

INTEGRATED REGIONAL BIOENGAGEMENT FRAMEWORK TO COMBAT BRUCELLOSIS

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Abstract: *Aim:* To evaluate the current practices in laboratory disease detection, biosafety and biosecurity measures and information-sharing systems available to the public health systems in R. Macedonia and the Balkan region.

Methods: Epidemiological studies were reviewed from the region to examine the high incidence of localized forms of human brucellosis.

Results: There is clearly a need for the development of a South Eastern European regional network for sharing information aimed at disease surveillance, early reporting and efficient containment of human brucellosis. Given the zoonotic nature of the disease's onset and progression, public health strategies aimed at containing and eventually eliminating human brucellosis require a broader national and regional bioengagement framework that involves human and veterinary diseases detection systems, deployment of medical countermeasures, epidemiology and a supportive laboratory infrastructure, strategic stockpiles and information sharing.

Conclusions: A systems-centric framework for a national and regional strategy to combat human brucellosis is essential, and should be comprised of: a) a disease threat and surveillance framework at the national and broader regional level, b) laboratory performance evaluation metrics, c) best practices for information-sharing and regional coordination, and d) a coordinated regional strategy to improve biosafety and biosecurity.

Key words: brucellosis, zoonoses, prevention and control, population surveillance.

Introduction

Threats posed by biological agents are not confined by geographical barriers, as the health and security of a nation is intertwined with regional and

global health and security. The spread of infectious diseases such as Brucellosis continues to be a major public health challenge for public health departments globally, requiring a multifaceted preparedness and coordinated response measures.

As one of the most common zoonotic infections worldwide, Brucellosis presents a unique national and regional public health burden in the Balkan region and other South Eastern European (SEE) countries. Brucellosis is among the most common zoonotic infections caused by bacteria of the genus *Brucella*. Although several domesticated animals serve as reservoirs, often the primary source for human exposure to the pathogen is in the form of contaminated animal products such as milk, cheese and other dairy products, inhalation of aerosolized pathogen, and direct contact with domestic animals and animal products. In the United States, brucellosis costs the dairy and beef producers \$30 million annually due to infections and mandatory elimination of populations with infected animals [1]. Over the past century, the livestock industry in the US has suffered billions of dollars in direct losses and costs to control and eliminate the disease.

An added concern with the *Brucella* species is that it has been traditionally considered a biological weapon, and the bacteria listed under the Select Agents and Toxins list by the US Department of Health and Human Services (HHS) and the Department of Agriculture (USDA), and Category B pathogen by the WHO. *Brucella* species are potential bio-threat agents due to: a) the relative ease of airborne transmission of the pathogen, b) ability to induce a chronic debilitating disease with low mortality but high morbidity, c) no human vaccine is currently available and treatment regimen with multiple antibiotics remains problematic, d) wide distribution in environmental reservoirs, and e) vague early clinical manifestations preventing rapid detection and identification.

Effective management of a public health disease burden such as brucellosis, which also has potentials for national and regional security, requires integrated biosurveillance information acquisition, management and sharing capabilities at national and regional levels. This requires an effective government agency level, and international level coordination such that data collected from multiple sources can be analysed and the results disseminated within the shareholder community in a reporting format that is meaningful and actionable to multiple and diverse government and regional entities. Such an effort to combat the threat of brucellosis in Macedonia and in the broader region appears urgent.

Published public health epidemiological findings reveal that whereas EU countries in general have declining incidence of brucellosis, with many western European countries now declaring the region as "Officially Brucellosis-Free" (OBF), the disease remains endemic in the Balkans and the Mediterranean countries, and there is a marked resurgence of the disease in parts of the former

Soviet Union [2]. The public health burden due to brucellosis in these regions is mostly linked to consumption of pathogen-contaminated dairy products, inadequate resources for early detection and reporting, reduction in support for veterinary health services, and an overall lack of healthcare networks.

Clearly, human brucellosis is an endemic public health disease burden with likely national and regional security implications for R. Macedonia and the broader Balkan region. Published studies from this region indicate the lack of a regional network and a systems-centric approach to early detection and reporting, as well as implementation of a national programme aimed at improved veterinary healthcare and effective management of human brucellosis disease. This paper will provide a conceptual framework with potential dual applications in the public health and national and regional security domains consisting of: a) threat assessment framework for disease surveillance, b) bioengagement-related information-sharing and coordination at national and regional levels, and c) implementation of biosafety and biosecurity practices to ensure the safety of the animal product supply chain, occupational and environmental safety measures.

