Brucellosis Control and Eradication in the South Eastern European Countries: Current Status and Perspective Strategies

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Abstract

Aim. To present main outputs of the International Scientific Conference on Brucellosis in South Eastern Europe (SEE) and Mediterranean Region, held in Struga, Republic of Macedonia, Nov. 12-14, 2009, and to summarize the weak points and constraints for implementation of the current brucellosis control programs in the SEE countries, as well as main components and directions for perspective developments of brucellosis prevention, control and eradication strategies at national and regional levels.

Methods. Retrospective study based on the presentations and discussions recorded at the conference, selected published papers from participants in the scientific journal thematic issues on brucellosis, and a review of the relevant literature.

Results. Networking and exchange of knowledge and experiences among the participants at the conference, together with the adopted declaration for intersectoral and regional collaboration and prepared thematic issues on brucellosis in three scientific journals will have important influence for the future control and eradication of brucellosis in SEE countries. Re-emergence or worsening the situation with brucellosis in many SEE countries indicates weaknesses in the control programs and insufficient organization and collaboration in their implementation. Vaccination and test and slaughter of infected animals need to be accompanied with appropriate herd management, public awareness and health education programs.

Conclusion. Brucellosis is a serious concern in many SEE countries which needs comprehensive approach and investments in long-term, with sound strategies and programs for control and eradication, strengthening intersectoral and regional collaboration between all countries in the SEE region, with technical and financial support from European Commission and relevant international organizations.

Introduction

Brucellosis is a global zoonosis and endemic disease in many countries of Asia and Middle East, Africa, Latin America, South Eastern Europe (SEE) and Mediterranean Region. Prevalence of brucellosis infection by Brucella melitensis in the SEE countries is very high, and affects primarily sheep and goats. Infection in animals is strongly correlated with abortions in the last trimester of pregnancy. Infections of humans are highly contagious through direct or indirect contact with infected animals or their products, causing a debilitating illness. It affects people of all age groups and of both sexes [1, 2]. This insidious and frustrating zoonosis, often neglected, under-recorded and underreported, has widespread impact on human and animal health and plays a significant role in the
The incidence of human cases is significantly correlated to the level of \textit{B. melitensis} infection in small ruminants. This is especially true among nomadic, rural and peri-urban communities where traditions and cultural practices contribute to disease transmission and where people live in close occupational contact with infected animals. Humans may be exposed to animal tissues, discharges or fetus membrane and fluids following abortion, or due to consuming raw contaminated milk, fresh cheese and other dairy products, and rarely raw meat or partly cooked offal (liver) from such animals. Aerosol and hand-to-mouth transmission may occur in abattoirs or laboratories. Hence, control of the disease in animals is a pre-requisite to reducing its burden on public health \cite{2, 5}.

Brucellosis has been a severe public health and socio-economic problem in the Republic of Macedonia for more than 30 years \cite{6-8}. This led the Government of Macedonia, together with the German Academic Exchange Service (DAAD) and Replek Pharm-Skopje to sponsor in 2009, the International MetaNET Project Thematic Scientific Conference: "Brucellosis in South Eastern Europe and Mediterranean Region", which was held in Struga, Republic of Macedonia, from November 12-14, 2009.

The primary aim of the conference was to gather international and regional scientists with an interest in brucellosis, as well as governmental and international authorities, in order:

- To review the current understanding, the state of the current strategies and approaches, and to identify the weak areas of prevention and control of brucellosis;

- To initiate exchange of knowledge and data from fundamental and applied research, experiences and views on various epidemiological and public health aspects of brucellosis, veterinary conditions and activities including vaccines and animal models, immunology, molecular biology and genomics, laboratory and sero-diagnostics, pathogenesis, clinical aspects and treatment of patients with brucellosis;

- To encourage the collaboration and to strengthen international ties and professional networks among the SEE and Mediterranean countries and broader; and

- To provide a forum for discussion and to recommend tools and procedures relevant to perspective developments in various aspects of brucellosis prevention, control and eradication at national and international levels.

