Chapter 13

TBE in Germany

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E-CDC risk status: endemic (data as of end 2023)

History and current situation

The beginning of research on TBE in Germany was influenced and inspired by the results and developments of TBE research in the former Czechoslovakia. There, TBE virus was detected in the Czechoslovak Republic in 1948. In Germany, the first evidence of the presence of TBE virus was found by Sinnecker and his group in the former German Democratic Republic (GDR).[1] The first virus strains were isolated also by Sinnecker's group in the early 1960s.[2] In the former Federal Republic of Germany (FRG), TBE research started with research on TBE virus in the region of Franconia by Scheid and Ackermann.[3,4] In the region of Lower Franconia, a virus was isolated which was called "Zimmern Virus'' after the location of the isolation.[5] Unfortunately, all these virus strains were lost but it can be assumed that they all belonged to the Western (European) subtype of TBE virus.

In the 1970s, a strong decrease of reported human TBE cases occurred in the former endemic areas of the German Democratic Republic.[6] In Western Germany, only few studies were conducted on the geographic appearance of human TBE cases, mainly led by the company IMMUNO, the first producer of a TBE vaccine in Western Europe. No systematic epidemiological studies are available from this time. TBE was not reportable during this time.

In 2001, TBE became a reportable disease by the new Infection Control Act. From this time on, reliable data on the prevalence of TBE in Germany are available. In the era of molecular detection studies in different areas of Germany on the prevalence of TBE virus in ticks were conducted. In non-engorged ticks the prevalence rates vary depending on the tick stage from 0.1% to 0.5% (nymphs) up to 5% (adult stages).[7,8] The molecular characterization of a number of virus strains isolated from ticks in Germany shows that so far all known strains belong to the European subtype of TBE virus.[8] *Ixodes ricinus*, the sheep tick, is the most important vector of TBE virus in Germany. In 2016, TBE virus was detected for the first time in Dermacentor reticulatus in the Federal State of Saxony. In 2016 and 2017, also for the first time in about 50 years, two goat milk-borne outbreaks of TBE were registered in Germany (districts of Reutlingen, Tübingen, Baden- Württemberg).

