Strengthening integrated surveillance for arboviruses in the Mediterranean and Black Sea regions in the framework of the *One Health* approach

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Summary - This article describes how the MediLabSecure European project contributes to the strengthening of One Health surveillance in the Mediterranean Basin and Black Sea Regions. We conducted a survey with 19 countries to assess and document the level of integration in surveillance of arboviruses between four disciplines: animal virology, human virology, medical entomology and human epidemiology across three different levels: policy and institutional, data collection and analysis, dissemination of results. Seventy-five contact points (CP) of the four disciplines from the 19 countries were invited to the survey. Responses were obtained from 63 CP (81%) of whom: 14 from the Black Sea, 26 from North Africa and the Middle East and 23 from the Balkans. Integration on all the explored levels was confirmed by all four disciplines independently in any of the countries included in the study. This suggests that implementation of fully integrated one health surveillance across the policy and institutional level to the data collection and dissemination level is yet to be fully developed in the Mediterranean and Black Sea regions with the four considered disciplines.

Key words: arbovirus, One Health, integrated surveillance, Mediterranean Basin, Black Sea

Riassunto - Questo articolo descrive come il progetto europeo MediLabSecure contribuisce al rafforzamento della sorveglianza integrata nel quadro strategico della "*One Health*" nelle regioni del Mediterraneo e del Mar Nero.
Abbiamo condotto uno studio con 19 paesi per valutare e documentare il livello di integrazione nella sorveglianza delle arbovirosi tra quattro discipline: virologia animale, virologia umana, entomologia medica e epidemiologia umana riscontrabile attraverso meccanismi di integrazione adottati in tre differenti livelli: politico e istituzionale, raccolta e analisi dei dati, divulgazione dei risultati. Settantacinque referenti delle quattro discipline sono stati invitati a partecipare allo studio. Hanno risposto 63 referenti (81%) di cui: 14 dal Mar Nero, 26 dal Nord Africa e dal Medio Oriente e 23 dai Balcani.
Nessuno dei Paesi coinvolti nello studio ha riportato l'esistenza di meccanismi di integrazione nei tre livelli considerati indipendentemente da tutte le quattro discipline. Questo suggerisce che l'attuazione della sorveglianza integrata per le arbovirosi non è stata ancora pienamente sviluppata nelle regioni del Mediterraneo e del Mar Nero con meccanismi integrativi che considerino le quattro discipline e i tre livelli considerati.

Parole chiave: arbovirosi, One Health, sorveglianza integrata, Mediterraneo, Mar Nero

INTRODUCTION

The emergence and reemergence of infectious diseases is linked to concurring determinants affecting the microbial agent, the human host and the human environment [1].
Among those determinants, human mobility and population growth, trade and climate change are recognized risk factors for the geographic expansion of diseases to new areas. In addition, globalization has been described as a determinant in redrawing pathogen distribution patterns in haphazard and unpredictable ways [2].
Emerging and reemerging infectious disease agents are for the most part (70%) vector-borne and/or zoonotic [3] and also include causative agents with

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bioterrorism potential [4]. These pathogens have been able to adapt to changing human and animal populations and to environments that have been altered by humans. They are also characterized by complex life cycles involving human and animal hosts and, in some cases, vectors. For this reason they require mutual animal and public health vigilance for rapid detection [4]. An example of the impact of inadequate surveillance and preparedness for zoonotic disease threats is the initially unrecognized emergence and establishment of West Nile virus in the US that led to 37,000 human illnesses and 1500 deaths [5].

Mosquitoes are the most important vectors of human diseases. The incidence of mosquito borne diseases like dengue, equine encephalitis, or West Nile Virus Disease has been increasing in recent years in tropical and temperate countries. Climate and environmental changes engender both short- and long-term impacts on vector-borne pathogen transmission. It is estimated that average global temperatures will rise by 1.0-3.58 °C by 2100, increasing the likelihood of many vector-borne diseases [6]. At the same time, deforestation causes drier conditions that will have an impact on the dynamics of infectious diseases, especially those associated with forest vectors and reservoirs, such as malaria, leishmaniasis, and arboviral infections. The fact that some pathogens can be transmitted by different competent vectors, such as Rift Valley Fever [7], further complicates this picture and explains rapid spread and establishment of diseases in new geographical areas.

Dengue virus and West Nile virus (WNV), two distantly related flaviviruses, are good examples of the rapid spread of arboviruses [8]. The widespread establishment of WNV in the US and in the Mediterranean basin also demonstrates the vulnerability of non-endemic countries to the introduction of arboviruses [6,9]. Furthermore, the presence of competent *Cx. pipiens* in southern Europe and North African countries represents a virtual risk for Rift Valley Fever virus epizootics in case of virus introduction in countries of the Mediterranean basin, even if the main vectors of the disease (*Aedes spp*) are not present [10].

