Chapter 13

TBE in South Korea

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E-CDC status: imperiled *(last edited in May 2025, update for 2024: no data)*

History and current situation

Although no human case of tick-borne encephalitis (TBE) has been documented in South Korea to date, 5 surveillance studies have been conducted to evaluate the prevalence of tick-borne encephalitis virus (TBEV) in wild ticks.[1-5] Four studies collected ticks by dragging or flagging in grassland and forest, while 1 study tested wild mammals (boars and rodents) by removing ticks from them. In the wild of South Korea, *Haemaphysalis* spp. were the predominant species found by tick dragging, while *Ixodes nipponensis* became predominant when harvested from small mammals.[6]

According to the results, TBEV was detected in numerous regions (Figure 1)[1-5]:

- Gyeonggi-do (Yangpyeong and Dongducheon), Gangwon-do (Pyeongchang, Jeongseon, Sokcho, and Chuncheon), Jeonllabuk-do (Gunsan and Gurye), Gyeongsangbuk-do (Hapcheon, Dongu, Andong, and Uiseong), Gyeongsangnam-do (Yangsan), and Jeju-do (Jeju).

The first study was conducted in 12 regions of 5 provinces of South Korea in 2005–2006.

TBEV was detected from *Haemaphysalis longicornis* (minimum field detection rate, 0.2%), *H. flava* (0.8%), *H. japonica* (0.9%), and *I. nipponensis* (1.6%), as depicted in Table 1.

The minimum field detection rate ([number of detection positive pools/ total number of examined ticks] × 100) was particularly high in Yangpyeong (5.9%–20.0%), Dongducheon (1.3%–6.7%), Pyeongchang (0.8%–1.3%), and Jeongseon (0.4%–8.3%) with variation by tick species. As usual, 1–30 ticks were included in each pool. Phylogenetic analysis revealed that the TBEV in South Korea belonged to the Western subtype, contrary to neighboring countries including Japan, China, and northeastern Russia, where the Far-Eastern subtype was only isolated (Table 1).

In the second study by the same research team, TBEV was also isolated from ticks feeding on wild rodents (*Apodemus agrarius*) captured in Hapcheon, Gyeongsangnam-do.[2] These TBEV isolates (KrM216, KrM219) caused symptoms of encephalitis in suckling mice and were able to grow from brain preparations in cell culture. In 2007, the third TBEV surveillance was conducted in the southern provinces of South Korea, including Jeju Special Self-Governing Province (Jeju Island), Jeollanam-do, Gyeongsangbuk-do, and Gyeongsangnam-do.[3] Among the 6,788 ticks collected, 4,077 were pooled (649 pools) by collection site. In Jeju Island, the minimum field detection rate was 0.17% in *H. longicornis* and 0.14% in *H. flava*. In accordance with the previous study, the Jeju strains were identified as Western subtype TBEV by phylogenetic analysis.

Later during 2011–2012, the fourth larger-scale surveillance study was carried out in 25 localities of 10 provinces of South Korea.[4] A total of 13,053 ticks were collected with *H. longicornis* as the most abundant species (90.8%, 11,856/13,053), followed by *H. flava* (8.8%, 1,149/13,053), *I. niponensis* (0.3%, 42/13,053), and *Ixodes persulcatus* (0.05%, 6/13,053). The minimum field detection rate for *H. longicornis, H. flava*, and *I. nipponensis* were 0.06%, 0.17%, and 2.38%, respectively, and the TBEV sequences obtained were identified as the Western subtype, consistent with the previous reports.[1-3]

In 2014, the most recent surveillance study was conducted to evaluate the prevalence of TBEV and other tick-transmitted viruses (Powassan virus, Omsk hemorrhagic fever virus, Langat virus, and severe fever with thrombocytopenia virus) among wild ticks.[4] A total of 21,158 ticks were collected by dragging at 139 sites in 6 provinces; *H. longicornis* was the dominant tick species (83.04%, 17,570/21,158), while other tick species, *H. flava* (15.68%, 3317), *I. nipponensis* (1.18%, 249), Amblyomma testudinarium (0.05%, 11), and *H. phasiana* (0.04%, 8), were much less common. TBEV was detected by nested reverse transcriptase-polymerase chain reaction (RT-PCR) in the Andong, Uiseong, Daegu, and Yangsan areas. The maximum likelihood estimation (estimated numbers of viral RNA-positive ticks per 1,000 ticks) for *H. longicornis, H. flava*, and *I. nipponensis* was 0.23%, 0.90%, and 8.02%, respectively. On phylogenetic analysis, the TBEV strains identified in this study belonged to the Western subtype also.

Two serological surveillance studies for TBEV were reported in South Korea.[7,8] The first study was conducted from January 2017 to August 2018; a total 583 sera were obtained from the forest and field workers in South Korea.[7] Seroprevalence of TBEV was 0.9% (5/583) by IgG ELISA, and 0.3% (2/583) by neutralization assay. One forest worker in Jeju had positive anti-TBEV IgG titer (56.1 RU/mL) and

neutralization titer (1:113). This man has been working as a forest worker for 6 years in Jeju. However, he immigrated to Jeju from Jilin (northern China) 8 years ago, so TBEV infection could have occurred when he lived in China. In the other forest worker in Hongcheon, neutralization titer against TBEV was marginally positive (1:10), but anti-TBEV IgG was not detected. In another study, serological surveillance was conducted for healthy farmers in Jeju island during 2015-2018 using TBEV ELISA kits.[8] This study revealed a 1.9 % seroprevalence of TBEV, but not confirmed by neutralization assay.

