Chapter 13

TBE in Hungary

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

History and current situation

Hungarian scientists were among the pioneers in Europe as the tick-borne encephalitis virus (TBEV) was isolated in 1952, 30 years after the TBEV had been described in Russia (see chapters 3).[1] However, most of their observations were published in the Hungarian language, and therefore did not become widely distributed. Between 1981 and 1997, the average annual number of TBE cases reported to authorities was around 300, and as of that year, it decreased to fewer than 20 patients per year (Figures 1, 2). It has been speculated that the decrease is a result of underreporting of TBE, following a change in the reimbursement system for payments related to serologic TBE diagnosis.[2-4] However, two main arguments contradict the 'underreporting hypothesis':

During the 5 years before 1997, a total of 1,800,000 FSME vaccine doses were sold by pharmacies (Figure 1), and this convincingly explains the observed reduction of TBE cases. Furthermore, after 1997, lethal TBE cases decreased in parallel with decreased incidence. If lower incidences had resulted from underreporting, then lethal cases would not have changed since the etiology of a lethal case is regularly determined by mandatory autopsy and other diagnostic tests.

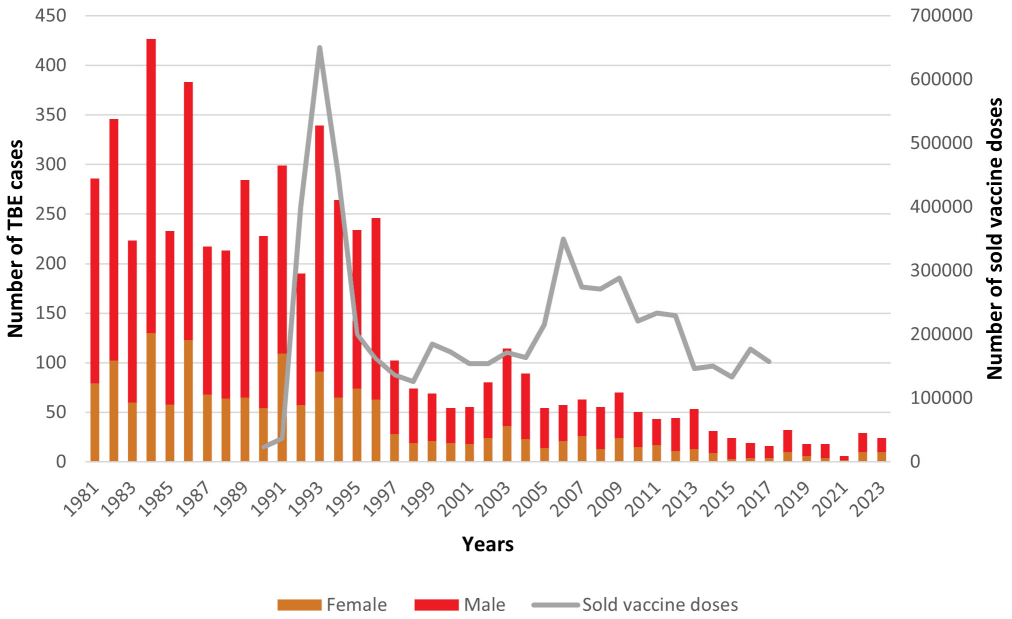
The incidence data from the Hungarian military are similar to that of the civilian population: no case has been reported since 2003. 'Underreporting'[5] in this context would be practically impossible. The reporting system for TBE has not changed, and a reduction of cases (most probably due to vaccination) sufficiently explains why the use of TBE serology was subsequently reduced.

