Problems in Anti-epidemic Control of Brucellosis in Bulgaria

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Abstract

Aim. To elucidate the distribution of brucellosis among humans in Bulgaria for the period 1950-2007 and to evaluate the official measures regarding brucellosis elimination.

Methods. We used data from the official registry of infectious diseases, survey data on epidemiological control, and data from epidemiological and epizootical surveys.

Results. Registered morbidity of brucellosis in Bulgaria varied between 0.01 cases (1959, 1974, 1985, 1993, 1996, 2000) up to 0.048 (2005) and 0.74 (2007) per 100,000 inhabitants. No cases of human brucellosis were recorded in Bulgaria for 35 years of the entire study period from 1950 to 2007. The periods without registered cases of brucellosis initially lasted about 7-10 years and later 2-5 years. Two deaths were recorded for the years 1958 and 2005. Of the 28 regions in the country, 17 (61%) were affected during multiple years between 1991 and 2007: Plovdiv for 4 years; and Varna, Ruse, Pazardjik, Yambol and Burgas for 2 years. The remaining 11 regions (39%) were affected in only one year during the same period. In all cases professional exposure or consumption of uncooked milk or milk products was identified as a risk factor. The infections persisted from months to years.

Conclusion. Anti-epidemic measures taken by health-care authorities implemented in collaboration with veterinary services can restrict the distribution of human brucellosis.
the counter measures implemented, to describe the clinical indications necessary for laboratory testing and related procedures and to reveal the connection between the epidemiological and epizootic processes in human and animal populations.

Material and Methods

Data sources and case definitions

This retrospective study used data for 1991-2007. Data were taken from notifications of brucellosis, as published in No. 85 report for recording acute communicable disease, and from analyses published by the National Centre for Communicable and Parasitic Diseases of main epidemiological indicators from 2002 to 2007. Additional data sources were epidemiological investigations, data from serological surveys of people and animals, microbiological surveys of the Regional Inspection for Prevention and Control of Public Health (RIPCPH) and the National Reference Laboratory at the National Centre of Infectious and Parasitic Diseases and the National Centre for Veterinary Medicine, Sofia.

Until 2005, in accordance with existing regulations, infectious disease cases were reported as being "questionable" or "confirmed". Since 2005, with implementation of Regulation 21 of the Ministry of Health [11], a three-stage scale of infectious disease incidence reporting was introduced: "possible", "probable" and "confirmed". The cases in the present study were reported as "probable" or "confirmed", since for brucellosis a "possible" case is not applicable. A case was classified as "probable" when it had a typical clinical picture and endemic relationship, or a single sample showed high antibody titer. A case was defined as "confirmed" when it had a typical clinical presentation and was positive by laboratory analysis.

The rate calculations per 100,000 are based on data from the National Statistical Institute of Bulgaria regarding mid-year population estimates for the corresponding regions of the country.

Diagnostic methods

The diagnosis of brucellosis was made at the Regional Inspectorate for Protection and Control of Public Health Laboratories. Until 1998, diagnosis was made using serological diagnostic procedures (Wright and Huddelsson agglutination); during 1999-2007, it was made using the Rose-Bengal test. Cases were confirmed by the National Reference Laboratory in Sofia when clinical evidence and an epidemiological connection was present. Culture testing was done on whole blood samples, and serum was re-tested after 17 – 21 days [12].

Diagnostic titers derived from the Wright agglutination reaction were interpreted as follows: 1:50, problematic; 1:100, weakly positive; 1:200, positive; 1:800, strongly positive. Diagnostic titers from the Huddelson agglutination reaction were interpreted as follows: 1:50, negative; 1:100, weakly positive; 1:200, positive; 1:800, strongly positive.

The presence of differences in titer values and possible cross reactions meant that both clinical and epidemiological criteria were used to confirm diagnosis of brucellosis. The differences in titer values were due to the different disease stages. The need to take into account the specific features of the different foci of infection and the time from onset requires the analysis and confirmation to be performed in the same laboratory.

