

## EPIDEMIOLOGICAL CHARACTERISTICS OF Q FEVER IN VOJVODINA PROVINCE, SERBIA, 1985-2009

GORANA ČOSIĆ, JELENA ĐEKIĆ, P. ĐURIĆ, Z. ŠEGULJEV, M. PETROVIĆ and S. RAJČEVIĆ

Institute of Public Health of Vojvodina, Center for Control and Prevention of Diseases, 21000 Novi Sad, Serbia

**Abstract** - Due to the atypical symptoms and signs of Q fever, the high incidence of mild infections and the fact that in our region the appearance of this anthropozoonosis is linked to the lambing season (the end of winter and beginning of spring), when the greatest frequency of respiratory infections is manifested, Q fever is not recognized very often. The possible lethal complications, the fact that *Coxiella burnetii* can survive for years in the environment and be transferred by air-stream in great breathing spaces, the small infectious dose necessary to cause the disease and speculation as to its possible use in bioterrorism, make it a significant public health problem. The aim of our study was to give some data on Q fever in the Autonomous Province of Vojvodina, Serbia, an area with a high degree of agricultural activity.

**Key words:** Q fever, epidemiology, Vojvodina, Serbia

### INTRODUCTION

Q fever is a worldwide disease, classified in zoonosporonosis. It is caused by the bacteria *Coxiella burnetii*. Q fever was for the first time described in Australia in 1935 when Derrick (1937) named it "Query fever". Burnet and Freeman (1937) detected and described the causative agent of the disease and classified it among the *Rickettsiaceae*. In 1937, in the USA, Cox isolated the same *Rickettsiaceae* from the tick *Ixodidae*. The bacteria was named *Coxiella burnetii*, and first classified in the order *Rickettsiaceae* and then in the order *Legionellales* (Kuzman et al., 2006).

Cattle, sheep and goats are the primary reservoirs, although a variety of species may be infected. Bacteria are excreted in the milk, urine, and feces of infected animals. During birthing, the organisms are shed in high numbers within the amniotic fluid and the placenta. *Coxiella burnetii* is an internal cell bacteria that is extremely hardy, resistant to heat, drying, and many common disinfectants, which al-

low the bacteria to survive for long periods in wool, straw, dust and dry feces. It is highly infectious and it is thought that only around ten transferred bacteria may cause disease. The infection of humans usually occurs by inhalation of these organisms from air that contains airborne barnyard dust contaminated by dried placental material, birth fluids, and the excreta of infected animals. Other modes of transmission to humans, including tick bites, ingestion of unpasteurized milk or dairy products, and human to human transmission, are rare (Punda-Polić, 2003; Kuzman et al., 2006; Thomas, 2000). There are data on the association of human Q fever with litters of pets – cats and dogs, which is a significant risk to human health (Marrie et al., 1988; Pinsky et al., 1991).

The incubation period lasts from 2 to 3 weeks, depending on the infectious level. In patients in the acute phase of the disease, Q fever is mainly expressed by nonspecific symptoms similar to flu, although more than 50% of exposed persons with confirmed antibodies to *Coxiella burnetii* can be

completely asymptomatic. In 1-2% of patients with Q fever, chronic complications are manifested that are evident for decades after infection. Data on Q fever in the area of Vojvodina have been continually followed up since 1966 on the suspicion that there were Q fever focuses in the whole area of the province (Šeguljev, 1976; Šeguljev et al., 1990).

The aim of this study was to give some data on Q fever in the Autonomous Province of Vojvodina, Serbia, an area with a high degree of agricultural activity.

#### MATERIALS AND METHODS

From 1985 to 2009 surveillance reports of serologically confirmed Q-fever cases sent to the Institute of Public Health of Vojvodina were analyzed using standard statistical methods by demographics (age, sex, current residence), seasonal and regional distribution of disease, and clinical signs of the disease and contact exposures. For comparative analysis of frequency, the  $\chi^2$  test was used. Presented data refer to the two million population of the territory of the Autonomous Province of Vojvodina (area of 21.500 km<sup>2</sup> or one quarter of the territory of Serbia).