Overview of TBE in Hungary

Table 1: Virus, vector, transmission of TBE in Hungary	
Viral subtypes, distribution	TBEV-EU[6]
Reservoir animals	*Apodemus agrarius, Apodemus flavicollis, Microtus arvalis, Myodes glareolus*[6] *Apodemus flavicollis, Apodemus agrarius, Myodes glareolus, Microtus subterraneus*[7]
Infected tick (Figure 3)	2/2485 = 0.08%[1] 6/8310 ≈ 0.07%[8] 40/51,746 ≈ 0.08%; the highest figure was 22/6738 ≈ 0.3% in this study[9] 1/17,500 ≈ 0.006%[10] 5/2196 ≈ 0.23%, only with PCR[11] 3/9616 ≈ 0.03%[7]
Dairy product transmission	Out of the 81 food-borne TBE cases registered between 1992 and 2011, 55.1% were male. Also, 4.4% of the total number of TBE cases were milk-borne. On average, 24.5% of people who drank infected goat milk suffered from clinical symptoms of neurologic infection. Historically, only 2 TBE epidemics in Hungary were caused by cow milk.[12] The largest epidemic came from a single goat (of the 75 tested animals) with 25 cases amongst 154 subjects who had consumed contaminated milk.[13] In that year (2007), almost half of the total number (30/63) of registered TBE cases were of alimentary origin.

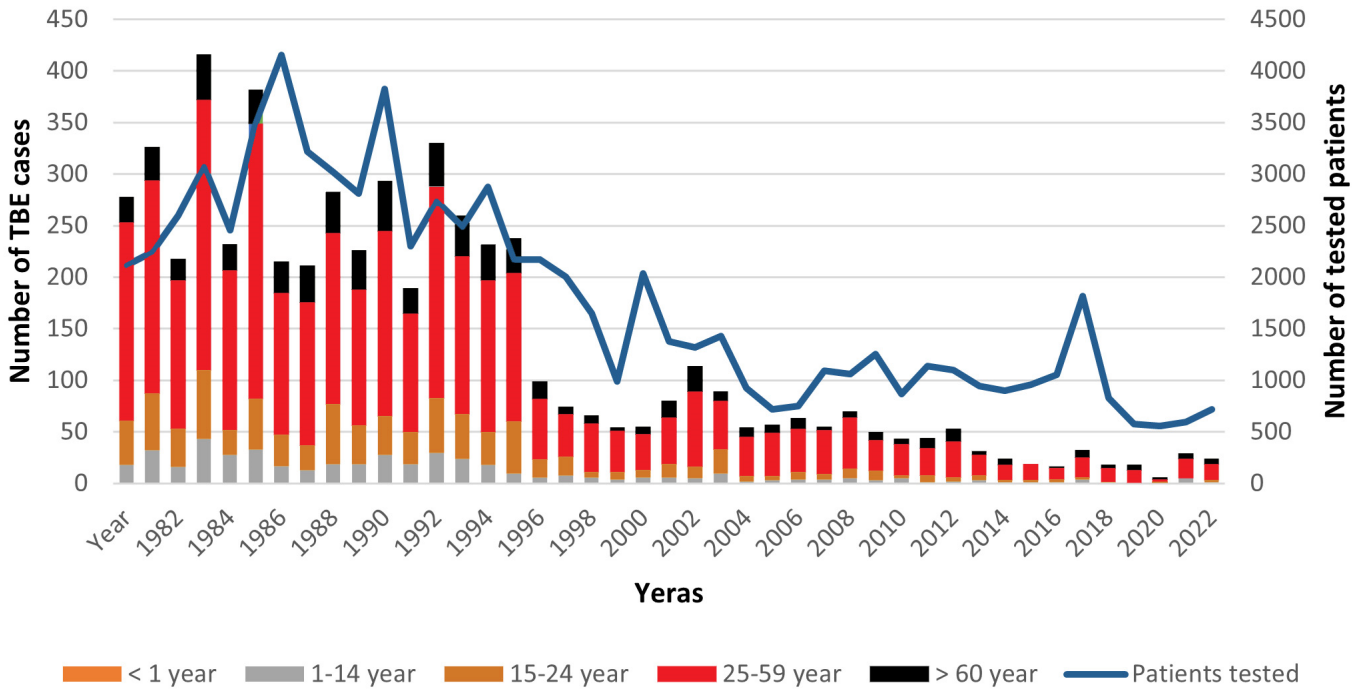
Table 2: TBE reporting and vaccine prevention in Hungary	
Mandatory TBE reporting	Every physician who establishes a diagnosis of TBE must report it. Practically, these are hospital-based specialists for infectious diseases, pediatricians, internists, and neurologists. Case definition: clinical symptoms of central nervous infection + presence of TBE immunoglobulin M (IgM) antibodies in serum and cerebrospinal fluid (CSF) OR TBEV-specific IgM in CSF OR isolation of infectious virus from clinical samples OR detection of TBEV RNA in clinical samples OR seroconversion and/or 4-fold specific IgG increase in a sample pair.[14]
Other TBE surveillance	No
Special clinical features	• In one study, 21% of retrospectively collected patient cases were agrarian, 16% forestry workers.[8] • Other work has shown 12% to 16% of patients with TBE were forestry workers.[9,10] • Similarly, another report found 10.4% of 5196 cases were forestry, 11% other agrarian workers.[15] • Also, 2% of the 1,670 forestry workers screened for Lyme borreliosis went through TBE (Lakos, unpublished data). • 65% of hospitalized patients could recall a biphasic course of their TBE.[16]
