

Mycobacterium bovis in human population in four Central European countries during 1990–1999

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ABSTRACT: A survey on *Mycobacterium bovis* and *M. tuberculosis* in humans has been performed in four Central European countries (Croatia, the Czech Republic, Slovak Republic and Slovenia) during the years 1990 to 1999. These countries cover an area of 204 688 km² with 22 135 million population. During the period, new cases of tuberculosis were bacteriologically diagnosed in 47 516 patients. *M. tuberculosis* was detected in 47 461 (99.88%) cases, whereas *M. bovis* was found only in 55 (0.12%) patients. The rate of infection due to *M. bovis* in humans did not exceed 0.29% in the study countries. The annual incidence of bacteriological confirmed *M. bovis* cases did not exceed 0.1 per 100 000 inhabitants. In the Czech Republic out of 44 tuberculosis patients due to *M. bovis*, 32 (72.7%) were older than 61 years and originated from rural areas, where they lived during childhood and worked in agricultural occupations. These patients may have suffered a reactivation of persistent (long-standing) *M. bovis* infection as they got older. Bovine tuberculosis in cattle was eliminated from these countries during the second half of the 1960s (Croatia in 1966, Czech Republic and Slovak Republic – former Czechoslovakia in 1968, Slovenia in 1973) and the incidence of outbreaks of bovine tuberculosis in cattle were very low, thus the disease in humans was unexpected.

Keywords: human tuberculosis; animal tuberculosis; risk assessment

In Central Europe, infection with *Mycobacterium bovis* was a serious cause of human and animal tuberculosis until the middle of the last century (Thoen and Steele, 1995; Grange, 1996). Since then, however, the epidemiological situation of this disease in cattle has improved as a result of successful national bovine tuberculosis eradication programmes. Similarly the incidence of bovine tuberculosis in other livestock was gradually declined (Thoen and Steele, 1995).

A reduction in the incidence of the disease was enhanced by an improved understanding of the pathogenesis of the disease, introduction of milk pasteurisation and meat inspection at abattoirs

(Mohelsky, 1954; Jelinek, 1959; Dobes, 1959; Holec and Kral, 1960; Drazan *et al.*, 1962). Other preventative veterinary hygiene measures in agriculture were also introduced to reduce the risk of infection to humans working with infected animals. As a result, human tuberculosis due to *M. bovis* infection gradually decreased in Central Europe to the current low level compared to the relatively high occurrence of *M. tuberculosis* cases (Thoen and Steele, 1995; O'Reilly and Daborn, 1995; Moda *et al.*, 1996; Grange, 1996).

In the second half of the 20th century the decreasing incidence of bovine tuberculosis in humans reflected that in cattle. For example, the last case

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of bovine tuberculosis in cattle was detected in Croatia in 1998, in the Czech Republic in 1995 and in Slovak Republic and Slovenia in 1993 (Pavlik *et al.*, 2002a,d). Following the successful control of bovine tuberculosis in cattle, the incidence and prevalence of *M. bovis* in other animals also decreased (Pavlik *et al.*, 2002c).

In the Czech Republic and Slovak Republic (former Czechoslovakia) bovine tuberculosis in cattle was eliminated in 1968 (Polak, 1969). *M. bovis* infection occurred in human until the end of 1960s, mainly in children, as a result of drinking unpasteurised milk from infected animals (Langerova and Zavadilova, 1968; Vojtek and Berkova, 1968; Grigelova and Turzova, 1969; Vojtek *et al.*, 1969; Mikova and Kubin, 1970; Vojtek *et al.*, 1975; Maar *et al.*, 1975). Tuberculous lesions were most frequently localised in the cervical lymph nodes (Sykora and Grigelova, 1967; Maar *et al.*, 1975). Subsequently, the annual incidence of human tuberculosis due to *M. bovis* gradually decreased to a few cases (Virsik *et al.*, 1973; Viznerova and Polanecky, 1974; Truksova *et al.*, 1978; Virsik *et al.*, 1978; Kubin and Svandova, 1980, 1982; Pavlas and Mezensky, 1982; Havelkova *et al.*, 1987, 1998; Havelkova and Pavlik, 1995; Pavlik *et al.*, 1998a,b).