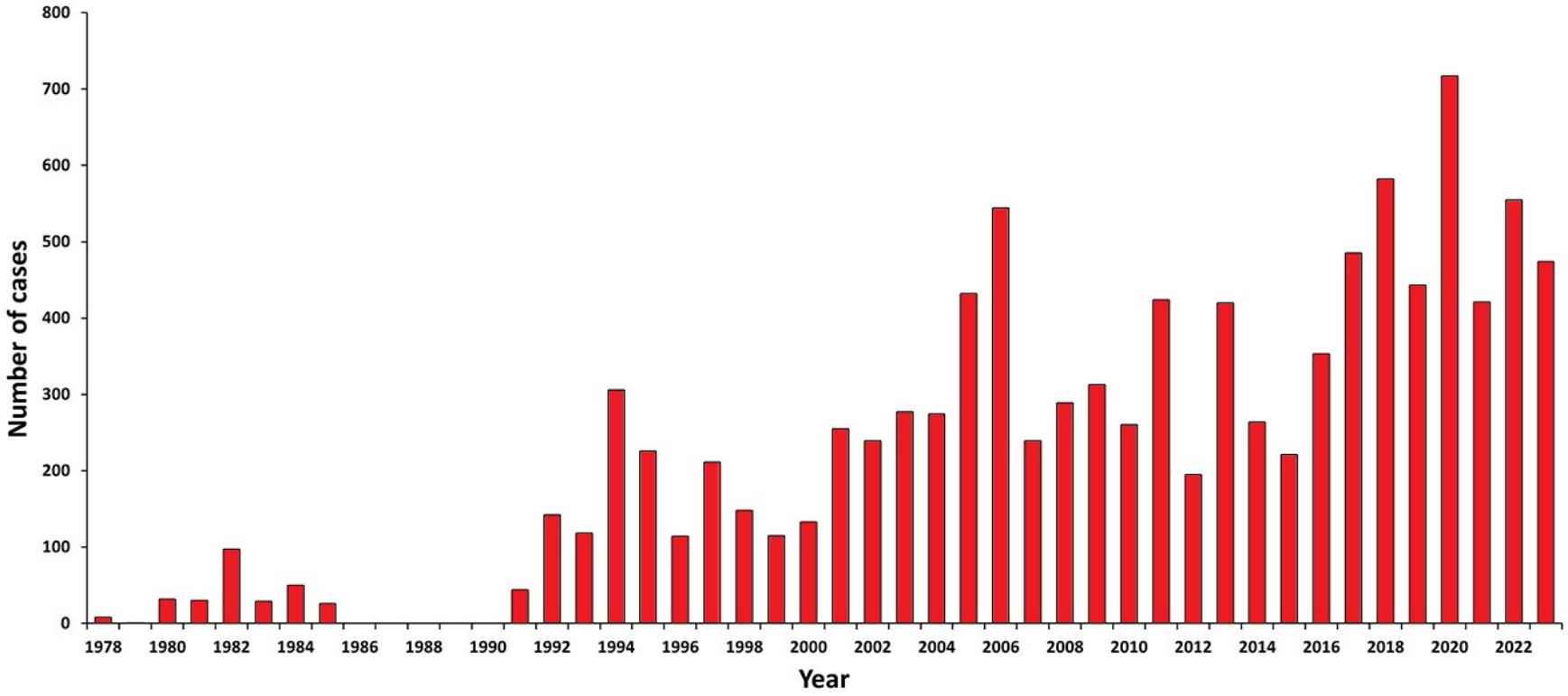
In Germany, TBE is found mainly in the southern part, with the federal states of Bavaria and Baden-Württemberg comprising 80% to 90% of all reported human cases in Germany. There is an increasing number of districts in Saxony, Thuringia and for the first time in 2019 in Lower Saxony and Brandenburg which are classified as risk districts by the RKI. The annual reported human cases range from 200 to >550 (RKI, SurvStat). Seroprevalence rates before vaccination programs started in endemic areas in the human population ranged between 3% to 8%, with high clustering in some human populations, indicating a highly focal geographic distribution within the endemic areas. Calculating the incidence of the overall German population is generally low (<0.1/100,000), but these figures may give a strongly underestimated risk for some districts in Southern Germany, where the highest incidence rates in Germany can reach >10/100,000 in particular districts (e.g., Amberg, Bavaria and Ortenaukreis, Baden-Württemberg). Actual studies in the district of Ortenaukreis show that the prevalence of antibodies indicating infection (NS1 IgG) is 5.6% in a population of blood donors and subtracting the vaccinated (and therefore protected) portion, the prevalence of antibodies indicating infection was 12.8%[17].

Overview of TBE in Germany

Table 1: Virus, vector, transmission of TBE in Germany

Viral subtypes, distribution	European TBEV subtype[7,8,13,14]
Reservoir animals	Main vertebrate reservoir animals assumed – *Myodes glareolus, Apodemus flavicollis, Apodemus agrarius, Apodemus sylvaticus, Microtus agrestis and Microtus arvalis, and Myodes glareolus*; detailed information and studies missing.[10]
Infected tick species (%)	*I. ricinus* (0.1%–5%); *D. reticulatus* (0.5%). (Chitimia-Dobler et al.[16]; Dobler, personal communication)
Dairy product transmission[14]	2016 first outbreak by goat milk and goat cheese for >50 years in Germany; 2 patients 2017 outbreak in school with 8 patients[18]

