>Completeness of case detection and reporting</b>	Unknown
<b>Type of reporting</b>	Mandatory
<b>Other TBE surveillance</b>	Detection in ticks, wild and companion animals <sup>3-13</sup>
<b>Special clinical features</b>	Encephalitis and meningitis with typical neurological symptoms. <sup>6,15-17</sup>
<b>Licensed vaccines</b>	No licensed vaccine
<b>Vaccination recommendations</b>	No
<b>Vaccine uptake</b>	No
<b>National Reference center for TBE</b>	NATIONAL INSTITUTE OF INFECTIOUS DISEASE, Toyama 1-23-1, Shinjuku-ku, Tokyo 162-8640, Japan, info@nih.go.jp

## Overview of TBE in Japan

Only five confirmed cases of TBE have been reported from Japan to date. The first patient was a 37-year-old female in 1993,<sup>2,6</sup> and the second patient was a male person in his 40s (2016).<sup>15</sup> The third and fourth patients were male in their 70s (2017).<sup>16</sup> The fifth patient was a female in her 40s (2018).<sup>17</sup>

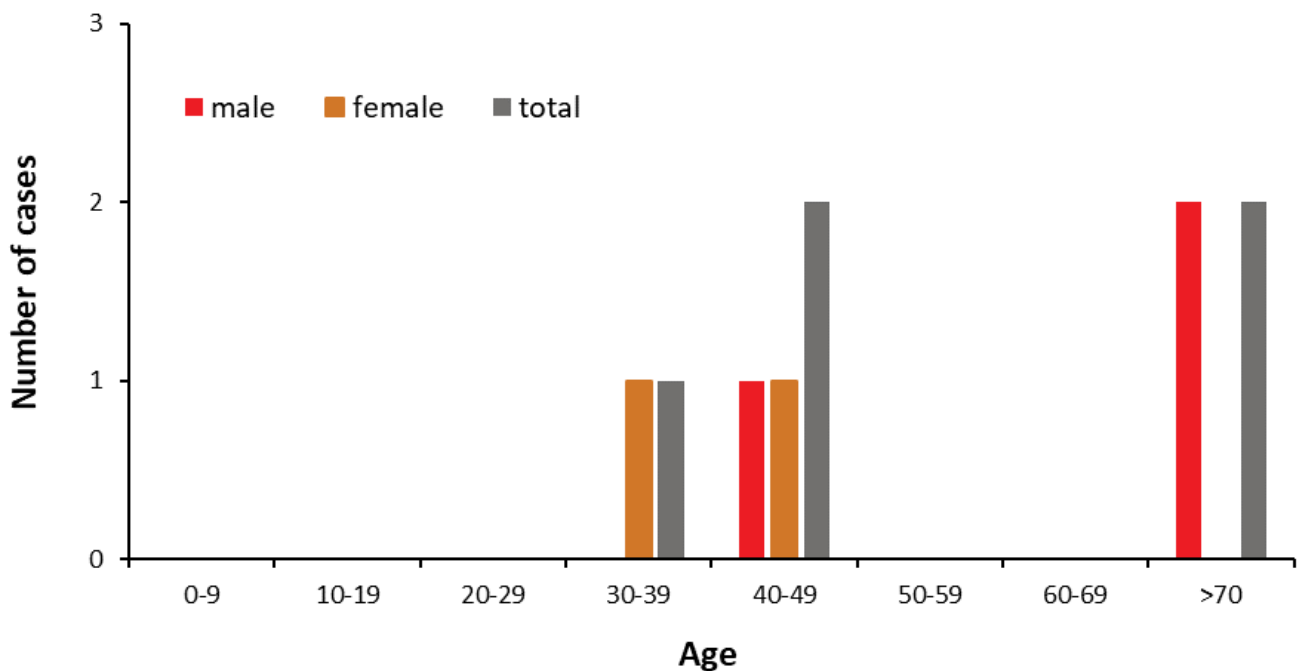
Retrospective survey revealed infection with TBEV in one Lyme disease-suspected patient with meningoencephalitis<sup>18</sup>, seven patients with neurological disorders<sup>19</sup> and two asymptomatic cases in Japan Self-Defense Forces members in Hokkaido.<sup>20</sup> Other surveys also revealed infection with TBEV in three patients hospitalized with encephalitis or meningitis of unknown etiology outside Hokkaido.<sup>21</sup>