Other methods

For analysis of the relation between epidemiical and epizootic processes we applied the recommendations of the Expert Group for Brucellosis and the recommendations of the Ministry of Health in 2005 and 2007. These were the years when two outbreaks were investigated using serological screening of contact persons and animals in a targeted anti-epidemic initiative under the supervision of the Ministry of Health. [9, 10].

Results

From 1971 until 1991, a period of 20 years, there were no registered cases of the disease, with the exception of a single case in 1985. Over the entire study period of 58 years, from 1950 to 2007, there were 35 years with no registered cases of brucellosis among humans. The periods free of registered cases of brucellosis initially lasted about 7 to 10 years, and later on were 2 to 5 years: 1951-1957 (7 years), 1961-1964 (4 years), 1975-1984 (10 years), 1986-1990 (5 years), 1997-1999 (3 years), and 2003-2004 (2 years).

For other years, cases were sporadic except for 2005, 2006, and 2007, when two communities had multiple infections within the same period: Smoljan and Haskovo each had 3 cases [6, 10]. Over the entire study period, the morbidity rate ranged from 0.01 per 100,000 inhabitants (1959, 1974, 1985, 1993, 1996, 2000) to 0.48 (2005) and 0.74 (2007).
Deaths were registered in only 2 years of the study period: one case in 1958 and one case in 2005. The fatality in the year 2005 occurred in the village of Karavelovo in the region of Yambol, and was proven only after exhumation. The patient had worked on two sheep farms in Greece in 2001, 2003, and 2004, for a total period of 20 months. Health began to deteriorate in 2003 and death occurred in 2005. The causes of death were unclear. After exhumation brucellosis was proven by DNA analysis of cadaver material. The epizoologic study carried out on the farm of the deceased did not reveal positive results for brucellosis [6].

During the period 1991-2007, 17 of 28 regions in Bulgaria (61%) were affected by brucellosis, mainly in southern Bulgaria and on the Black Sea Coast (Figure 1). The youngest age group affected was 5 – 9 years (1 case in 2007). Only single cases were reported during the other years, therefore age specific morbidity rates will not be indicative.

Agglutination diagnostic tests were widely used until 1999, and the tests were performed in different regional laboratories of the RIPCPH according to the patient’s place of residence. With Wright agglutination, 10 cases were confirmed: 2 with positive titers (>1:200) and 8 with strongly positive titers (>1:800). With the Huddleston agglutination reaction, 2 cases were diagnosed with positive titers (>1:200). Two more cases were confirmed using the passive hemagglutination reaction (RPH) with titres of 1:1280 and 1:3200, and 2 cases using ELISA (>1:150). All of these cases occurred sporadically.

Clinical indications for laboratory testing of some of the registered cases were: high temperature persisting for a long period (as long as years in some cases) and nonspecific symptoms: perspiration, anorexia, constipation, fatigue, depression, lymphonodulitis, arthritis, orchitis, pyelonephritis, neuralgia, leukopenia, lymphomonocytosis, and aneosinophilia [13, 14].

Some of the confirmed clinical cases can be described as follows:

1. A 62-year-old woman with pyelonephritis, high temperature, lower back pain and polyuria;
2. A 62-year-old man with pyelonephritis, joint pains, and orchiepidimitis;
3. A 74-year-old woman with high temperature, gastroenteritis, and weight loss.

In the outbreak of Haskovo (2007), where 561 cases were confirmed, the highest morbidity rate during a single year occurred in 2007 in Haskovo (11.92 per 100,000). Morbidity rates were calculated by age groups for 2005, the only year during the study period when multiple cases were reported. The rates were as follows: 50 – 59 years, 0.90 per 100,000; 40 – 49 years, 0.93; 30 – 39 years, 0.64; and 20 – 29 years, 0.71. No cases were reported in children under 1 year or from 2 – 5 years.

Table 1 shows the regions in Bulgaria affected by brucellosis in the period from 1991 to 2007, for which data are available for a retrospective study.

