

BOUTONNEUSE FEVER IN ROMANIA BETWEEN 2000 – 2008

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Abstract: We describe the geographical and temporal distribution of *boutonneuse fever* (MSF) cases in Romania in the 2000 to 2008 interval. All cases of *boutonneuse fever* recorded nationwide during the 2000 - 2008 interval came from the South of Romania and have exclusively evolved as sporadic cases. Highest incidence rate was registered in 2001 in Constanta (44.2% 000). *Boutonneuse fever* cases were recorded since May to October with a peak in August (38% of cases). Patients were living mainly in urban areas (80%). Most affected age group was 45-54 years (25%). Predominant clinical form of disease was the mild form (58%) and in 99.5% of cases the outcome was favorable. In the studied interval there were two deaths from *boutonneuse fever*. Of reported cases, 96% recognized the tick exposure by coming into contact with parasitized dogs (92%) or other domestic animals (3%). Exposure was most common at home (60%), but 4% of *boutonneuse fever* cases had professional exposure.

The geographical distribution of *boutonneuse fever* cases reported in Southern Romania between 2000 – 2008 overlaps the vectors distribution, while temporal distribution was respecting the maximum activity interval of vectors. However, a trend of extending the reporting interval was noticed, as our cases reporting interval was starting from May compared with the June-September previous pattern.

Sporadic case pattern evolution of *boutonneuse fever* cases demonstrated persistent natural reservoirs (foci) of infected ticks in Southern Romania.

Key words: cases, patients, *Rickettsia conorii*, geographical area.

1. Background

Boutonneuse fever is a vector borne zoonosis often severe and even fatal, transmitted in Europe mainly by *Rhipicephalus sanguineus*, by its popular name “the brown dogtick”. The disease is caused by *Rickettsia conorii*, which is an obligate, intracellular gram-negative coccobacillus.

Transmission of *Rickettsiae* in humans may occur directly, as a result of infected tick bite or crushing the tick on the skin, or indirectly, by mucosal entry, through contaminated hands. (1) *Rickettsiae* directly affect mammals, but humans may be accidental hosts. *boutonneuse fever* clinical onset is characterized by: high fever (present in 97-100% of cases), headache (56%),

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diffuse nonspecific pain (arthralgia, myalgia). Physical examination may detect the inoculation eschar (black spot) at the site of the tick bite. It is painless, erythematous or necrotic and may be confused with a scratch or a boil. Lymphadenopathy is usually present. Acute stage begins 3-5 days after the onset with clinical mucocutaneous manifestations including: non-itching generalized maculopapular rash initially starting from the legs or arms, spreading to the soles or palm, which is persisting for 6-7 days and accompanied by symptoms present at onset: fever (39-41°C), headache, myalgia, photophobia etc. Disease outcome is usually favorable in 10-14 days. Maculopapular eruption is 2-5 mm in diameter, edged red and imprecise, appears first on limbs and then quickly covers, by successive bursts, the trunk, neck and face.

Macules to papules are turning in typical bouton, which is a small, red nodule in the skin. Eruption diminishes by the end of convalescence disease, starting 10-14 days after onset [5,12,14].

There are complicated forms of disease that can lead to death.

Cases of boutonneuse fever are found in the maximum activity interval of ticks (May-October).

The disease is spread in the area of the Mediterranean littoral, of the Black Sea (Crimea) and of the Caspian Sea, and in Africa and India, areas well known as being endemic for boutonneuse fever (also known as Mediterranean Spotted Fever, Tick typhus, Indian tick typhus and tick fever).

Boutonneuse fever have a wide geographical distribution cases are reported in Italy (west **Sicily**), Spain, Portugal, Greece, Turkey, Cyprus, Palestine, Romania, and Bulgaria [4, 6,13]. In fact, *R. conorii* is prevalent around the Mediterranean Sea, south of the 45th parallel, and some foci have been detected.

In central and northern France, Belgium, and Switzerland and around the Black Sea in Russia. In northern parts of its zone of endemicity indoor heating allows *R. sanguineus* to survive indoors during the winter [10].

In Croatia Between 1982 and 2002, Mediterranean spotted fever (boutonneuse fever) was diagnosed in 126 (incidence rate 1.27/100 000 per year) [9].

Sporadic imported boutonneuse fever cases have been reported In Norway, Holland and Germany, related to the transport of parasitized dogs with infected ticks.

Asymptomatic cases represent a considerable number, fact demonstrated by serologic studies on the general population. Larger incidents are found in endemic areas where *Rhipicephalus sanguineus* is present, but disease cases are also reported in areas where the tick has been introduced. Moreover, current ecologic and climatic changes are leading to the enlargement of endemic areas that may favor an increase in the number of infections [15].