\textit{Aim} of the paper is to present main outputs of the conference and to summarize the weak points and constraints for implementation of the current brucellosis control programs in the SEE countries, as well as main components and directions for perspective developments of brucellosis prevention, control and eradication strategies at national and regional levels.

\textbf{Methods}

Retrospective study based on the presentations and discussions recorded at the conference, selected published papers from participants in the scientific journal thematic issues on brucellosis, and a review of the relevant literature.

\textbf{Results}

\textbf{Main outputs of the conference}

The Conference was attended by more than 150 experts from almost 20 SEE and other countries in Europe and beyond. Representatives from some international organizations also joined the conference, i.e. the Food and Agriculture Organization (FAO), European Commission and the World Health Organization (WHO), as well as 10 invited top-level experts in brucellosis as keynote speakers from various countries in the world. Total number of submitted abstracts, published in the Book of Abstracts, was 76, of which almost a half was accepted for oral presentation, and the rest of them for poster presentation.

Following the principles and practice of supportive editorial policy, including help to authors in the pre-review process who are less experienced in scientific writing, there has been achieved very high scientific productivity from the Conference by collecting 35 peer-reviewed papers divided for thematic issues in three different journals, all of them internationally visible, with full-text open access free of charge:

1. Journal "Prilozi - Contributions" of the Macedonian Academy of Sciences and Arts, thematic issue on "Diagnosis and Strategies for Control and Eradication of Brucellosis", published in July 2010 (www.manu.edu.mk/prilozi);

2. Croatian Medical Journal, thematic issue on "Bru-
Brucellosis Diagnosis and Epidemiology”, published in August 2010 (www.cmj.hr); and


The thematic issues on brucellosis would have permanent value in planning and implementation of further activities in the SEE countries and broader on prevention, control and eradication of brucellosis at national, regional and international levels.

The international importance of the conference was emphasized by the adopted Declaration (http://www.cmj.hr/2010/51/4/CMJ_51(4)_web-wxtra.pdf) as the first step of the future organized inter-sectoral and regional collaboration within and between countries in the SEE towards more successful control and eradication of brucellosis at national and international levels [9].

The conference has had special importance for R. Macedonia and the SEE Region. An appropriate problem formulation and broad dissemination of information during the preparation period prior to the conference, including creation of poster and the conference web-site (www.brucellosis09.iph.mk), induced awareness rising at all levels and very strong political commitment, support and sponsorship from the Government of R. Macedonia. In addition, the conference increased interest and cooperation among the experts from health, public health and veterinary sectors, as well as among the political leaders and decision makers responsible to provide and commit resources required for successful implementation of the brucellosis control program in R. Macedonia. Inter-sectoral networking and cooperation was an important output of the conference and benefit for all countries in SEE Region and broader.

**A view on the current brucellosis control programs in the SEE countries**

A big number of participants from the SEE and other countries, invited key-note speakers and representatives from FAO and European Commission, in their presentations and discussion at the Conference, and afterwards in the papers prepared for publication in the scientific journal thematic issues, expressed their views and experiences in control and eradication of brucellosis and pointed out that B. melitensis infection in sheep and goats and brucellosis in humans in many SEE and Mediterranean countries has re-emerged or situation has worsened over the last more than 10 years. Brucellosis, from low prevalence became an important endemic disease, especially in the Balkans, with high prevalence in sheep and goats, as well as in humans [5-7, 10-13]. In part, this has been the result of political changes, conflicts and wars in the new countries established in early 1990s after the breaking apart of the former Yugoslavia [8, 11, 14]. In addition, shortages of funds reduced vigilance or ceased implementation of the recommended control programs and, together with more intensive international travel of people, cross-border movement of animals, and insufficiently controlled trade in livestock and agricultural products, have resulted in a resurgence and worsening of the prevalence of brucellosis in the SEE countries.

