

## DIAGNOSTICS OF TULAREMIA IN THE EAST-BOHEMIA REGION

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### Introduction

*Francisella tularensis* is an aetiological agent of tularemia. It was isolated by E. Francis in Tulare, California in 1911. The type A predominates in North America, the strains are more virulent than in the continental Europe (hares, ticks). The type B occurs in rodents, birds and ticks. It is more resistant to external conditions, with a long-term survival in cadavers, it occurs in Europe. The disease can be characterized in several clinical forms according to the mode of infection (a direct inoculation, inhalation of an infectious aerosol, and attached tick).

Tularemia is a zoonosis. The infection can also have character of a transmissible zoonosis when transmission of *F. tularensis* from rodents to man occurs through ticks.

*F. tularensis* ranks among potential biological warfare agents (BW) - especially due to an easy applic-

ation in the form of infectious aerosol and its high morbidity and lethality.

In our conditions tularemia occurs in endemic regions. In the Czech Republic there are known endemic tularemia foci in South-Moravia, South- and East Bohemia. The first cases of tularemia in Bohemia were diagnosed by Drbohlav in 1936 (290 persons).

### Methods

The study started in 1961 and was completed in 1996. The patients visited the general practitioners' outpatient surgeries or infectious departments or surgeries of hospitals in the East-Bohemia region. On suspicion of tularemia (lymph node syndrome, lymphadenopathy, suppurative lesions on hands) they were hospitalized in the Infection Clinic in Hradec Králové. A complex clinical examination, blood

taking for serological examination and a detailed epidemiological history were conducted. Diagnosis of tularemia was confirmed by serological examination in agglutination reaction. Its positive titre was assessed 1:160 and higher (IgM, IgG), its dynamics, respectively. Further on, an epidemiological screening at the place of residence and sampling of material for serological and microbiological examinations were conducted. In case of a surgical intervention there was conducted a histological examination of the sampled lymphatic nodes or tissue. A microbiological examination aimed at demonstration of *F. tularensis* in immunofluorescence or a direct isolation of the infective agent on thioglycolate agar.

### Results

During the observed period there were described 13 epidemics. Altogether 587 persons were affected, either by a manifest or latent forms of infection. A sporadic incidence was registered in 302 cases.

Table 1

Year	Number of cases		
	Manifest	Latent	Total
1962	68	14	82
1963	32.18	18	68
1965	41.28	8	77
1969	18.12	16	46
1971	39	31	70
1976	21	15	36
1980	48	11	59
1982	56	8	65
1984	47	7	54
1988	21	9	30

Total number of cases - 889.

Altogether 4,826 pair sera were examined in the study course - positivity reached 6.26 %. In the manifest cases of tularemia the positive geometric titre reached values of 1:80 to 1:2,560.

Table 2

Presents a survey of the diagnosed clinical forms

Diagnosed forms	Epidemic incidence		Sporadic incidence	
Bronchopulmonal	220	37.5 %	89	29.5 %
Ulceroglandular	151	25.7 %	112	37.1 %
Abdominal	37	6.3 %	11	3.6 %
Glandular	98	16.7 %	29	9.6 %
Combined forms	48	8.2 %	33	10.9 %
Unidentified	33	5.6 %	28	9.3 %

### Incidence of tularemia

In the years:

1961-1981 it reached 0.1-7.38 per 100,000 inhabitants  
1981-1996 it was 0.1-5.2 per 100,000 inhabitants

### Seasonal distribution of tularemia

In the years 1961-1996 the highest incidence was during the winter months:

January to April - 52.5 %  
May to September - 20.5 %  
October to December - 27.0 %

### Distribution of tularemia according to age

The age of patients ranged from 6 to 71 years. The highest affection was in the cohort of 30 to 70 years (76.13 %).

### Distribution of tularemia according to sex

Epidemic incidence:

men: 401 (68.3 %)  
women: 186 (31.7 %)

Sporadic incidence:

men 171 (56.6 %)  
women 131 (43.4 %)

### A direct demonstration of *F. tularensis*

A direct demonstration of *F. tularensis* was successful 11x, namely from the lymph nodes or suppurative lesions (positivity 1.87 %). There were 158 (State Veterinary Institute, Hradec Králové) isolations from animals (rabbits or rodents). Virulence of the isolated strains reached LD<sub>50</sub> 10<sup>3</sup>-10<sup>6</sup> for guinea pigs at i.p. administration.

### Discussion

Tularemia was most often diagnosed by general practitioners as lymphadenitis or an influenzal illness with a high temperature (altogether in 18 different diagnoses). A positive epidemiological history facilitated the diagnostics - handling animal carcasses, a primary ulceration of hands and in the facial part of the head, a positive serological assay of antibodies.

An ulceroglandular form of tularemia was diagnosed most frequently - a pulmonary form in summer and in early autumn. The patients were usually hospitalized within 2-3 weeks after the first symptoms - in 10 % the correct diagnosis was confirmed within 2 months. At a differential diagnostics of a febrile lymphadenopathies it is necessary to distinguish in our conditions listeriosis, toxoplasmosis, and yersinia. In the therapy of tularemia tetracycline and aminoglycosides (MIC kanamycin 0.1 µg/ml, gentamycin 0.1-8 µg/ml) had a creditable record.

The maximum antibody titres were demonstrated in the 4<sup>th</sup>-5<sup>th</sup> week of infection, they persisted for 1 year or longer. The most frequent way of infection

was a direct handling with animal carcasses or killed hares (run over by cars). After getting over the disease in numerous persons in their 4<sup>th</sup> and 5<sup>th</sup> life decade there persisted symptoms of a neurovegetative alteration (sleeping disorders, concentration impairment, fatigue, etc.).

### Summary

The complex epidemic incidence (13 epidemics, 587 persons affected) and a sporadic incidence of tularemia (602 persons) in the East-Bohemia region in the Czech Republic from 1961 to 1996 are described.

Lymphadenopathy or influenzae was the most frequent first contact physicians' diagnosis. A clinical diagnosis was confirmed with a positive evidence of agglutinin antibodies (1:80 up to 1:2,560) as well as with an epidemiological screening at the place of residence, or with an isolation of *F. tularensis*, respectively.

In clinical aspect, ulceroglandular and bronchopulmonary forms with affection of mandibular, cervical and lymphatic glands were the predominant findings. A part of diseases had a subclinical course

(6 up to 8 %). In a differential diagnosis toxoplasmosis, listeriosis and yersinia have to be eliminated.

In the therapy of tularemia aminoglycoside antibiotics Kanamycin, Streptomycin proved best. In generalized forms, a period of recovery was prolonged, damages of the neurovegetative system persisted for half a year up to one year. In epidemic incidence, more men than women were affected in the ratio of 2:1 (401:186), in sporadic incidence a difference was not statistically significant. The affected persons were between 6 to 71 years of age.

Hares, mouselike rodents, rarely nutria, muskrat and raven were the sources of infection. The most frequent way of transmission was - a direct inoculation at the site of microtrauma of the skin or mucosa, via inhalation or after consuming an insufficiently heat-treated meat and meat products or contaminated water, and tick bite. Most diseases manifested in cold and winter months (79 %, October-December, January-April).

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