#### RESULTS

In a 25-year period, a total of 2154 serologically confirmed cases of Q fever were reported, with an incidence rate ranging from 0.0 to 20.5 per 100,000 population in different local districts of Vojvodina Province (Fig. 1, Fig. 2). Most of the cases were registered in outbreaks (76.6%). The mean annual incidence rate significantly decreased from 12.8/100,000 in 1980s, 3.7/100,000 in 1990s to 0.8/100,000 population in the last decade ( $p<0.01$ ). The male-to-female ratio of cases was 2.3:1 (Fig. 3).

The frequency of the disease differed significantly among age groups; it was highest for the group from 30 to 39 years of age ( $p<0.01$ ) (Fig. 4).

Seasonal distribution indicated the lowest incidence rate from June to December (range 0.6 to

6.3/100,000), while from January to May the incidence rate was 12.6 to 23.3/100,000 population ( $p<0.01$ ) (Fig. 5).

Overall, 75.4% had clinical symptoms of pneumonia. Among cases with reported exposure risks, 77.1% were related to individual household cattle handlers, and 22.9% to industrial exposure (livestock farms, slaughterhouses, research facilities).

#### DISCUSSION

Q fever has been endemic in large parts of Europe for several decades. Seroprevalence studies from in the period 1970-2009 show that 10-30% of rural populations in different parts of Europe have antibodies against *C. burnetii* (ECDC, 2010).

During the 2<sup>nd</sup> World War, epidemics appeared among the allied and German troops on our territories. They were described as "Balkan flu epidemics" as long as Q fever was confirmed. The local population was not affected owing to previous unrecognized infections. In Vojvodina, Q fever is principally registered as interstitial pneumonia with hepatitis. There are no data on possible complications appearing as the result of chronic infection, neither on fatal results (Šeguljev et al., 1990).

Q fever in Serbia was rare in period 2006-2010, with most of the cases registered in Vojvodina Province (Institute of Public Health of Serbia, 2011). In 2010, 24 cases of disease were reported, only two of them from outside the province.

In the European Union in 2009, 1988 confirmed cases were reported, with a majority of 1623 cases reported from the Netherlands (ECDC report, 2011). Large outbreak in the Netherlands resulted in an increase in the average incidence of Q fever in the EU since 2007. In our region, cases of Q fever are reported every year, but the incidence has been declining 1992, with an incidence of below 1 per 100,000 population since 2000, with the exception of year 2006. Probable reasons for this decline in Q fever incidence are: a) termination of the movement of