The Mediterranean and Middle East Regions have long been "hot spots" of the emergence and re-emergence of zoonosis [11,12,13,14]. For this reason, in 1978, the World Health Organization started an interregional (Mediterranean and Middle East) Programme on Zoonoses and Foodborne Diseases prevention, surveillance and control based in Athens with the participation of 17 countries. The Programme aimed at promoting prevention, surveillance and control of zoonoses and related foodborne diseases; strengthening collaboration between animals and public health services; implementing training activities; promoting veterinary public health activities and public health education; and fostering collaboration among Member Countries [15].

This initiative fathered what, in 2004, would become known as the concept of "One Health", underscoring the interdependency of human and animal health and their link with the ecosystems in which they co-exist. In the intervening years, much progress has been made at the international level to identify ways of collaboration between animal and human health agencies to reach the joint goal of One Health. However, the translation of this international success into national programs has been slow [16].

The "One Health" conceptual approach has seen unprecedented revival in the last decade with fostered awareness, scientific debate, research programmes [17], integrated disease surveillance [18] and an open toolbox in the fields of disease surveillance, epidemiological studies and health care provision.

The Global Health Strategy agenda, recently launched by the USA and endorsed by over 40 countries, seeks to forge interdisciplinary global health collaboration. It focuses on all aspects of health care for humans, animals and the environment to better prevent, detect and control human diseases with an aim to strengthen country compliance with the International Health Regulations. This programme can also potentially generate collaborations, surveillance, interventions, research, and improved policies through a One Health approach [19].

Also the European Commission, with the publication of the 'Decision on serious cross-border threats to health' in 2013, has stressed the need of interoperability between public health and veterinary sectors for preparedness and response planning [20].

The development of a business case for One Health has also been proposed to describe the origin and expansion of this concept, with five potential areas where One Health could add value and reduce costs: (1) sharing health resources between the medical and veterinary sectors; (2) controlling zoonoses in animal reservoirs; (3) early detection and response to emerging diseases; (4) prevention of pandemics; and (5) generating insights and adding value to health research and development [21].

But despite all efforts of cooperation between human and animal health, isolated silo thinking persists, particularly in the public health sector that struggles to perceive advantages of using a One Health approach [22].

One Health Surveillance is the latest conceptual tool being proposed to prove the added value of the One

Health concept, as per the business case described above, and to ultimately reduce the risks of infectious diseases at the animal-human-ecosystem interfaces. One Health Surveillance consists of the systematic collection, validation, analysis, interpretation of data and dissemination of information collected on humans, animals and the environment to inform decisions for more effective, evidence- and system-based health interventions [23].

At this stage, sporadic national success stories exist in implementing One Health Surveillance that could serve as examples for further implementation [23,24] and integrated surveillance systems have worked in specific situations and contexts [25]. International initiatives have been launched and supported by the Food and Agriculture Organisation (FAO), the World Health Organisation (WHO) and the World Organisation for Animal Health (OIE*)* and methodologies for the aggregation of existing databases at the human-animal interface have been tested (for example the GLEWS database and the establishment of the "4-way linking" platforms) [26,27].

Notwithstanding, barriers impeding the development of One Health Surveillance still need to be addressed [5]. Legal issues, hurdles to data sharing, unclear responsibilities, structural barriers between Ministries of Health, Agriculture and the Environment/Natural Resources and a lack of communication were all raised as obstacles to progress at the second International Conference on Animal Health Surveillance (ICAHS) in Havana (May 7-9, 2014). Moreover, the difference in priorities between Ministries of Health and Agriculture was found to be even more apparent when joint control strategies are discussed.

Also, the identification of criteria and methods to describe and assess existing levels of integration of surveillance for specific exposures is recommended to facilitate the evaluation of the impact and the added value of One Health Surveillance in the contexts where this integrated approach is being implemented.

In 2009, the EpiSouth Network [28] created a Directory of Human Public Health and Veterinary Public Health Officials for Zoonoses [29] in order to facilitate the surveillance of zoonosis in the Mediterranean basin in the framework of One Health. The network also identified two main recommendations towards integrated preparedness. Firstly, the establishment of formally appointed national multidisciplinary forums on zoonoses and risk assessment composed by epidemiologists, veterinarians, entomologists, laboratory officials from human public health (HPH) and veterinary public health (VPH). Secondly, the creation of a national network for preparedness and response, in line with the International Health Regulations, including the HPH and VPH authorities and all recognized actors of the process [30].