Threat assessment

The disease is caused by six variants of bacteria of the genus *Brucella*, of which *B. melitensis* accounts for nearly 90% of the reported cases of Brucellosis worldwide [3, 4]. A key concern is that an array of livestock animals serve as reservoirs that includes cattle (*B. abortus*), dogs (*B. canis*), sheep, goats, and camel (*B. melitensis*) and pigs (*B. suis*), enabling exposure to the biological pathogen in occupational and familial settings. Published reports are scanty on the nature and incidence of brucellosis in the Balkan and SEE region, but limited evidence from the region suggest most of the reported disease incidence is caused by *B. melitensis* in sheep, goats, and humans, and is a serious public health burden for R. Macedonia, Greece and the adjacent countries of the former Yugoslavia [5].

Figure 1 summarizes the reported annual incidence of brucellosis in R. Macedonia over the past decades. The nature and extent of the public health burden due to brucellosis in Macedonia is unclear, but limited published evidence suggests that a majority of over 54% of the disease incidence has a positive family history and remained localized in farms and exposure to home-produced milk and related dairy products [6]. Studies on the clinical and epidemiological characterization of Brucellosis have revealed interesting regional differences in the clinical profiles.

Studies in Macedonia over two time-periods of 1990–91 (group 1) and 2003–05 (group 2), illustrated in Figure 2, have revealed a generally compa-

rable clinical profile with arthralgia, malaise and fever as typical clinical manifestations. However, a higher rate of osteoarticular and cutaneous eruptions were observed in group 2 patients. Similarly, a much higher incidence of peripheral arthritis was reported in group 2 patients (41%) compared to 22% in group 1 patients [7]. A recent study summarizing the human brucellosis clinical scenario in the Indian subcontinent context reported a relatively comparable clinical profile, albeit with certain unique clinical features [8].

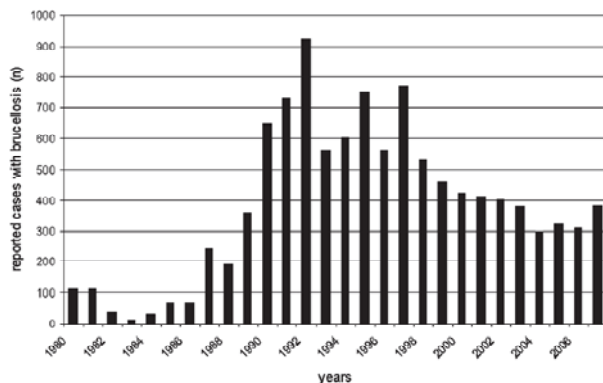


Figure 1 – Incidence of documented cases of brucellosis in the Republic of Macedonia for the Period 1990–2009 (Source: Bosilkovski et al. 2009).

Слика 1 – Инциденца на документирани случаи на бруцелоза во Република Македонија во периодот од 1990–2009 (Извор: Босилковски и сор. 2009)

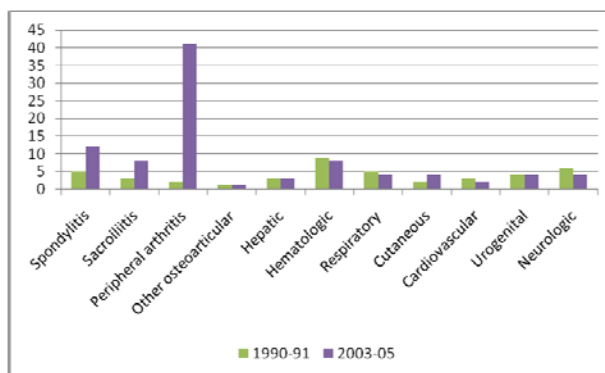


Figure 2 – Clinical manifestations serving as ideal indicators to brucellosis disease detection and surveillance in R. Macedonia (Source: Bosilkovski et al. 2007, 2009).

