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## CLINICAL, EPIDEMIOLOGICAL AND EPIZOOTIC FEATURES OF Q FEVER IN THE NORTHERN COASTAL PART OF CROATIA FROM 1989 to 1998

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Although Q fever is endemic in the northern coastal part of Croatia, it usually occurs sporadically. Analysis of 58 patients hospitalized for Q fever during the last 10-year period (1989–1998) revealed some differences in the clinical manifestation compared to a previous study (1954–1977). Most cases of Q fever (N=55; 91%), presented with pneumonia, but no rash was noticed, compared to 46% of patients with Q fever developing exanthema in the previous study. The previously observed high seropositivity to *Coxiella burnetii* among domestic animals was confirmed in this study. A two-peak seasonal distribution of Q fever observed in 1991 was connected with the imported Russian sort of sheep with special biology of delivery. The clinical outcome was favorable for all patients, since no complications or chronic forms of the disease were recorded. Disproportion between the number of registered and hospitalized patients, including a number of asymptomatic and several undiagnosed or misdiagnosed infections, leads to a conclusion that the real number of persons infected with *Coxiella burnetii* in the area is several times higher.

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### INTRODUCTION

Q fever is a zoonotic disease caused by a gram-negative proteobacteria *C. burnetii*. Since the first description of Q fever in 1937, the disease has been reported in most countries of the world<sup>1</sup>. Serologic evidence of Q fever in humans in the northern coastal part of Croatia was first described in 1954<sup>2</sup>. A systematic analysis of Q fever in this area was conducted during the 1954–1977 period, when 68 serologically verified cases were hospitalized<sup>3</sup>. Except for typical symptoms with pulmonary involvement following the infection with *C. burnetii*, a roseoliform rash was described in 46% of patients. Also, a seroprevalence of 78.7% was found in animals, so this part of Croatia was considered to be endemic for Q fever<sup>3</sup>.

Q fever occurs mostly as a limited outbreak in rural regions, however, cats, dogs and rats can also harbor *C. burnetii*, and can serve as a potential reservoir of infections among urban population, leading to sporadic occurrence of Q fever<sup>4</sup>. In spite of the usually benign course of Q fever, it is important to recognize and establish the presumptive diagnosis as early as possible, relying mostly on epidemiologic data, since there are no pathognomonic clinical characteristics. Introduction of specific therapy shortens the time of acute phase of the disease and probably reduces the risk of developing a chronic form of the disease<sup>5</sup>.

During the 10-year period, we have analyzed the characteristics of Q fever patients in order to determine if there were any pathomorphologic changes compared to the previously published data from this endemic region<sup>3</sup>.

### PATIENTS AND METHODS

A clinical, epidemiologic and epizootic retrospective survey was carried out in the northern coastal part of Croatia covering the period from 1989 to 1998. This area belongs territorially to the Primorsko-goranska County (2774 square kilometers, 339,527 inhabitants) which consists of two geographically distinct regions: the coastal region with a mild Mediterranean climate, and the thickly forested mountainous region with a continental climate. Agriculture and farming are not developed in either part, however, household cattle breeding is present in some areas.

Clinical features of 58 hospitalized patients were analyzed. Epidemiologic data were obtained from the Department of Public Health of the Primorsko-goranska County and the National Public Health Institute. All patients who had been hospitalized or registered for serologically verified Q fever were included in the study. The diagnosis of acute Q fever was established using a complement fixation test and/or microimmuno-fluorescence assay<sup>6</sup>. A fourfold increase in serum antibody titer between two blood samples obtained 3 weeks apart, or an initial high titer (at least 1:128) were considered diagnostic. Sera from domestic animals, especially in cases with a history of abortion, were also collected and tested for the presence of antibodies to *C. burnetii*. In epidemics, samples from animals were selected from the farms of patients with Q fever and the surrounding farms.