Started on the basis of the Network of countries established by EpiSouth, the European project MediLabSecure (2014-2017) aims to create a framework for collaboration to improve surveillance and monitoring of emerging arbovirosis in the Mediterranean basin and Black Sea regions [31].

This article describes how the MediLabSecure project is contributing to the strengthening of One Health surveillance.

MATERIALS AND METHODS

Under the coordination of Institute Pasteur - IP (Paris, France), an integrative network of four main disciplines: animal virologists (coordinated by INIA-CISA Madrid, Spain), human virologists (coordinated by IP Paris, France), entomologists (coordinated by IRD Montpellier, France) and epidemiologists (coordinated by ISS Rome, Italy) in 19 non-EU countries of the Mediterranean and Black Sea areas has been established to enhance the preparedness and response to emerging arbovirosis and to improve the integration of surveillance (IS) across the involved network.

A number of arboviruses were identified as present threats or with a potential risk of emergence in the Mediterranean and Black Sea regions as reported in Table 1.

Table 1 - Arboviruses representing an actual threat or a potential risk in the Mediterranean and Black Sea regions.

Arboviruses
• Representing a present threat in the region
• West Nile virus
• Crimean-Congo hemorrhagic fever virus
• Representing a potential risk of emergence in the region
• Dengue virus
• Chikungunya virus
• Yellow fever virus
• Rift Valley fever virus

Following a consensus workshop of the project the priority has been narrowed down to mosquito-borne viruses.

The project implements activities aimed at identifying laboratory and human surveillance contact points in all involved countries; assessing and documenting laboratory capacities and level of integration of surveillance activities; identifying training needs; designing and conducting trainings and capacity building. These activities take place within each discipline and in collaboration between them.

The selection of participating laboratories was performed based on the responses of potential participants of each beneficiary country to a questionnaire assessing their activities and capacities. One laboratory per discipline (human virology, animal virology, medical entomology) and per country was consequently identified. The first meeting involving all the Heads of the selected laboratories was held in January 2015 at IP in Paris.
Contact points for human surveillance were selected among experts working in the Ministries of Health/ Institutes of Public Health either already part of the EpiSouth Network or selected *ad hoc* through the contact points of the identified laboratories.
In order to assess and document the level of integration between the animal virology, human virology and medical entomology entities with the central national surveillance system we identified criteria, reported in Table 2, proposed on the basis of existing operational protocol and procedures [32]. On the basis of the three critical levels reported in the Table 2, we designed a survey targeting all the contact points of the project that could explore: 1) the existence of a national policy addressing integrated surveillance; 2) the existence of coordination mechanisms among the institutions involved; 3) the existence of integrated data collection tools and 4) the existence of joint result dissemination mechanisms such as bulletins, reports, papers, media reports and/or websites. We then assessed the level of surveillance integration in the 19 countries of the project splitting them in three regions (Tab. 3).
We performed a frequency analysis for all

Table 2 - Proposed criteria to describe existing levels of integration between human/animal/entomological surveillance for a specific exposure

Level of integration	Sublevels of integration	Criteria
Policy and institutional level	Policy level	1. Existence of a National policy addressing integrated surveillance for this specific exposure 2. Existence of a policy addressing integrated surveillance for this specific exposure at subnational level
	Institutional level	3. Existence of agreements among the institutions involved in human/animal/entomological surveillance for the specific exposure, 4. Existence of a coordination mechanisms among the institutions involved, 5. Existence of identified focal points for each of human/animal/entomological surveillance for the specific exposure
Data collection and analysis level	Interoperability mechanisms at data collection level	6. Existence of integrated data collection tools 7. Existence of activation mechanisms of human surveillance based on signals from animal/entomological surveillance 8. Other interoperability mechanisms at data collection level
	Interoperability mechanisms at data analysis level	9. Presence of DB exchange/merging/other mechanisms to facilitate joint analysis among sectors. 10. Performance of joint/integrated data analysis among the different surveillance sectors 11. Other interoperability mechanisms at data analysis level
Dissemination level	-	12. Existence of joint result dissemination mechanisms (e.g. bulletins, reports, papers, media reports, websites …)

Table 3 - Countries and regions involved

Balkans	Black Sea	North Africa and Middle East
Albania	Armenia	Algeria
Bosnia and Herzegovina	Georgia	Egypt
Kosovo	Moldova	Jordan
Montenegro	Ukraine	Lebanon
Serbia		Libya
The Former Yugoslav Republic of Macedonia		Morocco
Turkey		Palestine

categorical variables, and the proportions of responses were calculated on the basis of the number or respondents for each question.