Figure 1: Burden of TBE in Germany over time

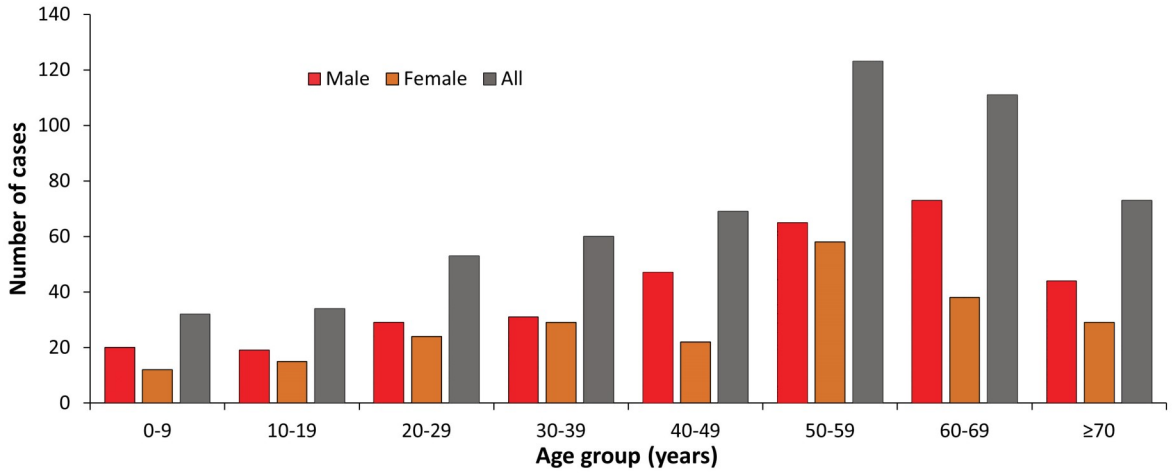


Source Data: Appendix—Figure 1

Please note that TBE is not evenly distributed throughout Germany; in some specific areas of the country, TBE incidence may be >10/100,000 (see text for details).
[Robert Koch-Institute, SurvStat. Available at: http://survstat.rki.de/Content/Query/Create]

Table 2: TBE reporting and vaccine prevention in Germany	
Mandatory TBE reporting	All patients with confirmed TBE by serological methods (TBEV IgM ± IgG) or by virus detection are reported to the State Public Health Authorities and to the Federal State Public Health Authority (Robert Koch-Institute: www.rki.de)
Other TBE surveillance	n/a
Special clinical features	Biphasic disease in about 50% Risk groups: permanent inhabitants and visitors of highly endemic areas; mainly acquired during leisure activities 40% of patients meningoencephalitis, 10% meningoencephalomyelitis; no reliable data available on neurological sequelae; in a large study 40%–50% of patients with long-term sequelae; mortality rate 1%–2%[9]
Available vaccines	Encepur Erwachsene, Encepur Kinder (Bavarian Nordic), FSME-IMMUN Erwachsene, FSME-IMMUN Kinder (Pfizer)
Vaccination recommendations and reimbursement	All inhabitants and visitors of known endemic areas with a risk of tick contact; (STIKO recommendation [www.rki.de])
Vaccine uptake by age group/ risk group/ general population	Vaccination rates in endemic areas 25% to 75%, depending on the district (Survey of the German Society of Consumption Research and personal seroprevalence studies).
Name, address/website of TBE National Reference Center	Robert Koch-Institute (Federal Authority of Public Health), Nordufer 20, 13353 Berlin, Germany (www.rki.de) Bundeswehr Institute of Microbiology, Neuherbergstrasse 11, 80937 München, Germany (gerharddobler@bundeswehr.org)

Figure 2: Age and gender distribution of TBE in Germany



[Robert Koch-Institute, SurvStat. Available at: http:// survstat.rki.de/Content/Query/Create.] *Source Data: Appendix—Figure 2*

TBEV-isolation and TBE cases in Germany			
Year of isolation	Strain name	Source of isolation	Location of isolation
1975[11]	K23	Tick	Karlsruhe, Baden-Württemberg
2006[8]	AS33	Tick	Amberg, Bavaria
2007[12]	Salem	Monkey brain	Salem, Baden-Württemberg
2009*	HM strains	Tick	Amberg, Bavaria
2011[13]	HB171/11	Tick	Heselbach, Bavaria
2014**	Bottnang	Tick	Stuttgart, Baden-Württemberg
2016*	HM-M1	Bank vole brain	Amberg, Bavaria
2016*,***	tbd	Goat milk cheese	Zwiefalten, Baden-Württemberg
2016[15]	tbd	Tick	Aubachstrasse, Baden-Württemberg
2017[15]	tbd	Tick	Schiltach, Baden-Württemberg
2017[16]		Tick (*D. reticulatus*)	Battaune, Saxony

**Dobler, personal communication; **Oehme, personal communication; ***Chitimia-Dobler et al.[16]; tbd, to be determined*

Appendix

Source data: Figure 1

Year	Number of cases	Incidence / 10^5
1978	8	
1979	1	<0.1
1980	32	<0.1
1981	30	<0.1
1982	97	0.17
1983	29	<0.1
1984	50	<0.1
1985	26	<0.1
1986	n.a.	
1987	n.a.	
1988	n.a.	
1989	n.a.	
1990	n.a.	
1991	44	<0.1
1992	142	0.18
1993	118	0.15
1994	306	0.38
1995	226	0.28
1996	114	0.14
1997	211	0.26
1998	148	0.18
1999	115	0.14
2000	133	0.16
2001	255	0.31
2002	239	0.29
2003	277	0.34
2004	274	0.33
2005	432	0.52
2006	544	0.66
2007	239	0.29
2008	289	0.35
2009	313	0.38
2010	260	0.32
2011	424	0.52
2012	195	0.24
2013	420	0.52
2014	264	0.33
2015	221	0.27
2016	353	0.43
2017	485	0.59
2018	582	0.70
2019	443	0.53
2020	717	0.86
2021	421	0.51
2022	555	0.66
2023	474	0.58