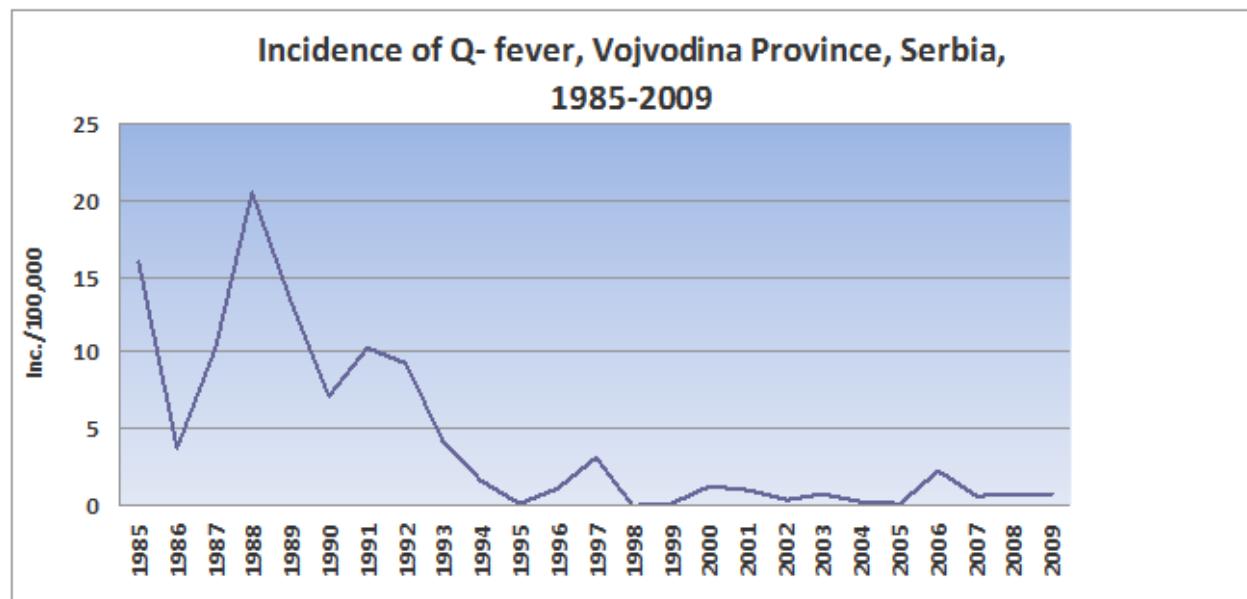


Fig. 1. Incidence of Q fever, Vojvodina Province, Serbia, 1985-2009