An aspect that should be taken into account is the fact that *Rhipicephalus sanguineus* can survive a long time in the protective environment of human habitats. Apartments infested with ticks have been discovered in the center of France and Switzerland, at a great distance from the ticks' natural distribution areas. Small epidemics of boutonneuse fever have appeared in Switzerland 6 years after the infestation of an apartment. The ticks were not only found on the dog, but also in the kitchen cabinets, dressers, between the furniture and the wall. Hence, dog infesting tick disinsection is sometimes insufficient to prevent boutonneuse fever cases [7, 8].

Boutonneuse fever is not common in the USA, however imported cases have been reported and confirmed by the CDC.

The real reservoir for *R. conorii conorii*. Is not known yet. Dogs serve as common transport hosts by bringing infected ticks closer to their owners. In certain zones of southern Europe, a correlation between the percentage of the canine population with antibodies to *R. conorii conorii* and the incidence of MSF in humans has been found [3]. Seropositivity was even higher in dogs belonging to MSF patients [3]. Dogs are transient reservoirs because of transient rickettsemia after infection; therefore, dogs do not seem to be an efficient reservoir for *R. conorii*. Evidence has recently been shown that dogs can exhibit febrile illness related to infection with this bacterium [11].

In Romania boutonneuse fever was first detected in 1931 in Constanta, being described by G. Barzanescu, V. Vasiliu [3]. D. Combiescu and G. Zotta studied the pathogenic and the transmission of boutonneuse fever [2].

An outbreak burst in 1948 in Bucharest. After the 1948 epidemic incidence decreased so that since 1959 only 1-2 cases per year have been reported.

Starting with 1988 sporadic cases were detected in Romania, in Constanta and Bucharest, during summer, the outbreaks being limited to family, neighborhood or community.

Between 2000-2008 all boutonneuse fever cases recorded nationwide came from the South of Romania and have evolved exclusively as sporadic cases.

Being in charge with Southern Romania public health duty, Bucharest Public Health Institute, nowadays the National Institute of Public Health conducted a systematic surveillance of boutonneuse fever starting with the 2000 year.

2. Method

A descriptive epidemiological study was performed on boutonneuse fever cases reported in Romania, in the 2000 – 2008 interval. Surveillance was conducted by the National Public Health Institute, May to October each year, considering the annual interval of maximum activity of *Rhipicephalus sanguineus*.

Features were analyzed by, time, place and person. The study took into account factors such as manifestation of the epidemiological process, symptoms, clinical form of disease, laboratory diagnosis, status at discharge, predisposing factors, source of infection, route of transmission.

The case definition used **clinical criteria** (i.e. person with fever, myalgia, not itching maculopapular rash, affecting limbs, associated or not with 2-5 mm lesion(s), with red halo, suggesting a tick bite), **laboratory criteria** (i.e. detection of *Rickettsia conorii* specific antibodies and their dynamics in serum pairs) and **epidemiological criteria**, as information about recent tick bite(s), exposure to high grass and tick-infested areas, contact with dogs, or professional exposure.

Results

All cases of boutonneuse fever (MSF) recorded nationwide during 2000-2008 came from Southern Romania. The highest rate of incidence, 1.6% 000, occurred in 2002 and represented 22.9% of all cases reported in the studied interval (Fig. 1).

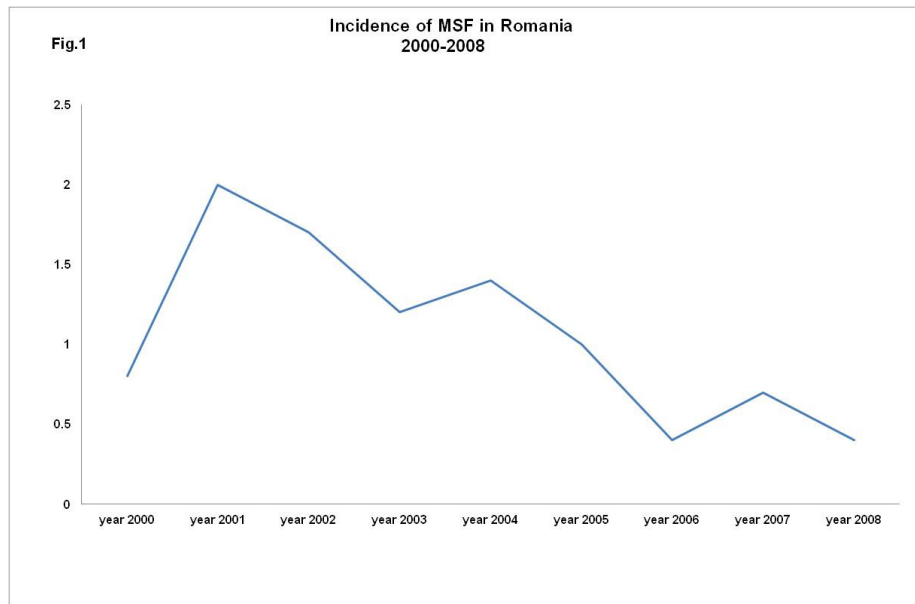


Fig.1.