Source data: Figure 2 (2023, with data for 2010–2022 also shown):

Year	Gender	Age group (years)							
		0–9	10–19	20–29	30–39	40–49	50–59	60–69	≥70
2010	Male	3	12	13	18	39	26	26	23
	Female	6	4	7	16	28	24	8	7
	All	**9**	**16**	**20**	**34**	**67**	**50**	**34**	**30**
2011	Male	18	19	18	15	76	62	34	27
	Female	7	13	8	23	42	25	18	18
	Unknown		1						
	All	**25**	**33**	**26**	**38**	**118**	**87**	**52**	**45**
2012	Male	3	5	10	14	34	27	13	17
	Female	3	3	9	7	15	19	7	9
	All	**6**	**8**	**19**	**21**	**49**	**46**	**20**	**26**
2013	Male	17	22	25	26	47	53	33	38
	Female	5	5	15	24	36	35	17	21
	Unknown				1				
	All	**22**	**27**	**40**	**51**	**83**	**88**	**50**	**59**
2014	Male	5	5	11	17	39	39	25	27
	Female	4	3	8	14	24	20	10	13
	All	**9**	**8**	**19**	**31**	**63**	**59**	**35**	**40**
2015	Male	5	11	11	11	17	30	27	18
	Female	4	5	6	6	23	21	12	14
	All	**9**	**16**	**17**	**17**	**40**	**51**	**39**	**32**
2016	Male	14	16	18	18	25	35	48	28
	Female	6	8	11	14	32	50	19	11
	All	**20**	**24**	**29**	**32**	**57**	**85**	**67**	**39**
2017	Male	13	14	22	36	43	81	52	50
	Female	7	14	13	16	27	52	25	19
	Unknown						1		
	All	**20**	**28**	**35**	**52**	**70**	**134**	**77**	**69**
2018	Male	25	16	34	30	57	74	68	66
	Female	15	11	15	27	42	48	28	25
	Unknown						1		
	All	**40**	**27**	**49**	**57**	**99**	**123**	**96**	**91**
2019	Male	16	19	23	26	39	58	47	43
	Female	4	6	14	15	29	48	37	20
	All	**20**	**25**	**37**	**41**	**68**	**106**	**84**	**63**
2020	Male	28	31	38	41	50	102	76	75
	Female	13	20	18	28	33	80	51	28
	Unknown							1	
	All	**41**	**51**	**56**	**69**	**83**	**182**	**128**	**103**
2021	Male	16	21	19	30	31	59	48	38
	Female	6	3	10	19	17	49	24	27
	Unknown			1					
	All	**22**	**24**	**30**	**49**	**48**	**108**	**72**	**63**
2022	Male	20	19	29	31	47	65	73	44
	Female	12	15	24	29	22	58	38	29
	All	**32**	**34**	**53**	**60**	**69**	**123**	**111**	**73**
2023	Male	10	16	24	31	32	62	64	23
	Female	5	9	8	26	25	47	37	18
	All	**15**	**25**	**32**	**57**	**57**	**109**	**101**	**41**