Слика 2 – Клинички манифестации кои служат како идеален индикатор за откривање на заболени од бруцелоза и за биолошко истражување и надзор во Р. Македонија (Извор: Босилковски и сор. 2007, 2009)

Figure 3 summarizes the clinical findings in 740 patients infected with *B. melitensis*. Although fever (78%) and arthritic pain (21%) were predominant features just as in the Macedonian medical epidemiological studies, a significantly higher percentage of splenomegaly (17%), hepatomegaly (10%) and splenohepatomegaly (15%) was observed in the Indian patient samples, pointing to a strong lymphatic and immune system component involvement in the clinical profile. Reliable clinical and medical epidemiological data is essential to develop evidence-based disease syndromic surveillance, taking into account differences in clinical profiles likely to be due to the pathogenic species or strain involved, demographic differences in populations exposed to the pathogen, and clinical criteria employed in the early detection of the disease by clinicians and public health specialists in various parts of the world.

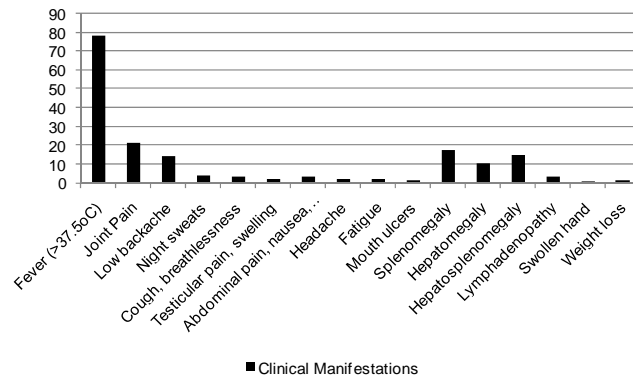


Figure 3 – Clinical manifestations key to disease detection and surveillance (based on Mantur et al. 2007).

Слика 3 – Клучни клинички манифестации за откривање на заболени и за биолошко испржавање и надзор (сијоред Манџур и сор. 2007)

As far as pathogen threat assessment and biosecurity are concerned, *Brucella* species *B. melitensis*, *B. abortus*, and *B. suis* are classified as select agents by the US Centers for Disease Control and Prevention (CDC) and the US Department of Agriculture (USDA). The European Union and most European countries classify these species under Risk Group 3 for select agents. *Brucella* species are highly infectious when transmitted by aerosol and incapacitate with flu-like fevers that generally do not respond well to antibiotic therapy. Hence, brucellosis was one of the prime candidates for weaponization due to its low lethality, ease of manufacture, and the fact that it does not cause uncontrollable epidemics due to its short shelf-life and sensitivity to light. It was considered a 'humane' weapon. Several nationals with active biological weapons were involved in large-scale production and field-testing activities. Much of the bio-

logical weapons related potential of the *Brucella* species remain a legacy topic of academic interest, although its potential as a biological weapon cannot be ruled out.

The infectious dose for human is unknown while the mode of environmental transmission and exposure are through ingestion, direct dermal contact accentuated by skin ruptures or wounds, and mucous membranes. Inhalation of aerosolized particles is a potential route under certain conditions and is considered one of the primary exposure pathways under laboratory conditions. *Brucella* species are extremely susceptible to environmental degradation in the aerosolized form and can be quickly inactivated by sunlight. Potential sources of infected materials included animal products, infected tissues, blood, urine, vaginal discharges, aborted fetuses, contacts in abattoirs, and laboratory-acquired diseases. A comprehensive threat assessment of the *Brucella* species requires a systematic biological hazard assessment and environmental hazard and risk evaluation based on weighted consideration of various intrinsic biohazard and environmental factors related to transmission, infectivity and fate [9–11].

Biosurveillance

Effective biosurveillance of brucellosis at the national and regional levels requires integration of heterogeneous data from relevant national agencies in the areas of human, animal and plant health to generate operationally relevant outputs in the form of alerts, warnings, and supportive quantitative analytics. The analytical elements would have to fundamentally delineate disease incidence either as a biological outbreak or a biological attack. Depending on the biosurveillance early indicators and warning (I&W), national and regional stakeholders are provided with near-instant access to information for decision support.