Between 1979 and 1983 the clinical occurrence of tuberculosis caused by *M. bovis* in the Czech Republic was analysed in 71 patients (Havelkova

et al., 1987). During the study period distribution of lesions, prognosis and course of the disease were similar to patients with tuberculosis caused by *M. tuberculosis*. Patients with tuberculosis caused by *M. bovis* however suffered relapses of the disease nearly twice as often as compared to tuberculosis caused by *M. tuberculosis*. Extrapulmonary lesions of bovine tuberculosis were found only rarely compared to the respiratory tract. The cavernous form of lung tuberculosis caused by *M. bovis* was detected in one patient in Slovakia (Svejnochova *et al.*, 1993).

In the last decades of the 20th century more attention has been put on the importance of tuberculosis in humans due to different reasons like antituberculous drugs resistance, increasing incidence of tuberculosis in some countries, immunodeficiency in HIV/AIDS infected individuals, etc. A summary analysis of *M. bovis* importance has not, however, been conducted although some papers were published (Havelkova and Pavlik, 1995; Badalik *et al.*, 1996, 1997a,b, 1998, 1999; Pavlik *et al.*, 1998a,b; Havelkova *et al.*, 1998).

The aim of our work was therefore to evaluate the occurrence of bovine tuberculosis in humans between 1990 and 1999 in four Central European countries (Croatia, the Czech Republic, Slovak Republic and Slovenia) which cover an area of 204 688 km² and have 22.135 million inhabitants (Table 1).

Table 1. Geographic, demographic and agricultural data of four Central European countries*

Country	Number of		National control programmes against bovine tuberculosis in cattle	Number of			Incidence of <i>M. bovis</i> in cattle herds during 1990–1999**
	inhabitants (mil.)	km ²		cattle (mil.)	cows (mil.)	herds	
Croatia	4.505	56 538	1953–1966	0.493	0.330	nk	32 (1998)
Czech Republic	10.330	78 864	1959–1968	2.030	0.830	5 410	7 (1995)
Slovak Republic	5.350	49 035	1959–1968	0.916	0.348	1 369	8 (1993)
Slovenia	1.950	20 251	1962–1973	0.504	0.210	nk	4 (1993)
Total	22.135	204 688	1953–1973	3.942	1.718		51

Explanations:

*source of the data: WHO (<http://who.int>), Surveillance of Tuberculosis in Europe (<http://www.ceses.org/euroth/eurotb.htm>) and OIE (FAO-OIE-WHO, 1997) from 1995

**published previously (Pavlik *et al.*, 2002d)

(1993, 1995, 1998) – years of the last outbreaks of bovine tuberculosis in cattle

nk = not known

tub.= tuberculosis

Table 2. Prevalence of bacteriological confirmed *M. bovis* infection in human patients in seven regions of the Czech Republic during 1990 to 1999

Region	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	Total
Prague	0	1	1	0	0	0	1	0	0	1	4
Centralbohemian	4	0	2	2	2	1	1	0	0	1	13
Southbohemian	0	0	0	0	0	0	0	0	0	0	0
Westbohemian	1	1	0	1	0	0	0	0	0	0	3
Northbohemian	1	1	3	1	1	0	1	0	0	1	9
Eastbohemian	1	2	0	2	1	1	0	0	2	0	9
Southmoravian	0	0	0	0	0	0	0	0	0	0	0
Northmoravian	1	3	2	0	0	1	0	1	0	0	8
Total	8	8	8	6	4	3	3	1	2	3	46

MATERIAL AND METHODS

Sources of statistical data

Statistical data were obtained for 1990 to 1999 from the relevant National Reference Laboratories. In the Czech Republic data on the prevalence of bovine tuberculosis were obtained separately from all seven regions (Table 2). In the Czech Republic, Slovak Republic and Slovenia data on the gender and age were obtained for 44 patients (Table 3).

RESULTS

During the period, new cases of tuberculosis were bacteriologically diagnosed in 47 516 patients. *M. tuberculosis* was detected in 47 461 (99.88%) cases, whereas *M. bovis* was found only in 55 (0.12%) patients. The rate of infection due to *M. bovis* in humans in Croatia was 0.05%, in the Czech Republic 0.29%, in Slovak Republic 0.07% and in Slovenia 0.03% (Table 4). The occurrence of bovine tuberculosis in the Czech Republic was also low (Table 2).

The data obtained for 44 patients with tuberculosis due to *M. bovis* in the Czech Republic, Slovakia and Slovenia indicate that the ratio of infection in men and women was 1 : 4. The number of individuals varied among age categories with none of the patients under 30 years of age. Twelve (27%) patients were in the age group 31 to 60 years and the remaining 32 (73%) were between the age group 61 to 90 (Table 3). Thirty (83%) of the 36 patients in

the Czech Republic, were either inhabitants of the rural area or had at least lived in the countryside and worked in farms in their youth.