Even though no confirmed human TBE case was reported in South Korea, TBEV might have been endemic in various localities and *H. longicornis, H. flava*, and *I. nipponensis* would be potential vectors of the Western subtype TBEV.

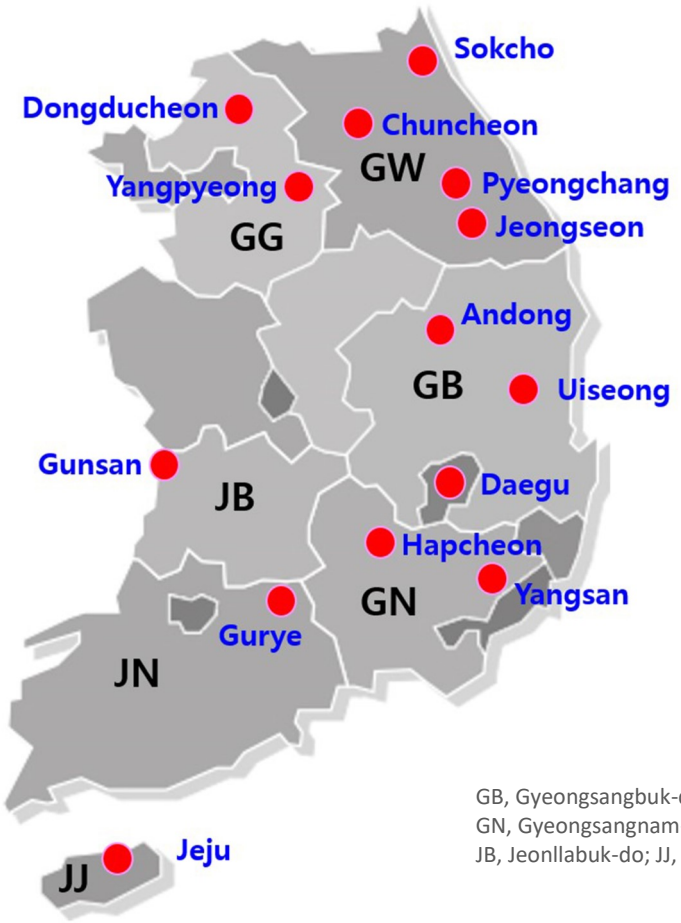
In South Korea, TBE is designated as a group 4 Nationally Notifiable Infectious Disease, requiring immediate reporting for laboratory-confirmed cases.[9] Although no case of TBE has been confirmed in South Korea, human encephalitis cases with unknown causes have been increasingly reported. TBE screening at the Korean Disease Control and Prevention Agency (KDCA) was started in 2006. As for undefined encephalitis cases or suspected TBE cases, blood and cerebrospinal fluid (CSF) samples are required to be sent out to KDCA to perform enzyme-linked immunosorbent assay (ELISA) and RT-PCR for TBEV. However, there are significant limitations of TBEV clinical surveillance in South Korea. First, TBE disease awareness is quite low, and diagnostic practice is limited in clinical settings. Neurologists often take care of undefined meningitis/encephalitis cases, but they are completely unfamiliar with TBE. Second, considering the short duration of TBE viremia, it is not easy to confirm the infection using blood and CSF samples collected at later clinical stages. To better characterize the disease burden of TBE in South Korea, serologic studies are required to evaluate TBE prevalence in high-risk populations such as forest workers and farmers in the endemic areas. At the same time, active surveillance with enhanced awareness would be essential to find missed TBE cases.

As of March 2024, no human cases of TBE have been reported.[10]

Table 1: TBE in South Korea

Viral subtypes, distribution	Western subtype[1-5]
Reservoir animals	Wild rodent *(Apodemus agrarius)*
Infected tick species	*Haemaphysalis longicornis, Haemaphysalis flava,* *Haemaphysalis japonica*, and *Ixodes nipponensis*
Dairy product transmission	Not documented
Mandatory TBE reporting	Yes: TBE is a group 4 Nationally Notifiable Infectious Diseases in South Korea[11] Case definition: laboratory-confirmed patient 1. Clinical criteria: person with symptoms of inflammation of the central nervous system, including meningitis, meningo-encephalitis, encephalomyelitis and etc. 2. Laboratory criteria • Detection of TBE-specific IgM antibody in the serum/CSF (confirmation of TBE-specific antibodies is required by serum neutralization assay) • Sero-conversion or ≥4-fold increase of TBE-specific antibodies in paired serum samples • Detection of TBE viral nucleic acid in clinical specimen
Other TBE-surveillance	None
Special clinical features	No information available
Available vaccines	None
National Reference Center	Korean Disease Control and Prevention Agency (KDCA)

Figure 1: Geographical location where tick-borne encephalitis virus (TBEV) positive ticks or wild rodents were identified in South Korea



GB, Gyeongsangbuk-do; GG, Gyeonggi-do; GN, Gyeongsangnam-do; GW, Gangwon-do; JB, Jeonllabuk-do; JJ, Jeju-do; JN, Jeonllanam-do.

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Citation:
Song JY. TBE in South Korea. Chapter 13. In: Dobler G, Erber W, Bröker M, Chitimia-Dobler L, Schmitt HJ, eds. *The TBE Book*. 7th ed. Singapore: Global Health Press; 2024. doi:10.33442/26613980_13-31-7

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