Figure 4 provides a notional outline of a biosurveillance system and information flow to support data analysis, generation of alerts and sharing of output with national and regional partners. The information flow outlines key elements of science and analysis approach: a) data source, b) data store, c) data analysis, and d) output. These enable detection of the disease at early stages in the endemic regions and accurately locate event clusters, pathogen identification and characterization and supportive evidence to justify further medical epidemiological or biosecurity investigations depending on the situation. Ultimately, the goal of a brucellosis biosurveillance system is to detect and characterize outbreaks through the collection and analysis of data, and is comprised of a) detection of individual cases, b) detection of clusters of cases, using a variety of grouping formats, c) disease outbreak characterization, d) number of individu-

als, families, and farming community clusters affected, e) pathogen agent identification, f) potential routes of environmental transmission and possible exposure pathways, and g) locating the source point for the disease origin.

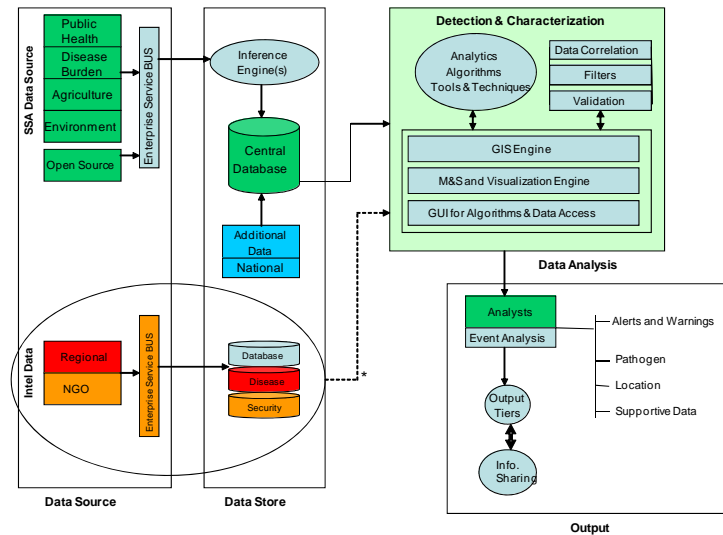


Figure 4 – Notional Outline of an Integrated System with Components of Syndromic Disease Surveillance and Biosurveillance Information Flow, Data Analysis, and Output for Sharing at the Local, National, Regional and International Levels

Слика 4 – Идејна рамка за интегриран систем со компоненти за истражување и надзор на синдроми на болести и за пројект на информации за биолошко истражување и надзор, анализа на податоци и размена на информации на локално, национално, регионално и меѓународно ниво

The public health disease burden due to brucellosis in Macedonia and the broader region remains murky due to lack of reliable data and under-reporting of the disease incidence. Going beyond routine syndromic disease surveillance and taking into account data from veterinary and environmental sources provides a better basis to define disease baselines and identify the disease process and related environmental factors associated with exposure.

Figure 5 is a box diagram illustrating a mathematical model of disease process and progression, in this case SARS, found consistent with the actual observations in the greater Toronto area. The disease process delineated in Figure 5 is fundamentally applicable to the brucellosis problem in Macedonia and the greater Balkan Region, since the disease to a considerable extent remains either undiagnosed or under-reported. Epidemiologists have applied mathematical models to predict whether isolation and quarantine would stop the spread of SARS in the greater Toronto area in Canada [12]. Adopting the overall simpli-

city of the mathematical model, an effort could be made in R. Macedonia and the greater Balkan region on the brucellosis-related health burden to assess the number of undiagnosed and underreported cases. The susceptible (S), and potentially exposed (E) populations consisting mostly farming communities in the rural areas form the population universe to develop brucellosis public health burden assessments. Intervention policies such as veterinary healthcare, easy access to healthcare networks and a policy related to food safety could be used to predict reduction of the disease burden. Reliable baseline disease burden data together with population demographics are necessary to compare model-based results with actual reductions in disease burdens.