Some of the major constraints of many brucellosis control programs and unsatisfactory results in prevention, control and eradication of brucellosis in the SEE and Mediterranean countries, that have been emphasized at the conference in Struga, Republic of Macedonia, include the following [5-8, 10, 15-21]:

- weak veterinary services and administration, often poorly funded, and insufficient mobilization of resources for control of the program’s implementation;
- absence of a clear defined veterinary legal framework for control program and action plans for epidemiology assessment and schemes for prevention, control and eradication of the disease;
- insufficient legislation on the inspection control systems and weak inspection services in the internal food market and imports;
- lack of efficient animal information systems for continued surveillance and providing accurate and reliable information on the disease in both animals and humans;
- lack of appropriate animal health policies and poor identification, registration and control of the movement and trade of animals across borders and within countries resulting in mixing infected animals/herds at the village level and during summer migrations (transhumance);
- ill-defined control strategies and poorly monitored efficiency and progress of the control programs,
- insufficient laboratories infrastructure capacities and laboratory tests conducted under poor conditions, with minimal or no quality assurance as well as poor diagnostics;
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- poor quality of some vaccines used, especially if the cold chain was not maintained;
- insufficient cooperation of farmers with the veterinary services, especially if the vaccine drawbacks and vaccine induced abortions have adversely affected farmer compliance;
- changes in livestock ownership patterns, from state-owned collectives to numerous smaller, privately-owned flocks and herds within communities, which resulted in more difficult implementation of bio-security measures, less effective monitoring and control of animal movements and spreading of infection among livestock, especially when various animal species were reared together;
- lack of inter-sectoral cooperation of medical and public health authorities with the veterinary authorities, failure to establish or lack of activities of the inter-ministerial/ multidisciplinary committees;
- lack of interregional collaboration between neighboring and other countries in the SEE Region.

Since 1996, FAO and several other donors, and the European Commission, have assisted several countries in the SEE, Mediterranean and Middle East regions in re-establishing control programs of brucellosis [5]. A number of lessons have been learnt, but still many practical answers for more efficient implementation of the control programs and for laboratory concerns are needed. Countries in these regions are encouraged to start or, if necessary, to modify existing strategies and prepare tailor-made design of the control programs in order to mitigate weaknesses and to improve performance based upon positive results of other countries. For example, in Greece the incidence of human brucellosis has been significantly reduced since 2000, from 5.0 per 100,000 (548 cases) to 1.9 per 100,000 (208 cases) in 2007, following extensive Rev.1 animal vaccination programs accompanied with health education efforts, which started in late 1990s [13, 22, 23]. Nonetheless, an increase in human cases has been reported in the last years (304 cases in 2008, as presented by the EC representative) possibly due to lack of sustaining the control program.

Main components of the brucellosis control and eradication strategies

Each brucellosis control program is aimed to minimize the health and economic burden of the disease by preventing, controlling, or eliminating the disease risks originating from direct or indirect contacts with infected animals, their products, or their environment. Based on the presentations and discussion with knowledge and experience exchange among participants of the conference, in accordance with the available broader scientific literature and international documents, the following approaches, tools and procedures for prevention, control and eradication of brucellosis at community, national and international levels might be summarized and recommended:

1. The fight against zoonoses begins by eliminating the pathogen at its animal source [4]. Three general methods of control of brucellosis in animals are often given: 1) hygienic measures with careful herd management, and health education, 2) vaccination of animals, and 3) test and slaughter of infected animals/herds. These are most effective when they are combined;

2. Capacity building and training for improving the quality of the veterinary services and appropriate diagnostic laboratories on the basis of adopted standards of the International Organization for Animal Health (OIE), including standardization and quality control of diagnostic kits/reagents and vaccines, are necessary [10, 17, 18];

3. Development and implementation of appropriate veterinary legislation and animal health policies, as well as adoption of appropriate control and eradication programs [19]. The selection of an appropriate and sound control and eradication strategy is of paramount importance. The final strategy should be established according to the epidemiology (extent and prevalence) of brucellosis, quality of the veterinary services organization, and economic resources available, including a baseline sero-prevalence epidemiological survey for assessing the real situation of brucellosis and defining the epidemiological units of intervention within the country and sometimes of a trans-boundary nature [1, 24]. It is necessary to give priority for support to brucellosis control and eradication programs as an essential prerequisite for efficient control and eradication of brucellosis, as well as having an impact on poverty reduction and food safety.