RESULTS

During the 10-year period (1989-1998), a total of 637 cases of Q fever were registered in Croatia. A large proportion of them (N=147; 23%) were recorded in the northern coastal part of Croatia. Out of these 147 cases to Q fever, 58 (39%) patients were hospitalized (Fig. 1). The mean age of the hospitalized patients was 36 (range 16-68) years, with a high male predominance (male to female ratio, 2.6:1) (Table 1). Since a high seropositivity was found in domestic cows (N=69 of 231; 29.9%), goats (N=38 of 131; 29%) and sheep (N=93 of 191; 48.7%) the Primorsko-goranska County should still be considered an endemic region for Q fever. Most cases (N=45; 78%) were registered from February to May of each year, however, a small peak was also noticed in December 1991 (Fig. 2). Two thirds of patients were residents of regions known for a high prevalence of Q fever: Krk, Rijeka, and Senj. A small number of cases occurred as outbreaks of Q fever, but mostly they appeared sporadically. Forty-one (71%) hospitalized patients had contact with animals or a marked occupational risk. Except for fever, which was present in 57 (98%) patients, other dominant clinical features were headache (N=39; 67%), cough (N=36; 62%) and loss of appetite (N=24; 41%) (Table 2). Chest radiographs were considered positive in 55, and elevated liver transaminases in 41 patients (91% and 70%, respectively). The clinical outcome after the treatment with tetracyclines was favorable in all patients, since no complications occurred. In

Table 1. Age and sex distribution of registered and hospitalized patients with Q fever in the northern coastal part of Croatia (1989-1998)

Age (yrs)	Registered		Hospitalized	
	N	%	N	%
0-10	3	2.0	0	0.0
11-20	9	6.1	2	3.5
21-30	25	17.0	17	29.3
31-40	50	34.0	22	37.9
41-50	34	23.1	9	15.5
51-60	19	12.9	3	5.2
61-70	7	4.9	5	8.6
>70	0	0.0	0	0.0
Total	147	100.0	58	100.0
Gender				
Male	104	70.8	42	72.4
Female	43	29.2	16	27.6
Total	147	100.0	58	100.0

contrast to the 1954-1977 data, no rash was recorded.