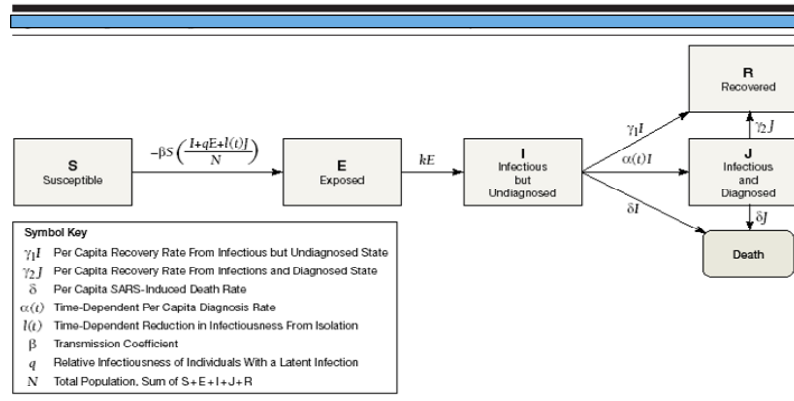


Figure 5 – A generic mathematical model for clinical intervention to stop spread of infectious diseases (adopted from Castillo-Chavezetal, 2003 based on a study to stop spread of SARS outbreak in Canada)

Слика 5 – Основен математички модел за клиничка интервенција за зајирање на ширењето на заразните болести (Приложено од Castillo-Chavezetal, 2003 базирано на студијата за зајирање на епидемијата на SARS во Канада)

Any effective public health or national security-centric efforts in combating Brucellosis at national and regional levels requires effective biosurveillance analysis comprised of an optimum mixture of computer processing of data collected from various human, veterinary and environmental related sources and human interpretation. Currently, the majority of the disease surveillance related analysis is performed by human analysts who are experts in the domain. Analysts interpret the biosurveillance data by applying individual and collaborative bodies of knowledge about biological agents and their propensities for certain routes of transmission. Over the past decade, there has been a growing appreciation of the potential to automate more of the cognitive work performed by analysts, as reflected in the growing body of research on appropriate supporting al-

gorithms. Several systems currently exist that would provide capabilities to: a) perform plug and play analytical modules, b) detect brucellosis disease subsets from clusters of reported cases with overlapping medical syndromic features, c) visualization of data for temporal and spatial analysis, to enable location of cases/clusters, regional distribution and overlapping multiple data sources. Brucellosis is an endemic public health problem in Turkey, just as it is in R. Macedonia and the Balkan Region. A recent study developed Geographic Information System (GIS) based disease maps to identify geographical distribution and disease etiology of data from multiple sources to perform spatial statistics and data analysis [13].

Figures 6 and 7 illustrate the tremendous value of biosurveillance systems using multiple data sources. Figure 6 illustrates disease clusters and spatial distribution by density of the total of farm animals (cattle, sheep and goats) for various provinces in Turkey during the years 1996 to 2006. Figure 7 is the result of a multivariate analysis of the brucellosis disease clusters visualized for various provinces in Turkey. Clearly the highest prevalence of brucellosis reported from the provinces of Turkey were also the same areas where the density of farming animal and family-owned farms were highest, clearly suggesting scenarios for exposure pathways for the disease centered on farming communities and the density of distribution of farm animals, which for the most part are the reservoirs and source of human exposure to the pathogens.



Figure 6 – The number of total farm animals (cattle, sheep, goats) distribution (1 : 1,000) for the provinces of Turkey for the period of 1996–2006
(Based on Demirel et al. 2009)

Слика 6 – Број и дис­т­ри­бу­ција на вк­у­ј­но жи­во­ј­ни на фар­ми (џо­ве­да, ов­ци, ко­зи) (1 : 1,000) во и­про­вин­ци­ј­не во Тур­ци­ја во и­е­ри­од­ој од 1996–2006
(Ба­зи­ра­но на Demirel et al. 2009)



Figure 7 – Multivariate LISA cluster map of number of farm animals against brucellosis rate of disease mapped for the provinces of Turkey, 1996–2006
(Based on Demirel et al. 2009)

Слика 7 – Мултиваријантна LISA-cluster мапа за број на животињи на фарма и стапак на заболени од бруцелоза мائирани во провинциите на Турција, 1996–2006 (Базирано на Demirel et al. 2009)

Table 1 is an illustrated set of detection and characterization algorithms applied for the detection of various disease outbreaks, and clustering and spatial analysis of disease outbreaks. The application of automated tools using disease detection and characterization algorithms could greatly assist disease outbreak assessment. Given the endemic nature of brucellosis in many parts of R. Macedonia and the adjacent region, sporadic reports of disease outbreaks are available. Any public health intervention measure under such circumstances would first have to detect individual cases followed by the detection of clusters of cases indicative of the nature and extent of the disease outbreak. A more crucial element of disease identification and characterization algorithms is their ability to identify the biological agent, potential routes of transmission, sources of pathogen, environmental receptors, release points, and the potential number of veterinary cases and humans affected.