	In the same department of the Central Hospital for Infectious Diseases, during the years 1976–1980 (n=100), 27 patients showed paresis, 2 died. In 1987–1991 (n=93), only 5 patients had paresis, none of them died.[17] From 1985 to 2008, the death rate from TBE in Hungary was 29/3987 (0.73%).[18] However, in an earlier period from 1977 to 1996, the fatality rate was higher – 43/5196 (0.83%). Most of the fatal cases were male (85%), while the proportion of male patients in the total TBE population was 70%.[15]
Available vaccines	FSME IMMUN Inject vaccine has been available for public use since 1992; another vaccine, Encepur, was launched in 1995. Previously, between 1977 and 1990, some 150,000 doses were distributed for the at-risk population. (Note: during 1979 to 1983, the FSME IMMUN Inject vaccine was considered to be ineffective both clinically and serologically.[19] It has to be mentioned that TBE vaccination in Austria at the same time showed a field effectiveness 79.4%–100% after the second dose and 97.3%–100% after the third dose.[26]) From 1990 to 2017, 6 million doses were sold. (The Hungarian population is 10 million.)
Vaccination recommendations and reimbursement	When FSME IMMUN Inject was first available in Hungary in the early 1990s, the reimbursement rate was 95%; the pharmacy price was 59 HUF (≈20 euro cents). After a gradual decrease, the reimbursement was cancelled for the FSME IMMUN Inject and Encepur vaccines in 2008 and 2012, respectively. The present price is around 13,000 HUF (40 euros). For occupationally exposed workers, vaccination has been mandatory at the employers' expense since 1999.[20]
Vaccine uptake by age group/ risk group/general population	Not available.
Name, address/website of TBE National Reference Center	National Public Health Center, National Reference Laboratory for Viral Zoonoses, Budapest, Hungary [https://www.nnk.gov.hu/].

