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Q-FEVER IN BULGARIA

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[Following is the translation of an article by A. Mitov, L. Shindarov and V. Serbezov, Higher Medical Institute in Plovdiv, the Institute for the Specialization and Improvement of Doctors in Sofia, and the Higher Military-Medical Institute, appearing in the Russian-language periodical Zhurnal Mikrobiologii, Epidemiologii i Immunobiologii (Journal of Microbiology, Epidemiology and Immunobiology), No 8, 1964, pages 101--106. It was submitted on 8 Feb 1963. Translation performed by Sp/6 Charles T. Ostertag Jr.]

The presence of Q-fever in Bulgaria (in the southern part of the country) was first established by Mitov in 1949. The first cases of the disease were serologically confirmed by Wisman and Shveitsar. At the same time it was known that the American Committee on Acute Respiratory Diseases (1946) identified an infectious agent with C. burneti. It was isolated by Caminopetros (1949) during illnesses that were similar in a clinical respect to those described under the name of Balkan Influenza during the Second World War in the Balkans (Imhauser, 1943; Dennig, 1947; Bieling, 1950).

More detailed data on Q-fever in Bulgaria was presented by Angelov et al. (1951, 1953), who showed that the diseases among the local inhabitants were connected with the frequently encountered rickettsiosis among domestic animals. Later they (1955, 1957) and also Shindarov (1957, 1960) and Serbezov (1959) studied the distribution of the disease among man and animals and showed the epidemiological significance of rural foci. Local strains of C. burneti were isolated (Shindarov and Serbezov, 1957; Shindarov, 1958).

As a result of complex work with the participation of virologists, epidemiologists, entomologists, clinical specialists and other specialists there has been a detailed study of the clinical aspects of the disease (Georgiyev, 1957; Despotov et al., 1951; Drachev et al., 1952, 1954; Drachev and Shishmanov, 1958; Zakhariyev, 1955; Zografskiy et al., 1959; Ivanov and Khristov, 1952; Mitov et al., 1954; Popov, 1954; Sprastranov, 1957; Turpomanov and Nikolayev, 1955; Tsvetanov, 1957; Tsonchev et al.) and the properties of local strains (Serbezov, 1959). Information was added concerning the territorial distribution (Vyzvyzov, 1959; Kuyumdzhiev, 1957; Serbezov, 1959; Tsvetanov, 1957; Tsonchev, 1955; Shindarov, 1960) and reservoirs (Shindarov and Mitov, 1960), and recently with the detection by Shindarov et al. (1959) of natural foci, work has begun on explaining the natural factors which support Q-fever in the country.

According to the data of a clinical analysis of 125 cases, the majority of which appeared in 3 epidemics and 30 cases of the disease which were reported in the press, Q-fever is encountered in Bulgaria mainly in two forms: Most often it is in the pulmonary form and less often in the febrile form.

After an incubation period of 12--20 days the disease begins with a common chill. The temperature reaches 39--40°, is maintained at this level for several days and drops lytically, sometimes in the course of 5--6 days. On the average the febrile period lasts 5--12 days, only in individual cases the temperature is maintained up until the 17th day, and in one patient -- more than two months. Temperature curves of a diphasic nature were observed very rarely.

During the beginning of the disease headache and muscular pains are the most frequent symptoms. Almost all the patients on the first day of the disease complained of a strong or intolerable headache, concentrated in the area of the forehead, temples or in the back of the head, becoming weaker in the following days and usually disappearing 3 or 4 days prior to the normalization of the temperature. Muscular pains, localized in the small of the back and the lower extremities, become weaker on the 4th or 5th day and disappear by the end of the febrile condition.

During the initial period, symptoms in the respiratory tract are scarce. The cough is the most frequent symptom (not observed only in five patients, in spite of a large infiltrate on the lungs). It appeared on the 2nd to 4th day, usually was weak, irritating and dry or with a meager discharge of sputum. Sometimes the cough became painful and was accompanied by bloody fibers in the sputum. Often complaints were noted of pains in the chest, and in those cases where there were large infiltrates or lesions of the pleurae, shooting pains were noted which predominated in the general picture of the disease.

The general condition of the patients was quite poor; they all had a strong fever and almost all of them were in bed on the first day of the illness. Cyanosis and labored breathing with a speeded up and superficial respiration was observed only in 5 cases. The tongue was moist and coated, very seldom dry, with a dirty brown film. Only in one patient was a point-like enanthema detected on the soft palate. A rash on the skin was determined only on one patient (there is talk of nodular rash turning into hemorrhagic).