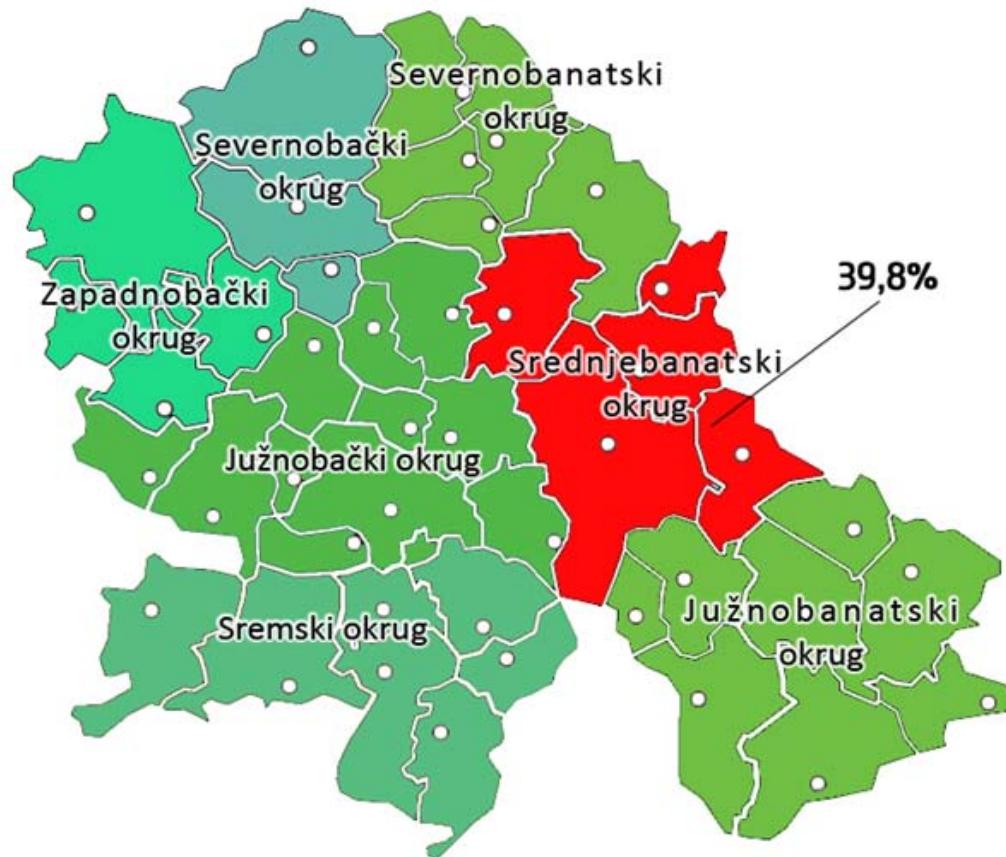
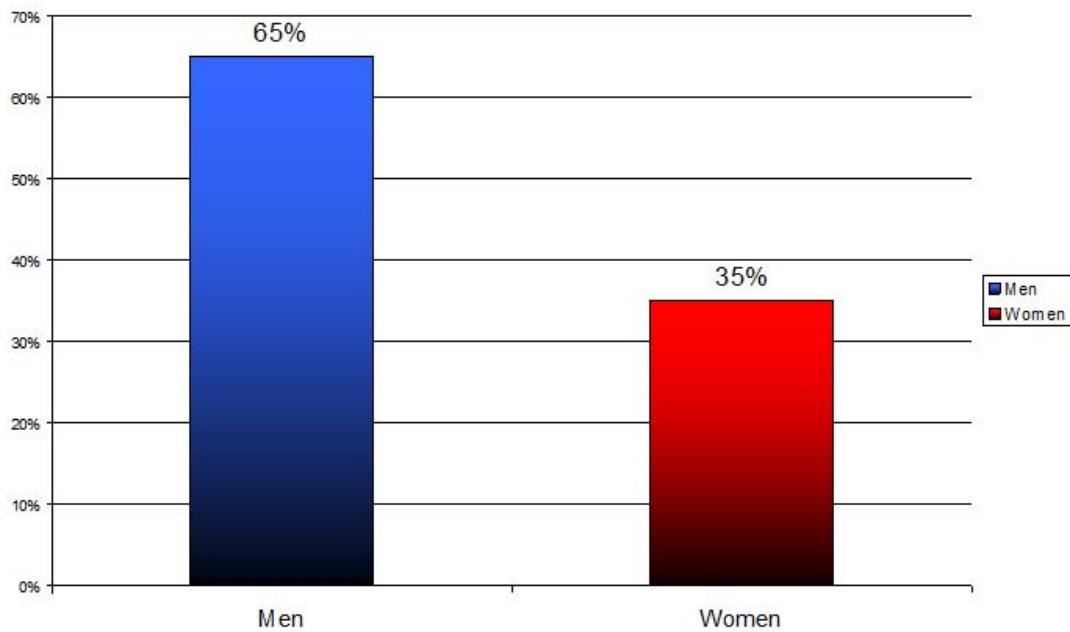
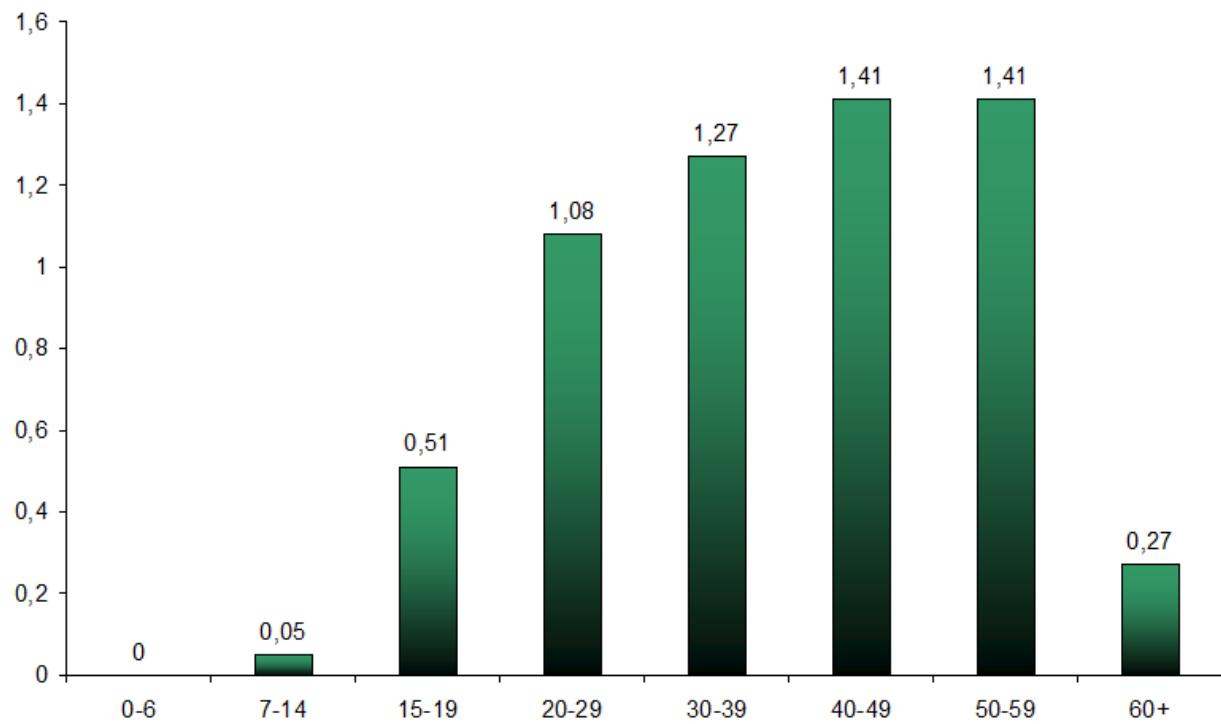