Results

Fifty-six contact points (CP) from laboratories (animal virology, human virology and medical entomology) and 19 contact points (CP) from Public Health Institutes (PHI)/Ministries of Health (MoH) (human epidemiology) from the 19 countries were invited to participate in the survey between December 2014 and September 2015.

We obtained responses from 51 laboratories (51/56; 91%) and 12 PHI/MoH (12/19; 63%), of whom: 14 were from the Black Sea, 26 from North Africa and the Middle East and 23 from the Balkans.

Human virology laboratories (19/63; 30%) were the most represented, followed by animal virology laboratories (18/63; 29%), medical entomology laboratories (14/63; 22%), and human epidemiology experts (12/63; 19%).

Thirty-four responders (34/63; 54%), of 17 countries, reported the availability of a *National policy addressing integrated surveillance* in their countries. When considering the result by sub-regions we found national policies to be available for 57% (8/14) of the Black Sea respondents, 62% (16/26) of North Africa and Middle East respondents and 43% (10/23) of Balkan responders.

Positive replies were given by 50% (9/18) of all animal virology respondents, 42% (8/19) of human virology respondents, 50% (7/14) of medical entomology respondents and 83% (10/12) of human epidemiology respondents.

Thirty-one respondents (49%), of 16 countries, reported the *existence of coordination mechanisms* among the institutions involved, of whom 57% (8/14) of the Black Sea respondents, 54% (14/26) of North Africa and Middle East respondents and 39% (9/23) of Balkan respondents. Positive replies were given by 56% (10/18) of all animal virology respondents, 47% (9/19) of human virology respondents, 29% (4/14) of medical entomology respondents and 67% (8/12) of human epidemiology respondents.

Integration mechanisms in data collection were reported by 29% (18/63) of all respondents, of 11 countries. This response was positive among 29% (4/14) of all the Black Sea respondents, 27% (7/26) of North Africa and Middle East respondents and 30% (7/23) of Balkan respondents. Positive replies were given by 11% (2/18) of all animal virology respondents, 32% (6/19) of human virology respondents, 21% (3/14) of medical entomology respondents and 58% (7/12) of human epidemiology respondents.

Thirty-four respondents (34/63; 54%), of 16 out of 19 countries, reported the availability of *joint results dissemination mechanisms* in their countries. This response was positive among 43% (6/14) of all the Black Sea respondents, 69% (18/26) of North Africa and Middle East respondents and 43% (10/23) of Balkan respondents. Positive replies were given by 44% (8/18) of all animal virology respondents, 58% (11/19) of human virology respondents, 57% (8/14) of medical entomology respondents and 58% (7/12) of human epidemiology respondents.

In 8 countries (42%), three in the North Africa and Middle East and Balkans and two in the Black Sea, all four contact points (animal virology; human virology; medical entomology; human epidemiology) answered the survey.

The positive replies given by the respondents of each discipline (animal virology; human virology; medical entomology; human epidemiology) in each region regarding the availability of national policy addressing integrated surveillance; existence of coordination mechanisms; integration mechanisms in data collection and joint results dissemination mechanisms, are reported in Figure 1.

A positive response to all the levels of integration explored in the survey was provided in one country by all four disciplines. In two countries, two disciplines replied positively to all the questions while in four countries one discipline indicated the existence of integration for all the levels explored.

Discussion

To our knowledge this is the first study in the Mediterranean and Black Sea regions aimed at assessing the level of integration in the surveillance of arboviruses across four disciplines: animal virology, human virology, medical entomology and human epidemiology.

We found that integration on all the explored levels was confirmed by all four disciplines independently in only one country included in the study and by two disciplines in two countries. This suggests that implementation of fully integrated one health surveillance across the policy and institutional level to the data collection and dissemination level is yet to be fully developed in the Mediterranean and Black Sea regions.

Notwithstanding, some integration mechanisms have reportedly been set up in a number of countries, more frequently directed to the joint dissemination of results. Conversely, fewer countries have reported the existence of mechanisms/procedures for integrated data collection.