**Figure 1: Reported TBE cases in Japan 1993–2023**<sup>6,15-17</sup>



Source Data: Appendix—Figure 1

**Figure 2: Age and gender distribution of TBE in Japan, 1993–2023**<sup>6,15-17</sup>



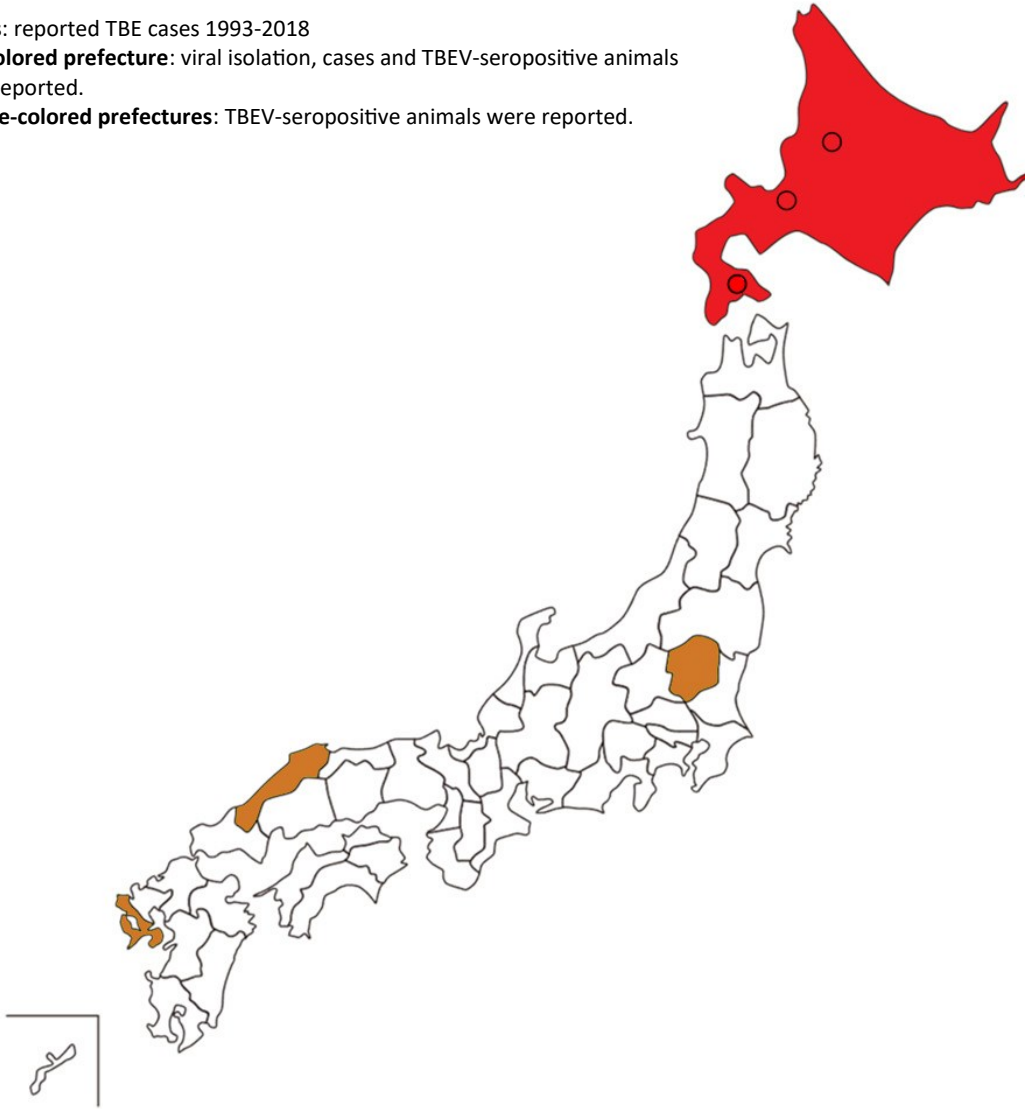
Source Data: Appendix—Figure 2

**Figure 3: Geographic distribution of TBE in Japan** <sup>4,5,8,11,13,15,16</sup>

**Circles:** reported TBE cases 1993-2018

**Red-colored prefecture:** viral isolation, cases and TBEV-seropositive animals were reported.

**Orange-colored prefectures:** TBEV-seropositive animals were reported.



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## Appendix

Source data: Figure 1

Year	Number of cases	Year	Number of cases
1993	1	2009	0
1994	0	2010	0
1995	0	2011	0
1996	0	2012	0
1997	0	2013	0
1998	0	2014	0
1999	0	2015	0
2000	0	2016	1
2001	0	2017	2
2002	0	2018	1
2003	0	2019	0
2004	0	2020	0
2005	0	2021	0
2006	0	2022	0
2007	0	2023	0
2008	0		

Source data: Figure 2

Age group (years)	Males	Females	All
0-9	0	0	0
10-19	0	0	0
20-29	0	0	0
30-39	0	1	1
40-49	1	1	2
50-59	0	0	0
60-69	0	0	0
>70	2	0	2

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