Fig. 2. Geographical distribution of cases registered in Vojvodina Province, Serbia, 1985-2009



**Fig. 3.** Distribution of Q fever by gender, Vojvodina Province, Serbia, 1985-2009



**Fig. 4.** Incidence of Q fever by age, Vojvodina Province, Serbia, 1985-2009



Fig. 5. Seasonal distribution of Q-fever cases (n=2154), Vojvodina Province, Serbia, 1985-2009

nomadic herds from the western regions of former Yugoslavia to Vojvodina Province; b) failure to implement routine serological diagnosis due to a lack of reagents (no serological confirmation), and c) significant reduction in livestock in the province.

In the EU, the highest rates were seen in the age group 45-64 years, with confirmed case rates of 1.09 per 100 000 population (ECDC, 2011). In our region, the highest incidence rate was found in the age group 30-39. Only 2.6% of cases of Q fever in the EU were reported among children under the age of 15, but in our study, it was even lower – 0.5%. This age distribution could be linked with exposures to sources of Q fever and the relationship of Q fever to professional exposure.

In the population surveilled, the male-to-female ratio was 2.3:1. The overall rate in the EU was higher in men than in women (0.76 and 0.48 per 100 000, respectively), with a male-to-female ratio of 1.58:1 (1.85:1 in 2008), (ECDC, 2011).

Q fever is a frequent professional disease because those affected are most often veterinarians, cattle breeders, employees in the slaughter industry and wool mills. It appears during the whole year but mainly in the period of late winter and in the spring. In the slaughter industry, employees in wool and fur processing, the disease is not seasonally dependant,

unlike cattle breeders, where Q fever has an extremely seasonal nature related to the birthing period. The main source of infection for humans is domestic animals, mostly sheep, goats, cows and their excretions. Infections in domestic animals mainly pass undetected.

In the period January-April, 71.7% of all cases of disease are registered, which correlates to the aero-genic route of transmission, dust inhalation contaminated by animal excretions and contact with postpartum ejects in birthing season of domestic animals.

Most cases of Q fever in Vojvodina occurred in the period January-April. In the last few years, the highest number of infected is registered during the summer season (July), which is in correlation to lesser family epidemics. The transfer of infected aerosol by wind has resulted in epidemics among humans who had not been in direct contact with infected animals (Šeguljev et al.; 1990, Ristić et al., 2010).

In the EU, most cases were reported in 2009 in May, June, and July, due to an outbreak in the Netherlands later than was usual in the previous years (ECDC, 2011). In France, most of the cases occurred from April to September (Frankel et al., 2011). The predominance of Q fever occurrence earlier than in the EU could be linked with microclimate, especially to the winds present in the region during the winter

months. The importance of winds to the local epidemiology of Q fever is well known (Tissot-Dupont 2004, Morović et al., 2008).

Most of the cases of Q fever in our study were linked with outbreaks, but about 30% were sporadic. It is well known that Q fever is an underreported disease. The report rate increases during outbreaks, but many mild infections are not confirmed and thus not reported. The unavailability of test kits in the country in last two decades and the absence of clear case definitions are important factors for this under-reporting.