This might indicate that each laboratory collects surveillance data separately and that results are

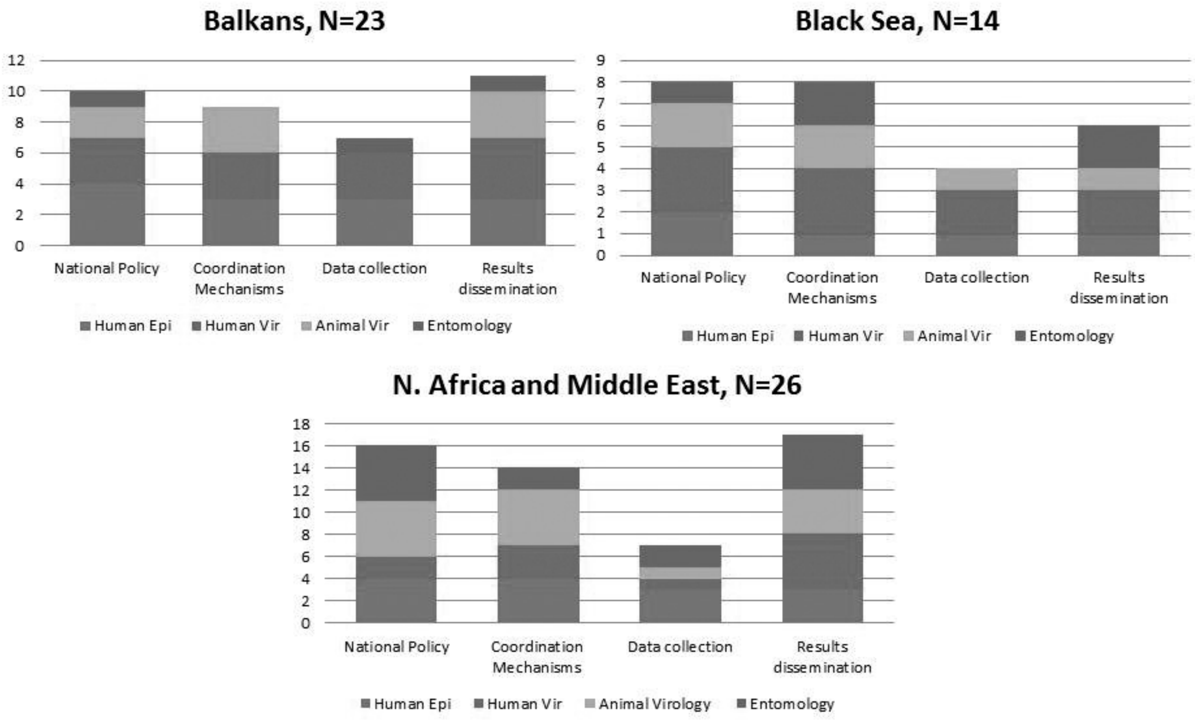

Figure 1 – Existence of policy and mechanisms for integrated surveillance

collated in a second step for coordinated dissemination.

The fact that all the contact points of the four disciplines answered the survey in eight countries might be indicative of a more defined role of each discipline and possibly increased motivation to report surveillance in an integrated way .

However, it has to be noted that the disciplines of the countries involved have not always replied consistently. Where one discipline reported integration in surveillance at one or more levels, in the same country this integration was commonly described differently by the other disciplines.

The questionnaire addressed purposely only some of the proposed criteria for levels of integration with the aim of acquiring a preliminary description of the situation in the 19 countries involved in the MediLabSecure Project without overloading participants with questions and thus enhancing the response rate. Detailed assessment of existing links and procedures will be carried out in selected countries which have disclosed a certain level of integration in this survey.

CONCLUSIONS

One Health surveillance should lead to faster disease detection, more efficient disease control and tangible financial savings when formally compared against separated surveillance streams [23,33].

While there seems to be a broad consensus about the value of One Health in the published studies, there is an evident lack of metrics and associated methods to estimate One Health benefits in a systematic way [34].

The first step to estimate the One Health benefits could be the assessment of the level of integration between relevant sectors/disciplines in the surveillance of specific emerging and re-emerging infectious diseases as described above in the study conducted in the framework of MediLabSecure Project.

Additional studies should describe procedures and mechanisms adopted by those countries with a certain level of integration, and good practices collected and shared to increase awareness.

Finally, the outcomes of integrated surveillance (in terms of disease detection, more efficient disease control and tangible financial savings) for the countries adopting it should be assessed and compared to the outcomes of countries with scarce or absent integrated surveillance mechanisms and procedures.

This should provide data and information to feed in an evidence based "business case" on One Health surveillance which can legitimately guide the development of national and international One Health policy.

ACKNOWLEDGEMENTS

We are very grateful to all the MediLabSecure contact points of all four discipline (animal virology; human virology; medical entomology; human epidemiology) who replied to the survey. Moreover we thank Antonella Lattanzi for her support in the references of this article.
The MediLabSecure Project is supported by the European Commission (DEVCO: IFS/21010/23/_194).

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