DISCUSSION

The low incidence of tuberculosis in humans due to *M. bovis* (Tables 2 and 4) in the study countries can be largely attributed to the successful control of bovine tuberculosis in cattle (Straka, 1985; Kouba, 1988, 1999; Pavlas, 1999). In the terms of the Office International des Epizooties Animal Health Code definition, these four countries are classified as free

Table 3. Incidence of bacteriological confirmed *M. bovis* infection in age groups of patients in the Czech Republic, Slovak Republic and Slovenia during 1990 to 1999

Age in years	Total			%
	Female	Male	Total	
1–10	0	0	0	0
11–20	0	0	0	0
21–30	0	0	0	0
31–40	0	2	2	4.6
41–50	1	5	6	13.6
51–60	1	3	4	9.1
61–70	3	7	10	22.7
71–80	9	3	12	27.3
81–90	4	6	10	22.7
Total	18	26	44	100

Table 4. Incidence of bacteriological confirmed *M. tuberculosis* and *M. bovis* infection in human population in four Central European countries during 1990 to 1999

Year	Croatia			Czech Republic			Slovakia			Slovenia			Total number of patients with tuberculosis caused by						
	<i>M. tuberculosis</i>		<i>M. bovis</i>	<i>M. tuberculosis</i>		<i>M. bovis</i>	<i>M. tuberculosis</i>		<i>M. bovis</i>	<i>M. tuberculosis</i>		<i>M. bovis</i>	<i>M. tuberculosis</i>		<i>M. bovis</i>	%			
	abs.	rel.	abs.	rel.	abs.	rel.	abs.	rel.	abs.	rel.	abs.	rel.	abs.	rel.					
1990	2 576	55.0	0	0	1 505	14.5	7	0.07	1 191	22.7	2	0.04	419	22.1	0	0	5 691	9	0.16
1991	2 158	45.0	0	0	1 549	14.9	6	0.06	1 197	22.7	1	0.02	363	19.1	0	0	5 267	7	0.13
1992	2 185	46.0	2	0.04	1 420	13.8	8	0.08	1 180	22.6	0	0	388	20.4	1	0.05	5 173	11	0.21
1993	2 279	48.0	5	0.10	1 222	11.8	4	0.04	1 139	22.4	1	0.02	420	22.1	0	0	5 060	10	0.20
1994	2 217	46.0	2	0.04	1 161	11.2	3	0.03	1 165	22.5	0	0	334	17.6	0	0	4 877	5	0.10
1995	2 114	44.0	0	0	1 188	11.5	1	0.01	961	17.9	2	0.04	345	18.2	0	0	4 608	3	0.07
1996	2 174	45.0	1	0.02	1 095	10.6	2	0.02	849	15.8	1	0.02	423	22.3	0	0	4 541	4	0.09
1997	2 054	43.0	1	0.02	1 047	10.2	1	0.01	783	14.5	0	0	356	18.7	0	0	4 240	2	0.05
1998	2 118	44.0	0	0	1 065	10.3	1	0.01	744	13.8	0	0	346	18.2	0	0	4 273	1	0.02
1999	1 770	37.0	0	0	0 999	9.6	3	0.03	651	12.9	0	0	316	16.6	0	0	3 727	3	0.08
Total	21 649		11		12 242		36		9 860		7		3 710		1		47 461	55	0.12

Explanations:

abs. = absolute number of bacteriological confirmed cases

rel. = relative number of bacteriological confirmed cases per 100 000 inhabitants

¹per cent of patients with tuberculosis caused by *M. bovis*

of bovine tuberculosis, because the prevalence of infected cattle herds is below 0.2% (Pavlik *et al.*, 2002d).

Detection of *M. bovis* predominantly in patients of the high age groups in our study (Table 3) was also recorded in Slovak Republic between 1972 and 1990, and after 1968 in the Czech Republic (Kubin and Svandova, 1982; Pavlas and Mezensky, 1982; Havelkova *et al.*, 1987; Badalik *et al.*, 1995). Most patients (80%) with bovine tuberculosis infection also came from rural areas, as has been observed previously by others. In Slovakia for example 80% of 68 patients with bovine tuberculosis lived in the countryside in their youth (Badalik *et al.*, 1995). The cases in older patients are the legacies of bovine tuberculosis which had occurred before the elimination of the disease from cattle population in the former Czechoslovakia in 1968 (Hrstka, 1957; Kladny, 1958; Canda, 1962; Holzer, 1964; Kouba, 1965; Laktis *et al.*, 1969; Grigelova and Turzova, 1969; Bajan, 1983; Pavlas, 1999).