In some regions the disease was observed during several years (Table 1): Plovdiv (2000, 2005, 2006, and 2007), Burgas (2000, 2007), Russe (2000, 2003), Varna (2005, 2006, 2007), Pazardjik (2000, 2005) and Yambol (2005, 2006). The disease was observed in 11 regions only in 1 year during the study period from 1991-2007. The highest morbidity rate during a single year occurred in 2007 in Haskovo (11.92 per 100,000).

persons were examined using serological tests, 47 cases (8.38%) turned out to be serologically positive without any apparent symptoms. In 46 cases (8.2%), the epidemiological investigation revealed that the most significant risk factor was the consumption of milk products prepared without the appropriate heat treatment. In 35 cases (6.24%) contact with animals positive for brucellosis was observed. Of 47 farms, where brucellosis-seropositive persons were found, animal testing was positive in 20 (42.55%).

In 2007, in parallel with testing the people in contact with brucellosis, serological testing of 90,345 animals in 10 settlements was also performed. Positive reaction for brucellosis was revealed in 403 small ruminant animals (sheep and goats) and 7 cattle. A total of 83 infectious foci were identified across several municipalities of the Haskovo region.

Our investigation revealed the following case groups:
1. Symptomatic, brucellosis-positive cases in association with farm animals that tested negative;
2. Symptomatic, positive cases linked to brucellosis-positive farm animals;
3. Positive cases without clinical manifestations linked to brucellosis-positive farm animals;
4. Positive cases without clinical manifestations and without direct connection to animals; these cases were people who had worked for a long time on dairy farms.

The most significant risk factors identified in our investigations were profession (12.5% of cases) and animal raising and consumption of uncooked milk and other uncooked products (34, 65.6%).

Discussion

Compared to other countries with epizootic foci, the morbidity rate in Bulgaria during the study period was lower. The rate in Spain ranged from 7.35 to 10.30 in 2002, it was 1.10 in Greece in 2006, and in the European Union as a whole, it was 0.18 in 2006. The morbidity in the world is higher: annually there are 500,000 cases but this is thought to be an underestimate [13, 15-18].

After the transition to a democratic government in 1989, intensive population mobility processes across Bulgaria and its neighboring countries as well as the long working residence in endemic regions abroad contributed substantially to the import of brucellosis infection into Bulgaria. The morbidity rate for brucellosis ranged from 0.01 per 100,000 (1959, 1974, 1985, 1993, 1996, 2000) to 0.048 (2005) and 0.74 (2007). Epidemic outbreaks were reported in 2005 and 2007.

The diagnosis of brucellosis in Bulgaria is generally done by serological tests: Wright or Huddelson agglutination reactions and ELISA. Testing is initiated based on clinical evidence, i.e. nonspecific symptoms. The genitourinary, the gastrointestinal and the musculoskeletal systems are affected regularly, and sepsis can be noted.

Risk factors were present in 94% of the cases: contact and raising of animals (65.6%), and profession (12.5%). Epidemiological anamnesis is helpful for the commencement of countermeasures in both humans and animals. Endemic cases and cases imported from Greece and Spain were noted.

Cases were identified across several municipalities in the Haskovo region, which shows that the region was substantially affected. After the occurrence of these human cases, anti-epidemic control measures were implemented based on the epidemiologic indicators. The measures were fast and adequate, and were the result of close cooperation with veterinary specialists [10].

Conclusion

Collaboration of human and veterinary specialists contributes to the fast and adequate implementation of countermeasures. Indeed, the most important preventive measure for the country is the control of brucellosis in animals. The presence of both diseased individuals and serologically positive animals revealed in our study shows the need for regulation of the efforts of veterinary and human health workers and public health specialists, as well as the need for their cooperation. Further development of the serological surveillance of contact persons and infected individuals is required. A multidisciplinary approach for seeking symptoms of brucellosis in populations at risk is also highly important for the control of brucellosis in Bulgaria.

The sporadic character of the disease in Bulgaria is a reason for the absence of intensive serological testing of contact persons. Nevertheless, our results indicate the need for regulations concerning regular serological screening of animals. In addition, education of the rural population and of farm workers in endemic regions is of utmost
importance for the control of brucellosis in Bulgaria.

References

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