4. A baseline sero-prevalence survey with test combinations for diagnosis of infection in animals and continuous surveillance and reporting are necessary for animal/herd identification and risk analysis, to monitor the presence/absence of brucellosis in herds/flocks, to monitor the efficacy of the control programs, and to
ensure early warning against spread of disease/infection to new areas. The surveillance and reporting systems should include domestic animals and wildlife disease control methods, including the use of vaccination under certain circumstances, with a relevant corresponding human continuum [5, 10, 18, 25-28].

5. There is a wide agreement that vaccination is the most economic, effective and practical method for reducing the prevalence of brucellosis in sheep and goat herds/flocks (B. melitensis strain Rev. 1 vaccine), and in cattle (B. abortus strain 19 vaccine). Vaccination increases resistance to infection and decreases the risk of abortion, as well as minimizing spreading of infection in animals, and consequently decreases the incidence of the disease in human populations. Vaccination of animals, with good quality vaccines, can be promoted to livestock owners, not only on the basis of protection of the animals from abortion, but also for improved lamb/kid viability, improved fertility and milk production, added value of livestock and lowered risk for human illness. The international community has not yet identified a sound solution to prevalence of brucellosis infection at high rates (if more than 10% of flocks are infected). A mass (whole-flock) vaccination of adult animals under the extensive breeding practices, in only one intervention/vaccination campaign, is considered to be the first step and the choice to control the disease, independently of the socioeconomic situation. This is however debatable due to adverse results such as abortion amongst pregnant animals and inadequate sero-diagnosis of vaccinated livestock due to false positive response to vaccine antibodies. In the subsequent years vaccination of young replacements (3-4 months old) is necessary (15-25% of the animals within the herd). It is possible to reinforce the immunity in previously vaccinated animals by repeating the vaccination at regular annual or biannual intervals maintaining it for a period of at least 6-12 years in endemic areas depending on the breeding systems and animal species involved [5, 24].

The methods used in developed countries to control/eradicate brucellosis may not be appropriate for developing countries and those in transition. However many veterinary services can manage Rev.1 vaccination programs successfully and high prevalence can be reduced within two to three years, if good quality vaccine is used in proper vaccination procedures and high coverage attained. Identifying and keeping records of vaccinated animals by ear tagging or other individual identification is essential to monitor coverage. Vaccination is feasible in high prevalence situations and extensive breeding systems for control programs to reduce the prevalence to minimum, but it is insufficient alone to eradicate brucellosis [4, 14, 15].

6. Once effective control of the disease and very low prevalence has been accomplished (less than 5%), eradication of brucellosis might be feasible introducing complex and expensive combined strategy with further vaccination of young replacements and “test and slaughter” of the adult animals found sero-positive until achieving brucellosis free or officially brucellosis free status. An eradication strategy might be based on exclusive “test and slaughter” of sero-positive adult animals without vaccination, which is a very expensive approach both for developing and developed countries, or combined with vaccination of just young replacements in case herd/flock annual prevalence is low to moderate (5 - 10%). For successful eradication a sustainable program must be prepared, in addition to maintaining an adequate organization and quality of the veterinary services, as well as strict control of animal movements with permanent individual identification, political long-term commitment with available financial resources and provision of adequate economic compensation to affected farmers [4, 24]. Test and isolation/ slaughter (partial or full depopulation) of sero-positive animals/herds is usually a part of organized governmental programs where the goal is eradication. Adequate economic compensation to livestock owners for the real market value of their culled animals, as well as control of animal movement, are essential parts of the brucellosis control and eradication strategies [5, 15].