The continuous presence of Q fever in Vojvodina and its link with professional exposure lead us to conclude that improvement in the appliance of preventative measures is necessary. There is a need for studies of the seroprevalence of Q fever, both in livestock and humans. Intensive education and appliance of individual preventative measures for professionals, including consideration of the vaccination of exposed professionals, should be a priority (Parker, 2006).

## REFERENCES

- Burnet, F. and M, Freeman (1937). Experimental studies on the virus of "Q" fever. *Med J Aust.* **2**, 299-305
- Derrick, E.H. (1937) "Q" fever: a new fever entity: clinical features. diagnosis, and laboratory investigation. *Med J Aust.*; **11**, 281-299.
- European Centre for Disease Control and Prevention – ECDC (2010). ECDC Technical report – Risk assessment on Q fever. ECDC, Stockholm, 1-42.
- European Centre for Disease Control and Prevention – ECDC (2011). ECDC Annual epidemiological report – Reporting on 2009 surveillance data and 2010 epidemic intelligence data. ECDC, Stockholm, 1-239.
- Frankel, D., Richet, H., Renvoise, A. and D. Raoult (2011). Q fever in France, 1985-2009. *Emerg Inf Dis*, **17**(3), 350-356.
- Institute of public health of Serbia (2011). Report on infectious disease in Republic of Serbia in 2010 (in Serbian). Institute of Public Health of Serbia, Belgrade.
- Kuzman, I. (2006). *Coxiella Burnetii - Q groznica*. In: *Infectiology* (In Croatian) (Ed. J. Begovac), 546-550. Profil, Zagreb.
- Marrie, T.J., Durant, H., Williams, J.C., Mintz, E. and D.M. Waag (1988). Exposure to the parturient cats: a risk factor for acquisition of Q-fever in maritime Canada. *J. Infect. Dis.*, **158**, 101-108.
- Morović, M., Babić-Milutin, M., Grgić, D. and O. Đaković-Rode (2008). *The open tropical medicine journal*, **1**, 63-67.
- Punda-Polić, V. (2003). Rickettsiaceae i Coxiella. In: *Special medical mikrobiology and parasitology* (in Croatian), (Eds. G. Mlinaric-Galinovic, M. Ramljak-Šešo), 199-211. Merkur A.B.D., Zagreb.
- Parker, N.R., Barralet, J.H., and A.M. Bell (2006). Q fever. *Lancet*, **367**, 679-88.
- Pinsky, R.L., Fishbein, D.B., Greene, C.R. and K.F. Gensheimer (1991). An outbreak of cat-associated Q fever in the United States. *J. Infect. Dis.*, **164**, 202-204.
- Ristić, M., Šeguljev, Z., Vidić, B., Petrović, V. and S. Ilić (2010). Structure and distribution of leading zoonoses in Vojvodina in 2000-2009 period (in Serbian). *Arh. Vet. Med.*, **3**, 63-72.
- Šeguljev, Z. (1976) . Infections by *Coxiella burnetii* in humans and domestic animals in Autonomous Province of Vojvodina [dissertation] (in Serbian). Medicinski fakultet, Novi Sad.
- Šeguljev, Z., Vuković, B., Stefanović, S., Stošić, Ž., Samardžić, V. and M. Bačić (1990). Seroepidemiological investigation of Q fever in Vojvodina (Yugoslavia). *Giornale di Malattie infettive e parassitarie*, **42**, 424-426, 1990.
- Šeguljev, Z. and B. Vuković (1990). Epidemiological and clinical characteristics of Q fever in Autonomous Province of Vojvodina (in Serbian). In: *Novelties in medicine* (Ed. D. Popović), 249-254. Medicinski fakultet, Novi Sad.
- Tissot-Dupont, H., Amadei, M.A., Nezri, M., and D. Raoult (2004). Wind in November, Q fever in December. *Emerg. Inf. Dis.* **10**, 1254-1259.
- Thomas, J.M. (2000). *Coxiella burnetii* (Q Fever). In: *Principles and Practice of Infectious Diseases*, 3 (Ed. G.L. Mandell), 2043-2050. Churchill Livingstone, New York.