Figure 1: Gender distribution of TBE cases and the sold number of doses of TBE vaccines



The data of TBE cases in this graph originated from the National Reference Laboratory for Viral Zoonoses and from the Department of Epidemiological and Vaccination Surveillance of the National Public Health Center. The data for 1998 is missing, an estimation is plotted in the graph. No reliable information on the number of vaccine doses sold in 1995 could be found; estimated information was used. (The number of vaccine doses sold is not available from 2018.)

Figure 2: Burden of TBE in Hungary from 1981 to 2023.[24-25] Age distribution and the requested number of tested patients

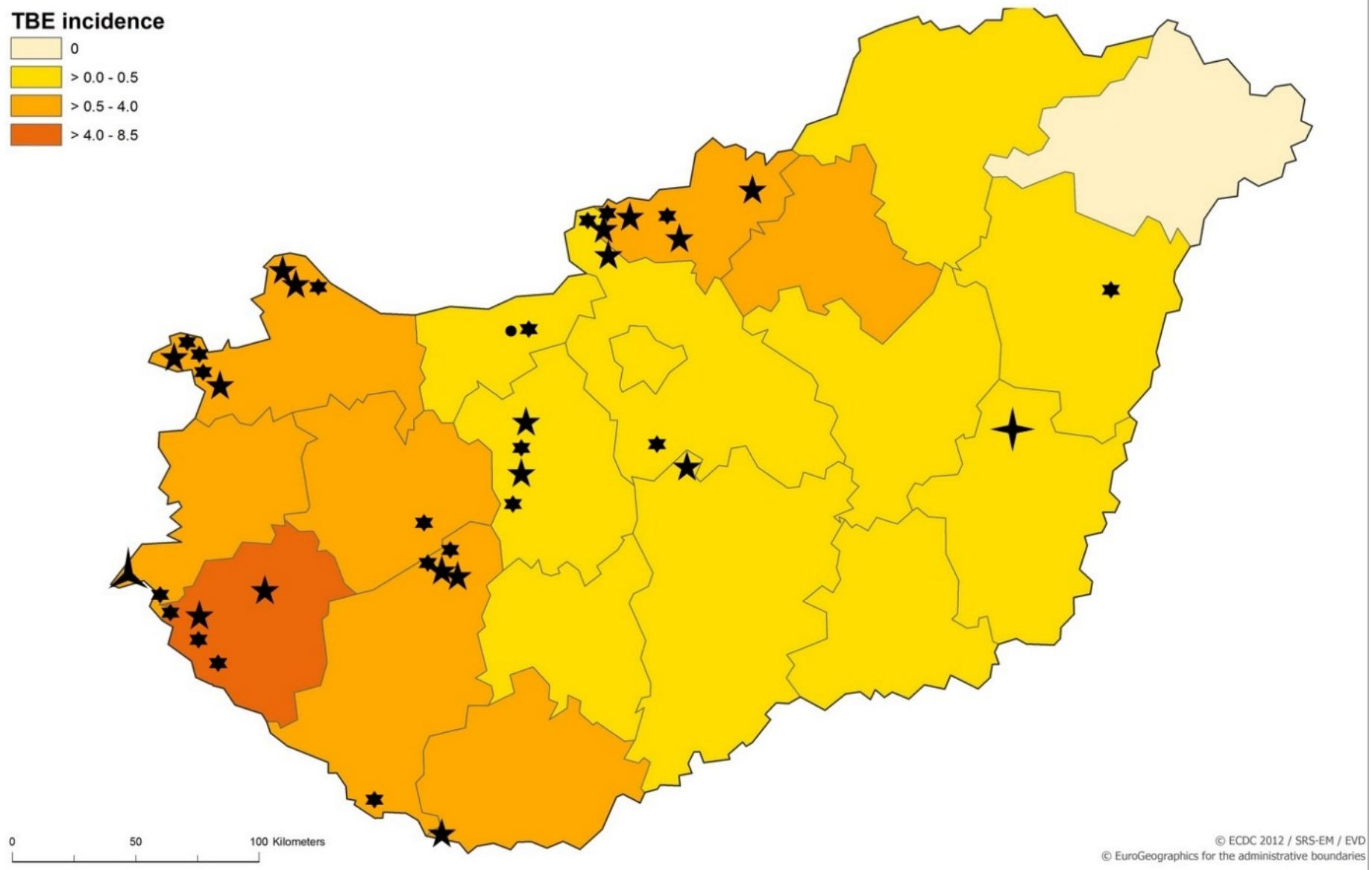


Source Data: Appendix-Figure 2

The data of TBE cases in this graph originated from the National Reference Laboratory for Viral Zoonoses and from the Department of Epidemiological and Vaccination Surveillance of the National Public Health Center.