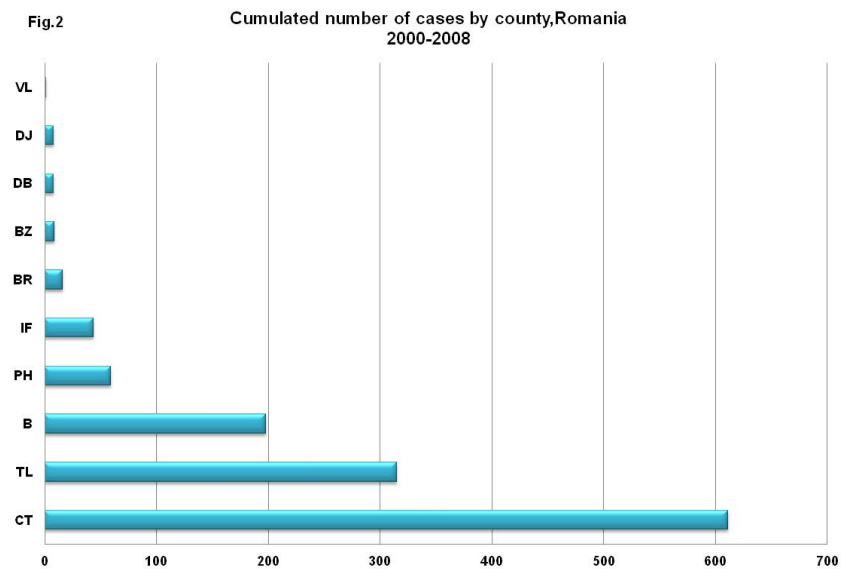


Fig. 2. The distribution of cumulated cases reveal that the most affected county are Constanta, Tulcea and Bucharest

The highest incidence rate, of 44.2‰, was registered in 2001 in Constanta county (table 1).

Table 1

Incidence rate of BOUTONNEUSE FEVER by reporting county

Year	2000	2001	2002	2003	2004	2005	2006	2007	2008
CT %000	20,2	44,2	24	14,6	19,6	8,9	8,5	8,23	11,5
TL %000	1,98	17	39	27	27,4	26,2	0	5,16	32
BB %000	1,65	2,89	3,15	2,43	2,53	1,19	0,2	0,72	0,41

Legend:

- CT = Constanta
- TL = Teleorman
- BB = Bucharest

Reported date range of boutonuse fever cases has extended from April to November, while the traditional evolution was June to September with a maximum in August, registering 38% of cases (Fig. 3).

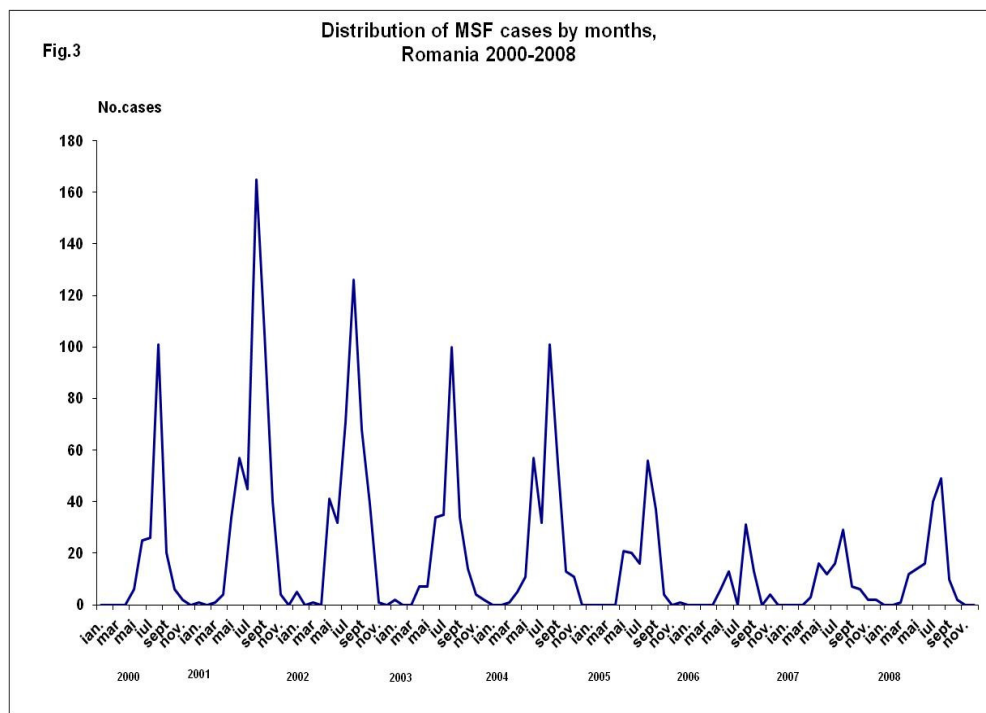


Fig. 3. Patients were mainly from urban residency (80%)