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References

1. Sinnecker H. Zeckenenzephalitis in Deutschland. *Zentralbl Bakteriol Orig*. 1960;180:12-18.
2. Apitzsch L, Sinnecker H, Wigand R, Berndt D. Zeckenencephalitis-Virusisolierungen in der DDR 1965-66 und einige Stammdifferenzierungen [Tick-borne encephalitis virus isolation in the German Democratic Republic in 1965-66 and some strain-specific differences]. *Zentralbl Bakteriol Orig*. 1968;207(4):429-434.
3. Queisser H. Beobachtungen über verschiedene Fälle von Zeckenenzephalitis in Deutschland. *Münch Med Wochenschr*. 1962;47:2288.
4. Scheid W, Ackermann R, Bloedhorn H, Löser R, Liedtke G, Skrtic N. Untersuchungen über das Vorkommen der Zentraleuropäischen Enzephalitis in Süddeutschland. *Dtsch Med Wochenschr*. 1964;89:2313-7. doi:10.1055/s-0028-1113279
5. Ackermann R, Scheid W, Küpper B. Infektionen mit dem Virus der Zentraleuropäischen Enzephalitis in Südwest-Deutschland. *Dtsch Med Wochenschr*. 1966;91(25):1141-3. doi:10.1055/s-0028-1110717
6. Süss J, Sinnecker H, Sinnecker R, Berndt D, Zilske E, Dedek G, Apitzsch L: Epidemiology and ecology of tick-borne encephalitis in the eastern part of Germany between 1960 and 1990 and studies on the dynamics of a natural focus of tick-borne encephalitis. *Zentralbl Bakteriol*. 1992;277(2):224-35. doi:10.1016/s0934-8840(11)80617-1
7. Süss J, Beziat P, Rohr HP, Treib J, Haass A. Detection of the tick-borne encephalitis virus (TBEV) in ticks in several federal "Länder" of Germany by means of the polymerase chain reaction (PCR) – characterization of the virus. *Infection.* 1996;24:403-4. doi:10.1007/BF01716096
8. Kupča AM, Essbauer S, Zoeller G, et al. Isolation and molecular characterization of a tick- borne encephalitis virus strain from a new tick-borne encephalitis focus with severe cases in Bavaria, Germany. *Ticks Tick Borne Dis*. 2010;1(1):44-51. doi:10.1016/j.ttbdis.2009.11.002
9. Kaiser R. Tick-borne encephalitis: Clinical findings and prognosis in adults. *Wien Med Wochenschr*. 2012;162 (11-12):239-43. doi:10.1007/s10354-012-0105-0
10. Achazi K, Růžek D, Donoso-Mantke O, et al. Rodents as sentinels for the prevalence of tick-borne encephalitis virus. *Vector Borne Zoonotic Dis*. 2011;11(6):641-7. doi:10.1089/vbz.2010.0236
11. Heinz FX, Tuma W, Kunz C. Antigenic and immunogenic properties of defined physical forms of tick-borne encephalitis virus structural proteins. *Infect Immun*. 1981;33(1):250-7. doi:10.1128/iai.33.1.250-257.1981
12. Süss J, Dobler G, Zöller G, et al. Genetic characterization of a tick-borne encephalitis virus isolated from the brain of a naturally exposed monkey (Macaca sylvanus). *Int J Med Microbiol*. 2008;298(S1):295-300.
13. Dobler G, Bestehorn M, Antwerpen M, Överby-Wernstedt A. Complete genome sequence of a low-virulence tick-borne encephalitis virus strain. *Genome Announc*. 2016;4(5):e01145-16.
14. Brockmann SO, Oehme R, Buckenmaier T, et al. A cluster of two human cases of tick-borne encephalitis (TBE) transmitted by unpasteurized goat milk and cheese in Germany, May 2016. *Euro Surveill*. 2018;23(15):17-00336. doi:10.2807/1560-7917.ES.2018.23.15.17-00336
15. Bestehorn M, Weigold S, Kern WV, et al. Phylogenetics of tick-borne encephalitis virus in endemic foci in the upper Rhine region in France and Germany. *PLoS One*. 2018;13 (10):e0204790. doi:10.1371/journal.pone.0204790
16. Chitimia-Dobler L, Lemhöfer G, Krol N, Bestehorn M, Dobler G, Pfeffer M. Repeated isolation of tick-borne encephalitis virus from Dermacentor reticulatus ticks in an endemic area in Germany. *Parasit Vectors*. 2019;12(1):90. doi:10.1186/s13071-019-3346-6
17. Euringer K, Girl P, Kaier K, et al. Tick-borne encephalitis IgG antibody surveillance: vaccination- and infection-induced seroprevalences, south western Germany, 2021. *Euro Surveill*. 2023;28(12):2200408. doi:10.2807/1560-7917.ES.2023.28.12.2200408
18. Chitimia-Dobler L, Lindau A, Oehme R, et al. Tick-Borne Encephalitis Vaccination Protects from Alimentary TBE Infection: Results from an Alimentary Outbreak. *Microorganisms*. 2021;9(5):889. Published 2021 Apr 21. doi:10.3390/microorganisms9050889