The number of TBE cases decreased dramatically after a mass vaccination campaign from 1992 to 1995. The Hungarian population is approximately 10 million, so the incidence for 100 cases is 1/100,000. A West Nile virus epidemic resulted in 225 infections in 2018 (https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2019.24.28.1900038). That was the reason for the striking elevation of the requested TBE serological tests. The elevated number of tests coincided with the elevated number of verified TBE cases.

Figure 3: TBEV-isolation and TBE cases in Hungary



Map of Hungary showing human TBE incidence (ECDC, 2017).[22] TBEV isolation sites are marked by circles (Fornosi, 1954),[1] six-pointed stars (Molnár, 1979),[23] five-pointed stars (Gerzsenyi, 1980 and 1985),[9,10] four-pointed star (Pintér, 2013),[11] and three-pointed star (Zöldi, 2015).[7]
A map with more detailed incidence data[21] can be downloaded from http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20128.

Appendix

Source data: Figure 2

	Female	Male	<1 year	1–14 years	15–24 years	25–59 years	>60 years	Unknown age	Total TBE cases	Sold vaccine doses	Samples tested (IgG)
1981	79	207	0	18	43	192	25	8	286	N/A	2113
1982	102	244	0	32	55	207	32	20	346	N/A	2241
1983	60	163	0	16	37	144	21	5	223	N/A	2595
1984	130	297	0	43	67	262	44	11	427	N/A	3074
1985	58	175	0	28	24	155	25	1	233	N/A	2456
1986	123	260	0	33	49	267	33	1	383	N/A	3486
1987	68	149	0	17	30	138	30	2	217	N/A	4157
1988	64	149	0	13	24	139	35	2	213	N/A	3215
1989	65	219	0	19	58	166	39	2	284	N/A	3016
1990	54	174	0	19	37	132	38	2	228	23251	2809
1991	109	190	0	28	37	180	48	6	299	36,720	3823
1992	57	133	0	19	31	115	24	1	190	400,000	2301
1993	91	248	0	30	53	205	42	9	339	650,000	2737
1994	65	199	0	24	43	153	40	4	264	450,000	2488
1995	74	160	0	18	32	147	34	3	234	200,000	2875
1996	63	183	0	10	50	144	34	8	246	161,717	2168
1997	28	74	0	6	17	59	17	3	102	136,394	2168
1998	19	55	0	8	18	41	7	0	74	125,843	2000
1999	21	48	0	6	5	47	8	3	69	184,555	1649
2000	19	35	0	4	7	40	3	0	54	172,615	988
2001	18	37	0	6	7	35	7	0	55	153,941	2036
2002	24	56	0	6	13	45	16	0	80	154,165	1379
2003	36	78	0	5	11	73	25	0	114	171,151	1315
2004	23	66	0	10	23	47	9	0	89	163,347	1428
2005	14	40	0	2	5	38	9	0	54	215,238	927
2006	21	36	0	3	4	42	8	0	57	349,206	467
2007	26	37	0	4	7	42	10	0	63	274,396	750
2008	13	42	0	4	5	43	3	0	55	271,092	1636
2009	24	46	0	5	9	50	6	0	70	288,629	1527
2010	15	35	0	3	9	30	8	0	50	221,095	1154
2011	17	26	0	5	3	30	5	0	43	233,579	1003
2012	11	33	0	1	7	26	10	0	44	229,794	1095
2013	13	40	0	2	4	35	12	0	53	146,518	1099
2014	9	22	0	3	5	20	3	0	31	150,507	840
2015	3	21	0	1	2	15	6	0	24	132,878	855
2016	4	15	0	1	2	16	0	0	19	177,064	958
2017	4	12	0	1	3	11	1	0	16	157,687	1050
2018	10	22	0	4	2	19	7	0	32	N/A	1814
2019	6	12	0	0	1	14	3	0	18	N/A	830
2020	4	14	0	0	0	13	5	0	18	N/A	578
2021	2	4	0	0	1	3	2	0	6	N/A	553
2022	10	19	0	5	0	19	5	0	29	N/A	597
2023	10	14	0	1	2	16	5	0	24	N/A	719

N/A: data not available

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