While spatial analysis detects disease clusters and data visualization and overlay of multiple data sources link likely environmental factors associated with exposure and assist detection and characterization of the pathogen, temporal analysis provides a time-line on the origin and development of the disease process for biosurveillance and disease outbreak investigations. Temporal analysis components in disease surveillance systems would depend on data processing and filtering techniques to detect any temporal anomaly in reported data streams and apply temporal correlation methods using standard statistical data analysis methodologies. Whereas spatial analysis and GIS displays and data overlays of raw counts and clusters result in disease maps, temporal analysis will reveal the timeline and trajectory of the progression of the outbreak.

Table 1 – Табела 1

Disease Detection and Characterization Algorithms Bring Computational Power and Automated Processes for Biosurveillance

Откривање на болести и карактеризација на алгоритми со компјутерска техника и автоматско процесирање за биолошко истражување и надзор

Detection and Characterization Tasks	Algorithms
Detecting a single case	Bayesian diagnostic network. Rule engine
Detecting temporal anomaly in university time series data	Cusum, recursive least squares (RLS), change point statistic, wavelet, moving average
Detecting spatial anomaly in univariate time series data	Kulldorf spatial scan Bayesian spatial scan
Computing posterior probabilities over existence of outbreak, causative biological agent, source, route of transmission	Bayesian Aerosol Release Detector (BARD)
Projecting future extent	Gaussian Plume and other aerosol dispersion models
Providing economic information	BioEcon

Spatial and temporal analysis of the disease outbreak together with visualization tools are essential components of a biosurveillance system. For visualization helps analysts understand large amounts of data and locates well-defined relationships among various entities displayed as they become immediately apparent. In order to more effectively manage medical and veterinary health investments to combat brucellosis and facilitate outbreak investigations, public health agencies in R. Macedonia and the greater Balkan region could benefit much from a shared technology platform that allows broader data analysis and visualization of high risk regions and locates potential risk factors linked to exposure and disease etiology.

Regional bioengagement framework

The threat posed by endemic or new and emerging diseases is not confined by geographical barriers to the point that the effectiveness of any public health intervention strategy depends to a large measure on regional and global responses to the threat. The outbreak of SARS and the threat of H1N1 (swine) flu are examples of an emerging landscape where a disease outbreak would require a concerted, multifaceted preparedness and response measures from national agencies, regional networks and international partners and NGO organizations.

Brucellosis as one of the most common zoonotic infections worldwide has dramatically altered the public health landscape in many parts of the world including R. Macedonia and the greater Balkan region. Factors ranging from sanitary, environmental and socioeconomic factors together with increased international travel have alerted us to the global landscape of brucellosis. Therefore, given the nature of the complex systems involved: nature, society, and technical domains compounded by an assortment of stakeholder communities, a multitude of national agencies, regional networks and NGOs participating at national, regional and international levels, a systematic bioengagement strategy to combat brucellosis requires a systems-centric approach. A System of Systems (SoS) bioengagement approach to combat brucellosis offers multiple advantages compared to approaching the problem in isolated vertical silos. Conceptually, the SoS approach is premised on the arrangement of interdependent systems and connections to provide a capability greater than the sum of the member systems. The SoS is attained either by grouping subsystems based on common characteristics, or by functional elements.

Table 2 – Табела 2

Systems-Centric Approach Provide Greater Capabilities to Combat a Multifaceted Public Health and Biosecurity Threat such as Brucellosis.

Systems-Centric присти́ајој обезбедува по̀големи можнос̀ти за сузбивање на по̀векеслојни́е закани по̀ здравје́то и биолошката́ безбеднос̀т како шти́о е бруцелоза́та

Brucellosis Problem Element	Features of a System of Systems Approach and Benefits
Autonomy of component systems	Autonomy of individual component systems is retained, while working to fulfill the overall purpose.
Belonging of various component entities	Decision to belong is based on cost/benefit assessment of each entity; and a desire to meet the broader goals.
Connectivity of programme areas by design or function	Dynamically supplied by participating entities/systems, connections at multiple levels; highly enabled by a net-centric architecture.
Diversity of management hierarchy, interplay of various systems and functions	Autonomy of component systems, and committed belonging and connectivity at multiple levels increases diversity.
Emergence of capabilities to address desirable and undesirable outcomes.	A new set of emergent capabilities attained, a shared platform for information exchange, prevention, early detection and management better enabled.