When the disease is fully eradicated, a surveillance strategy has to be implemented for the early detection of eventual new outbreaks or accidental disease reintroduction from the neighboring epidemiological units which remain infected [5, 24].

7. Besides general and occupational hygiene measures from veterinarians and cattlemen, awareness programs and health education, especially for the rural populations by utilizing a wide variety of media technologies, and education of all personnel involved are essential [8, 10, 29].

Ensuring safe food is paramount for the protection of human health and for enhancement of the quality of life. Special attention should be paid to milk and dairy products in regard to obligatory milk pasteurization or heating. Risk based programs should aim at prevent-
ing or decreasing the transmission of zoonoses, including brucellosis, through adequate policy frameworks, prevention and control measures, public awareness and targeted education of producers and entire population on the methods and ways how to prevent and control the spread of brucellosis [10, 20, 29, 30].

8. Prompt diagnosis and appropriate treatment and health care of diseased persons (proper case management) are very important to prevent chronicity and complications, as well as continuous surveillance and providing necessary information to those concerned in occupational and community education programs [1, 4]. Data from human cases may be used to identify possible animal sources of the infection.

9. There is a need to establish or strengthen effective inter-sectoral cooperation both between and within sectors by the joint efforts of all the relevant factors/stakeholders in cooperation with the veterinary service and laboratories, support of primary health care approaches, animal production, food safety and consumer education in the prevention and control of brucellosis. Cooperation between the veterinary services and public health services, governmental and non-governmental agencies involved, together with farmers and shepherds, are essential for efficient implementation of the brucellosis control and eradication strategies. It is necessary to carry out careful herd management and control of animal movement within countries and between neighboring countries. Animals should be individually identified by brand, tattoo or ear tag. Unauthorized sale or movement of animals from an infected area to other areas should be forbidden and prevented. Similarly, importations and replacement of livestock into clean areas must be restricted to animals that originate from brucellosis-free certified farms and areas that have given negative reactions to recently performed diagnostic tests. Livestock aimed at the market should be monitored by serological tests prior to moving the animals from the farms. Beside implementing basic biosecurity measures, suitable budgetary allocations for disease preventive measures and health education, and for support of the activities of the national multidisciplinary committees, aimed at permanent inter-sectoral consultation and cooperation, are necessary [10, 15, 31].

10. Regional collaboration among the SEE countries is necessary for coordination of activities and information sharing at national and the SEE regional level for efficient control and eradication of brucellosis in this region. Collaboration at the SEE regional level and beyond is necessary, with technical and financial support for co-financing of appropriate brucellosis control and eradication programs from the European Commission, FAO and other international organizations, that will include all countries in the region, regardless of the magnitude of the brucellosis incidence [5, 6, 10, 32].

Conclusion

The eradication of brucellosis offers unquestionable benefits to the whole society, of each country and of the SEE Region. In broader terms, supporting the efforts on eradication of brucellosis in the SEE countries is a continuous interest of the whole European Society towards completion of the European Single Market and its impact on competitiveness. But, brucellosis control and eradication is not a simple and “quick-fix” procedure. On the contrary, it needs comprehensive approaches and investments in the long-term, including vaccination, serologic testing with isolation and culling of infected animals (test and slaughter), public awareness, and health education activities, strong political commitment and providing sufficient financial resources for successful and continuous implementation of the control and eradication program. Most important, sustainability must be kept until complete eradication of the disease has been achieved at national level, as well as at the SEE regional level.

In support of such efforts, FAO, OIE and WHO, through coordinated action, intend to develop a transparent “peer review” evaluation process of national and regional brucellosis control and eradication programs, which must be properly planned, coordinated and resourced. Country specific programs might be submitted to FAO for review and be a subject of modifications at the country level. While FAO and OIE can advise on the agricultural and international trade aspects of animal brucellosis, the WHO can advise on human brucellosis aspects. Public health and animal care, first of all, must be the interest of the governments, stakeholders and policy makers within the countries in the SEE Region.

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