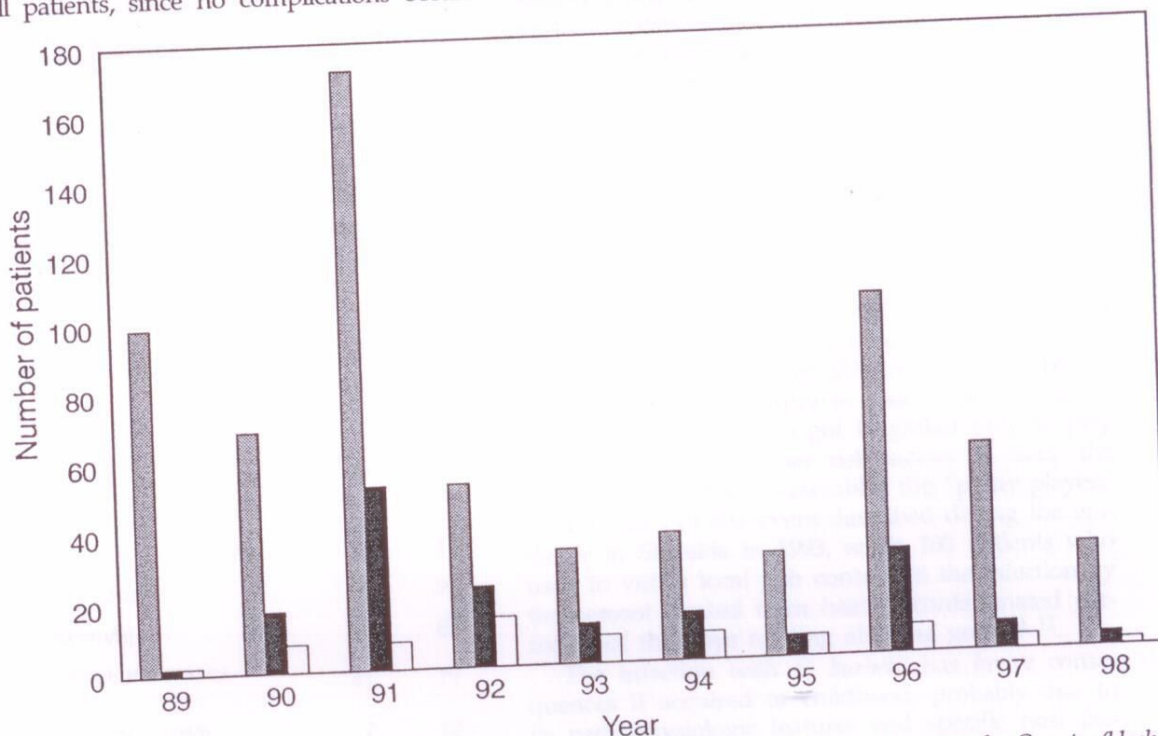


Fig. 1. Number of registered patients with Q fever in Croatia (filled bars), and Primorsko-goranska County (black bars), and patients hospitalized for Q fever (white bars) in the Primorsko-goranska County from 1989 to 1998.

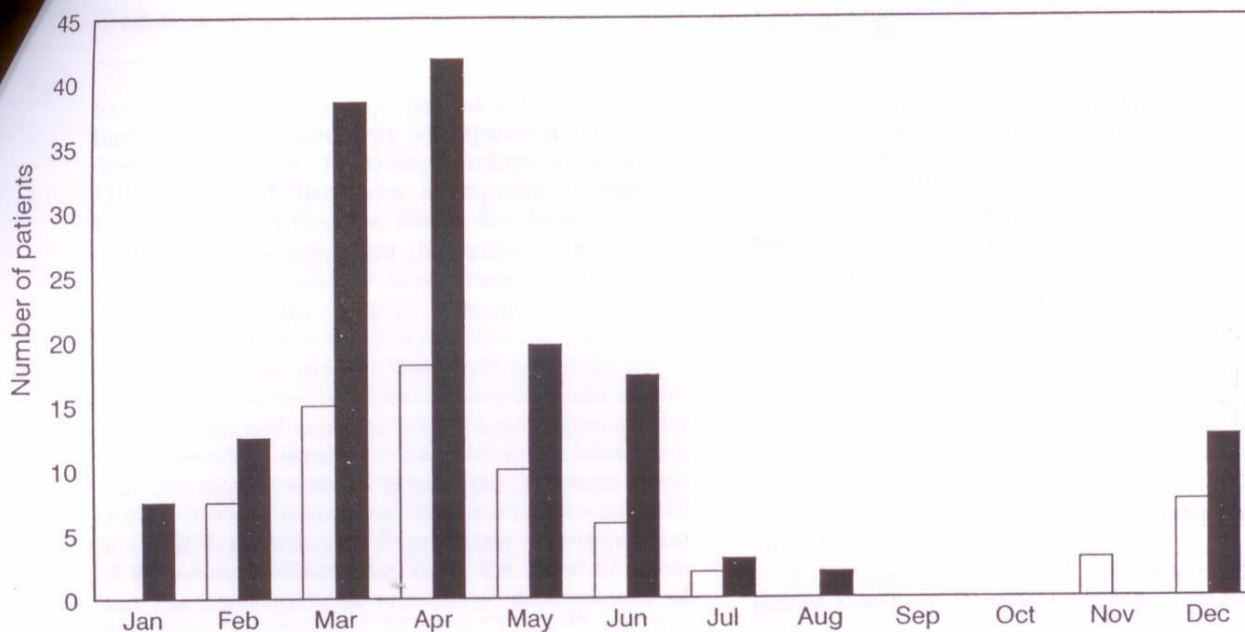


Fig. 2. Seasonal distribution of hospitalized (white bars) and registered (black bars) patients with Q fever in the northern coastal part of Croatia (1989-1998).