Table 2 summarizes the advantages of a system-centric approach to brucellosis by problem elements. Ownership of data systems by a stakeholder

community requires a well-articulated data sharing agreement, identifying shared resources to a SoS based entity without compromising system autonomy, but allowing connectivity to data systems aimed at creating new capabilities that cannot be achieved by a stand-alone system. Many of the current challenges in combating brucellosis centre on difficulty in information-sharing, collective threat assessments, quality standards in prevention and medical intervention approaches and harmonizing guidelines to protect veterinary and human health, together with measures for environmental monitoring.

Figure 8 illustrates a high-level, conceptual system-centric biological architecture of a shared system to combat brucellosis. As seen in the architectural layers, the primary operational domain remains a global layer comprised of national, trans-boundary (regional) and international layers where multiple and often overlapping investments are made to combat a public health menace such as brucellosis. Also, the threat layer investments made in the domain of national security, covering threat of infectious diseases, overlap public health and disease prevention related investments. These investments, grouped either as public health oriented for endemic disease burdens such as brucellosis, new emerging outbreaks and potential misuse have national and/or regional security consequences.

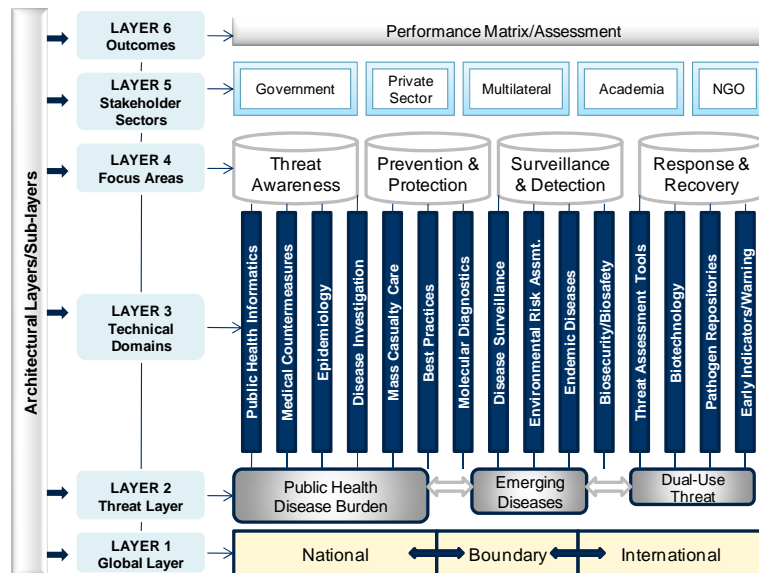


Figure 8 – Systems-centric biological architecture to combat brucellosis as a public health menace and a potential national/regional biosecurity threat
Слика 8 – Систем-центрична биолошка архитектура за сузбивање на бруцелоза како закана за здравјејо на луѓејо и како потенцијална национална/регионална закана по биолошката безбедносјо

The technical domain layer is perhaps the most versatile and highly distributed capability that requires a careful assessment of resident capabilities and how they contribute to key focus areas defining the next layer, the focus areas (Layer 4). Layer 4 represents combined investments in technology base development by government-sponsored research and development capabilities, academia and private sector investments in medical countermeasures development both for veterinary and human health and, finally, the combined technology capability development by the international agencies vested with global disease prevention and health protection. The technology base and capabilities developed in this layer are uneven, since priorities in investments are driven by the government entities and public sectors with vested responsibility to protect the public from threatening new/emerging diseases and provide a lasting solution to systemic public health disease burdens.

Nations and regional groups have invested significant resources based on threat awareness, biosurveillance and early detection and characterization, prevention and protection measures and, finally, response and recovery related operations either due to major disease outbreaks having far-reaching public health/national security implications such as foot and mouth disease (FMD), Bovine Spongiform Encephalopathy (BSE), Severe Acute Respiratory Syndrome (SARS), or H1N1; or threats having potential for bioterrorism involving dual-use biological materials. A systems approach allows leveraging of investments in public health oriented programmes to gain insight on potential national/regional security threats, and vice versa. A systems-centric biological architecture will afford the overlapping emergence of capability based on efficient information-sharing platforms and optimum utilization of resources committed to prevention, biosurveillance, and emergency response functions. What follows are two examples illustrating how biological architectural layers interplay in the development of new capabilities for brucellosis detection and management.