Also, in the first decade after the elimination of bovine tuberculosis in Czechoslovakia, new infected cattle herds arose mainly because of outbreaks of infection in the anergic animals occurred more frequently (Rossi and Dokoupil, 1969; Rossi *et al.*, 1969; Hejlíček *et al.*, 1970; Poláček and Bajan, 1971; Popluhar *et al.*, 1974; Hejlíček and Chloupek, 1982; Pavlik *et al.*, 1998a,b). This later disease was then most probably an endogenous reactivation of a persisting *M. bovis* infection in their organism (Havelkova *et al.*, 1987; Thoen and Steele, 1995; Grange and Yates, 1996; Grange, 1996). This assumption is confirmed by the age structure of the patients presented in Table 3. The same may be true in animals which may be persistently infected and in which *M. bovis* infection may suddenly break out at a higher age (Brown *et al.*, 1994; Pavlik *et al.*, 2001, 2002a).

Although the question of the means of the transfer of the infection to humans was not the subject of our study, it is possible on the basis of data in literature from the Czech Republic and Slovak Republic to assume similar means for the infection of people in Central Europe. Because 80% of patients lived in the countryside, it is more likely that the source of *M. bovis* was direct or indirect contact with infected animals or their products. These people were most probably infected with *M. bovis* by oral (above all drinking infected, non-heat-treated milk) or aerogenic route by the contact with infected animals (Riha, 1957; Potocky, 1959; Jezek *et*

al., 1963, 1965, 1966a,b,c; Simek *et al.*, 1964; Kacin *et al.*, 1966; Klimsa, 1966; Kouba, 1968; Sykora *et al.*, 1971; Viznerova and Polanecky, 1974; Truksova *et al.*, 1978; Pavlas and Mezensky, 1982; Burjanova and Nagyova, 1985; Bajan and Burjanova, 1986). During an autopsy or handling with the infected carcasses or cadavers, butchers, veterinarians and others may also become infected (Robinson *et al.*, 1988). Concerning the human to human transmission of *M. bovis*, the paper published by Kubin *et al.* (1984) refers about a very seldom intra-human transmission of tuberculosis cause by this mycobacterium species. This fact indicates the “disappearance” of *M. bovis* infection in humans.

Milk may have been an important vehicle for the transmission of bovine tuberculosis to susceptible hosts. Culture demonstration of *M. bovis* in 1992 from cow's milk was reported by Pavlik *et al.* (1998a,b). In the Czech Republic for example, according to the current law No. 166/1999 Sb. **on veterinary care** and § 49 of regulation No. 287/1999 Sb. **on veterinary requirements for animal products**, under certain conditions selling of raw milk and milk products is permitted but this probably presents a low risk of infection given the virtual absence of tuberculosis in cattle.

CONCLUSIONS

Although bovine tuberculosis is eradicated from the cattle population of the study countries, considerable attention should also be given to the following risk factors:

1. Infected wild animals manifesting clinical signs of weakness and a loss of timidity may become a source of *M. bovis* for their self-sacrificing human rescuers.

2. Wild animals kept in captivity at zoological gardens and deer farms and domestic animals like cats, horses, dogs and others may pose the risk of infection for humans (Krejci, 1958; Pavlas *et al.*, 1965; Pavlik *et al.*, 2002b).

3. The transmission of *M. bovis* from an infected human being to animals is possible, like it was described in many works in the Czech Republic (Krivinka, 1957, 1959; Meissner, 1959; Raska, 1959; Illes, 1960; Sery *et al.*, 1963; Pavlas *et al.*, 1964, 1966; Pejsek, 1968; Hejlíček *et al.*, 1970; Hejlíček and Chloupek, 1982) and in other countries (Fromm and Wiesmann, 1953; Kuslys, 1958; Goerttler, 1962; Röder, 1964; Baldwin, 1968; Englert and Milbrandt, 1977).

4. Products from infected animals like milk and milk products processed from unpasteurised milk, total absence or inconsistent meat inspections in slaughterhouses and inadequate laboratory examination of organs with tuberculous alterations may leave a dangerous window of infection for humans.

5. Refugees from third countries with high prevalence of *M. bovis* and working in the farms may also represent a risk in spreading the infection.

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