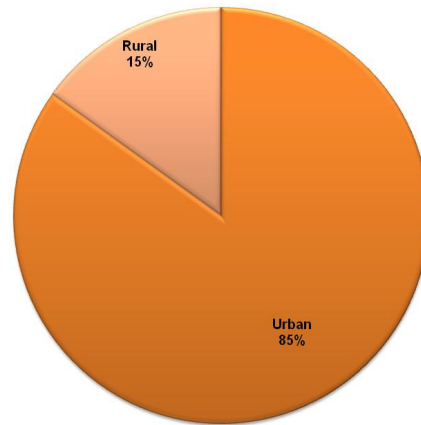


Fig. 4. *Distribution of patients by place living criteria MSF cases, Romania 2000–2008*

The most affected age group was 45-54 years (25%) and no statistically significant difference in terms of distribution of cases by sex was noticed. However in the most affected age group, there was a slight predominance of males.

Analyzing the clinical aspects we found that the predominant clinical form of the disease was the mild form (58%) and the outcome was favorable in 99% of cases.

In the studied interval there were two deaths due boutonneuse fever.

For laboratory diagnosis we used indirect immunofluorescence assay (IFA), performed on two paired serum samples to demonstrate a significant (four-fold) rise in antibody titers, but relevant were just in 38% of cases, while in the rest of cases the diagnosis was supported only by clinical symptoms and epidemiological link. (Fig.5)

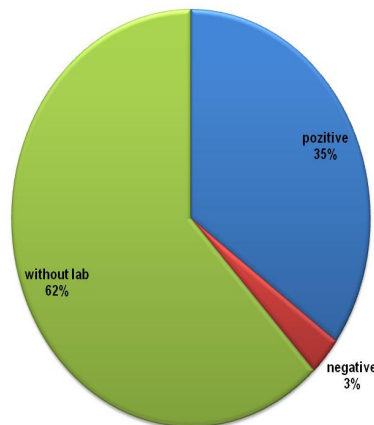


Fig. 5. *Laboratory diagnosis – indirect immunofluorescence assay, MSF cases Romania 2000–2008*

Exposure: 96% of cases recognized the tick exposure by coming into contact with parasitized dogs (92%) or other domestic animals (3%). (Fig.6). Exposure was most common at home (60%), but 4% of boutonneuse fever cases had professional exposure.

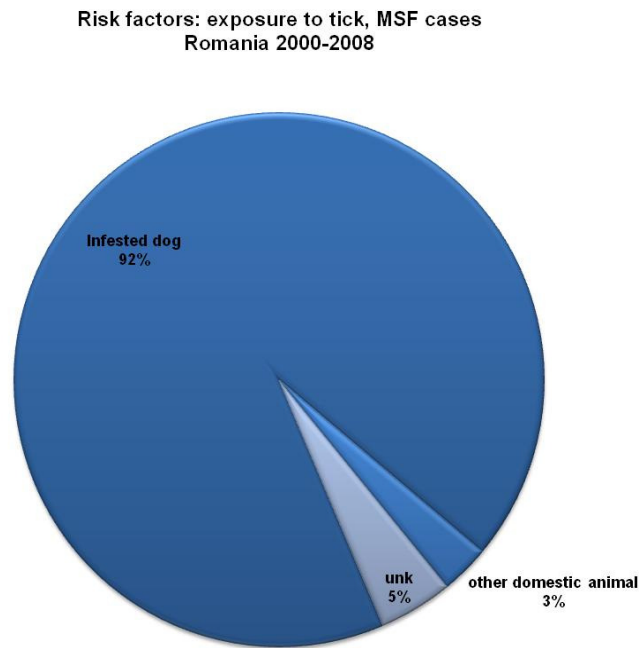


Fig. 6. *Risk factors: exposure to tick, MSF cases Romania 2000–2008*

Conclusions

The geographical distribution of boutonneuse fever cases reported in Southern Romania between 2000 – 2008 overlaps the vectors distribution, while temporal distribution was respecting the maximum activity interval of vectors.

However, a trend of extending the reporting interval was noticed, as our cases reporting interval was starting from May compared with the June-September previous pattern.

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