First, food safety programmes are a critical component of any effective brucellosis prevention programme. Measures aimed at evaluating the microbiological safety of food, and especially milk and milk-based products generated from small farming communities, is an essential element if the goal is to eliminate at the sources of exposure the pathway to most of the infected population (Layer 3). Brucellosis is very rare in much of the industrialized world, but remains a public health challenge stemming mostly from direct human contact with infected animals, or through exposure to animal products such as unpasteurized milk, cream, cheese and other dairy products (Layer 4). A food microbiological safety surveillance programme based on a rapid field test to detect and identify the pathogen in infected environments and food products would have considerable impact in reducing the exposure burden at the source level (Layer 5). Second, biosurveillance of livestock and free-ranging wildlife that constitute reservoirs of *Brucella* spp. is the other key intervention layer in the bioengagement architecture. Risk assessment for disease transmission using both unidirec-

tional and bidirectional models for contact between disease-borne and disease-free animals, either in livestock or free-ranging wildlife, provide a fairly accurate estimate of the probability of infection in wildlife, which could be used as the basis for serological field testing plans. According to published risk assessment studies, it would take approximately 2 years before a brucellosis infected animal is detected in wildlife and livestock either clinically or through serological testing [14]. Quantitative risk measures for the detection of infected animals drives investments in Layer 4 and information sharing capability at the global layer (Layer 1).

Conclusions

Regions where the disease has remained endemic for a long period, such as France, Latin America and Israel, have attained a measurable level of control, whereas parts of Central Asia, Central and Eastern Europe, Russia and the FSU nations, the Balkans and the Middle East have generally witnessed a worsening of the disease burden. Human brucellosis is illustrative of an endemic threat in R. Macedonia and the Balkan region. Clearly a need exists in the region for a systems-centric framework as part of a broader strategy to combat human brucellosis. The key features of a systems-centric approach should be centred on a disease threat and surveillance framework with a service-oriented architecture for information-sharing at the national and broader regional level. Subsystem components should consist of laboratory performance evaluation programmes and a coordinated regional strategy for biosafety and biosecurity.

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Резиме

**ИНТЕГРИРАН РЕГИОНАЛЕН БИОАНГАЖМАН
ЗА БОРБА СО БРУЦЕЛОЗАТА**

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Цел: Да се евалуираат сегашните практики за лабораториско откривање на бруцелозата, мерките за биолошка безбедност и сигурност, како и системите за информирање достапни на јавно-здравствените системи во Р. Македонија и Балканскиот регион.

Методи: Направен е преглед на епидемиолошки студии од регионот со цел да се анализира високата инциденца на локализираните форми на бруцелоза кај луѓето.

Резултати: Постои јасна потреба од развој на регионална мрежа во Југоисточна Европа за размена на информации насочени кон надзорот на болеста, раното известување и ефикасното ограничување на бруцелозата кај луѓето. Поради зооноската природа на почетокот и прогресијата на заболувањето, јавно-здравствените стратегии насочени кон ограничување или евентуално елиминирање на бруцелозата кај човекот, имаат потреба од пошироко национално и регионално ангажирање на биолошките ресурси во вид на конструкција која вклучува системи за детекција на болести кај човекот и животните, употреба на медицински противмерки, инфраструктура за епидемиолошка и лабораториска поддршка, стратешки групирања на ресурсите и размена на информации.

Заклучоци: Системски насочената конструкција за национална и регионална стратегија за борба со бруцелозата кај луѓето е есенцијална и се состои од: а) Систем за набљудување и надзор на законите од болеста на национално и пошироко регионално ниво, б) Систем за евалуација на лабораториските перформанси, в) Најдобри протоколи за размена на информации и регионална координација, и г) Координирана регионална стратегија за подобрување на биолошката безбедност и биосигурност.

Клучни зборови: бруцелоза, зооноза, превенција и контрола, популациски надзор.

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