#### DISCUSSION

Although Q fever is a well-known disease in the endemic parts of Croatia, the real incidence remains unknown since the most common outcome of in-

Table 2  
Symptoms and signs of Q fever in 58 patients hospitalized from 1989 to 1998 in the northern coastal part of Croatia

Symptoms and signs	N	%
Fever	57	98
Headache	69	67
Cough	36	62
Loss of appetite	24	41
Malaise	21	36
Chills	19	33
Arthromyalgia	18	31
Constipation	16	28
Vomiting	13	22
Sweats	10	17
Positive chest radiographs	55	95
Elevated ESR (>20mm/h)	39	67
Elevated level of aminotransferases (>25 U/l)	41	71
Thrombocytopenia (>135 x 10 <sup>9</sup> /l)	7	12

fection with *C. burnetii* is an inapparent infection or a mild flu-like disease<sup>7,8</sup>. As a characteristic zoonotic disease in the Primorsko-goranska County, Q fever mostly occurs sporadically as it does in Slovakia<sup>9</sup>. However, when data on the last 40-year period are summarized, it becomes evident that the incidence of Q fever is rising. This is in accordance with the sustained high seroprevalence of *C. burnetii* antibodies in domestic animals. Seasonal distribution of Q fever clearly depends on the biology of animal delivery, so the peak noticed in winter 1991 could be explained by the imported Russian breed of sheep with one parturient time in winter. In general contact with animals, especially parturient, but also occupational hazards were found to be the major risk factors for contracting Q fever. However, in almost 30% of our patients no significant epidemiologic data could be obtained. It is interesting to mention a case of secondary aerosol transmission through a jacket, which was previously used to warm up a lamb (A. Vučemilović, unpublished data). Antibodies to *C. burnetii* were found in four acquaintances of the jacket's owner who got to gather only to play cards and had no other risk factors to catch the infection. This closely resembles the "poker players' pneumonia", or the event described during the epidemic in Slovakia in 1993, when 103 patients who used to visit a local pub contracted the infection by the aerosol created from heavily contaminated garments of the boys tending aborting goats<sup>10, 11</sup>.

The infection with *C. burnetii* has fewer consequences if acquired in childhood, probably due to its pathophysiological features and specific host fac-

tors<sup>12, 13</sup>. In our series, no patient younger than 16 had been hospitalized, but we registered three children younger than 10 having serologic evidence of Q fever. Two of them were asymptomatic, while in one child a mild flue-like illness developed.

There was a significant difference in the clinical presentation of acute Q fever compared to a previous study in the region<sup>3</sup>. Namely, the previous observation of rash in Q fever was not supported during the recent period. This could be explained by the changed virulence of the *C. burnetii* strain and/or by misdiagnosed cases of febrile exanthemas in the latter period. Q fever was formerly categorized as a rickettsial disease without exanthema, although some studies showed occurrence of a maculopapular rash in 4%-20% of patients<sup>14, 15</sup> providing no explanation of its nature. Furthermore, since the route of infection has been taken as one of the determinants of the clinical manifestation of acute Q fever<sup>16</sup>, we cannot exclude a changed route of infection as the reason for the absence of rash in our patients. However, the dominant clinical presentation of Q fever remains pneumonia. As in other parts of Croatia, there was no evidence of chronic forms of Q fever<sup>17</sup>.

The disproportion between the number of registered and hospitalized patients, including a number of asymptomatic and undiagnosed or misdiagnosed infection leads to a conclusion that the real number of persons infected with *C. burnetii* in the area must be several times higher. Therefore, we suggest that in every fever-associated illness in springtime, sometimes even in winter, in the regions endemic for Coxiellosis, Q fever should be included in differential diagnosis, irrespective of the presence or absence of contact with animals in the history.

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