During a physical examination of 30 of the 125 patients observed by us no symptoms of pulmonary affection were detected, and with x-ray examination only in a small part were infiltrated dark spots recorded. In the remaining cases following x-ray investigation, infiltrates were detected which attained the size of the palm of the hand, but physically perceptible symptoms were also lacking. The relative dullness of the percussion tone was detected in 46.6% of the patients. During auscultation no changes were observed in 21.5% of the patients, but in many cases there was foundation to suspect consolidation of lung tissue in places which corresponded to the sites of the x-ray determined infiltrates. On the 4th--5th day weak bronchial respiration with rales appeared and it lasted 3--4 days. Most often of all a weakened vesicular respiration was noted. Cases of pleurisy were also observed, and in one patient -- double hemorrhagic pleurisy with intense stabbing pains and coughing. During x-ray examination, which was usually conducted on the 3rd--5th day, the presence of infiltrates was detected. These disappeared, while maintaining only an amplified pulmonary structure on the 15th, and often on the 20th--28th day of illness.

On the part of the cardiovascular system a relative bradycardia was noted, but not constantly.

In individual cases the liver was palpable under the costal rib. Most often an enlargement of the spleen was noted.

In several patients symptoms were observed on the part of the nervous system: Meningism with rigidity and delirium appeared in 5 persons, in 3 the loss of consciousness was noted and in 3 -- neuralgia.

Included in the complications were dry and exudative pleurisy, arthritis, thrombophlebitis, and acute tubular insufficiency.

In a considerable number of the patients, initially leukopenia was observed (up to 3150 leukocytes in 1 mm^3), and leukocytes in the amounts of 3000--5000 in 1 mm^3 were established in 48.8% of the patients. Initially a considerable increase in the number of monocytes was observed; the number of lymphocytes was already increasing during the febrile period, in some cases reaching 55%. There were no eosinophiles during the first days, but during the recovery period their number reached normal. In the beginning of the illness the ESR (erythrocyte sedimentation rate) was normal in the majority of cases, but later it speeded up.

In 28.5% of the patients a weak albuminuria was detected, and in the precipitate -- single leukocytes, erythrocytes and cells of renal epithelium. Very rarely and for a short time it was possible to detect hyaline and granular casts. The diazo test was positive in 5 patients.

After recovery, loss of strength was observed over a period of 2--3 weeks. Relapses were not noted. The use of biomydin turned out to have a good effect, only in two patients was an effect observed after the 6th and 12th day of use.

The results of investigating the sera of 3534 domestic animals, 1357 humans and 130 wild animals, and also the isolation of C. burneti from man, domestic animals and wild animals and ticks lead to the conclusion that in Bulgaria, Q-fever has the nature of a prevalent endemic disease, in the support of which the main role is played by agricultural and partially natural foci.

The disease is encountered almost throughout the entire country, but between different regions considerable differences are noted in the degree of its distribution among animals and the morbidity of the local population. It is most widespread in the southern part of the country, especially in the central oblasts, where the frequency of occurrence is greater and where several particularly intensive agricultural foci exist with a wide scattering of infections among various types of cattle. The disease is more weakly distributed in the north where the average percentage of affection is lower.

Agricultural animals are the basic reservoir of the causative agent and the source of the disease. Complement fixing antibodies (in a titer of 1:10) were detected by us in 31.1% of the large cattle -- cows, oxen, calves and

buffaloes (all told 1232 head), in 17.1% of the sheep (1013 head) and in 19.2% of the goats (327). The average percentages of positive serological finds in various localities fluctuated in the following limits: In large cattle --6--14.2--41, in sheep --12--15.9--23, and in goats --3.7--8.1--35. As is apparent from the data presented, in Bulgaria in contrast to some other countries with a one-sided development of animal husbandry, it is impossible to connect the rural focalness of Q-fever with a specific species of animal.

Along with cattle, other species of domestic animals are involved in the circulation of the causative agent. Thus, positive serological tests were obtained in 7% of perissodactyl animals -- horses, mules, asses (171 animals examined), in 4.2% of the pigs (165 animals investigated), in 11.5% of domestic fowl -- hens, geese, turkeys (604 birds examined), and also in dogs.

Investigations in the area of epidemiology, in particular the study of conditions and factors which support Q-fever in the country, obtained a new trend after natural foci of the disease were discovered in 1957. As a result of these investigations, clarification was made of the role of the suslik (Citellus citellus) and several pasture ticks in the formation of natural foci. The role of the suslik was proven by means of isolation of two strains of C. burneti from the internal organs of 53 specimens, captured in various parts of the country, and also serologically by means of detection of complement fixing antibodies in 32 out of 90 animals investigated. By an experimental method it was possible to establish that the suslik maintains C. burneti in its tissues for a long time, including throughout the entire period of winter hibernation. This also proved its role as a natural reservoir of the disease. Positive serological findings in hares (Lepus europeus), common voles (Microtus arvalis), rats (Rattus sp.) and storks (Passer domestica) lead to a suspicion that they also are included in the natural focalness of Q-fever.

From the investigations of 9 species of the most frequently encountered ticks of the family Ixodidae the carrying ability for Rickettsia could be proven in Rhipicephalus sanguineus and Hyalomma plumbeum. With the presence of this limited information it is not possible to resolve the problem of the existence of isolated circulation of Rickettsiae under conditions of natural biocenoses independent of the animal source of agricultural foci. Stemming from the natural geographical nearness of field biotopes of the suslik with agricultural foci, and also from the biocenotic bond of ticks with individual species of warm-blooded animals in agricultural and natural foci it must be considered without a doubt that there is a tight bond between both types of foci of Q-fever. It is impossible to answer the question of which of these foci is primary and which is secondary.

The historical process of the emergence of Q-fever in Bulgaria, in contrast to several other European countries, was concluded long ago. The fact that Q-fever in Bulgaria has a relatively old history testifies to its wide distribution and the simultaneous presence of two forms of focalness.

Morbidity with Q-fever among the local inhabitants is observed in many regions of the country. The number of cases in the southern part of the country is two times greater than in the north. During the investigation of 971 doubtful and recovered cases the presence of Q-fever was proven in 158 (16.2%). During an analysis of the occurrence of these illnesses it was established that in the majority of cases there was a doubtless infecting ability in agricultural foci. Rural residents become sick most often of all, but epidemic outbreaks and individual cases have been noted in cities also. In a significant number of cases it is possible to show clearly their occupational association -- that category of the population becomes ill which most often has contact with animals or products of animal husbandry (stock breeders, butchers, furriers, drivers and others). The occupational association of morbidity also finds support during serological investigations. Thus, 197 healthy persons were investigated who lived in 11 various populated points and were related by the nature of their activity with animal husbandry or the processing of animal products (workers at slaughter houses, dairy plants, tanning and wool-spinning plants, stock breeders and hunters). Of these, 16.2% turned out to be serum positive. The highest affection was exposed in hunters (24.4%) and stock breeders (17.3%). Morbidity was also observed in all the remaining categories of the population. Thus, positive serological reactions were detected in 4.7% out of 189 donors in Sofia (administrative workers, workers in paper and carton factories, students at a railroad school, etc.).

The most frequent mechanism of infection is the inhalation method, the inhalation of infected dust. Such was the method of infection during the epidemic outbreaks studied by us. These emerged during the transporting of cattle or animal products.

Morbidity was noted throughout the entire year, with a maximum in March--April; the number of cases in the first half of the year was four times greater than in the second half. This distribution is directly connected with the period of the mass dissemination of cattle infections (during calving and abortions) and testifies to the epidemiological significance of agricultural foci of the disease.

Up until now cases of infection in natural foci in the country have not been established.

In Bulgaria 13 strains have been isolated: From the blood of humans -- 7, blood of a goat -- 1, milk of a cow -- 1, internal organs of a suslik -- 2, and ticks -- 2. All the strains were isolated by means of intraperitoneal or subcutaneous inoculation on guinea pigs. In a morphological respect the local strains possessed all the morphological peculiarities of C. burneti. They all cultured well on chick embryos according to the method of Cox.

The method of cultivating Rickettsiae by Cox's process or the combined method of Shindarov was used for the purpose of producing the antigen. It was established that by irradiating the chick embryos with the optimum doses of x-rays (Greiff et al., 1957), 1.3 -- 2 times more of the antigen was obtained than during cultivation according to Cox.

Antigenic analysis by means of the cross reaction of complement fixation and the immunological analysis by means of the cross immune test on guinea pigs showed that there were no differences between the local strains isolated from ticks, from domestic and wild animals and man, and that they were identical with the standard strain.

Conclusions

1. Q-fever in Bulgaria has the nature of a widespread endemic disease.
2. The main reservoir of Q-fever are the domestic animals, among which cattle have the most importance. Together with this, natural foci of the disease exist in the country.
3. In man the disease proceeds mainly in two forms -- pulmonary and less often, purely febrile.
4. Based on their properties, the local strains of C. burneti isolated from man, domestic and wild animals and from ticks are no different from the European strains.

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[Following is the English summary which appears with the Russian article.]

Q-fever in Bulgaria is a widespread endemic disease, affecting almost the whole of the country, being most widespread in the south of it. The chief reservoir of infection are domestic animals, among which the greatest role is played by cattle, sheep and goats. In examining the sera of 3,534 domestic animals the complement-fixing antibodies were revealed in 31.1 per cent of cattle (1,232 animals examined), in 17.1 per cent of sheep (1,012 animals examined), in 19.2 per cent of goats (327 animals investigated), in 7 per cent of the perissodactyls, in 4.2 per cent of swine, etc. Natural foci of the disease also exist in the country. It was possible to isolate C. burneti from the Citellus citellus and from the Rhipicephalus sanguineus, Hyalomma plumbeum. Positive serological results were obtained in 32 of 90 Citellus citellus, as well as in Lepus europeus, Microtus arvalis, etc. A close relationship exists between both types of the foci.

In man this disease occurs throughout the whole year with the peak in March--April, which is due to the mass spread of infection in cattle, sheep and goats (during calving and abortions). Infection by inhalation is the most frequent route. Clinical examination of 125 Q-fever cases showed that in human beings the disease occurs principally in two forms -- the pulmonary, and more rarely, the febrile one.

Antigenic analysis demonstrated that the properties of local C. burneti strains isolated from man, domestic and wild animals and ticks were the same as in the European strains.