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RESPONSE IN FRONT OF OUTBREAKS AND EPIDEMICS CAUSED BY VECTOR BORNE DISEASES, THE ECDC EXPERIENCE

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Abstract Outbreaks of vector borne diseases represent a major challenge for preparedness and response to infectious diseases. The European Centre for Disease Prevention and Control supports the investigation of outbreaks of infectious diseases detected within the European Union/Economic European Area and internationally. We summarize several ECDC contributions to investigate a dengue outbreak in Madeira (Portugal), a yellow fever epidemic in Angola, a plague outbreak in Madagascar and an investigation on community preparedness, following the detection of two cases of Crimea Congo in Spain. In the mentioned examples, ECDC contributed to the investigation of the outbreaks and epidemics, by supporting the activities performed by the national authorities in charge of the investigations. ECDC's contribution to preparedness and response to outbreaks and epidemics of vector borne diseases represents a valuable support to the affected countries and it comes as a result of the cooperation between experts from emergency and vector borne diseases together with those of preparedness and response.

Key words Outbreak, vector borne diseases, preparedness, response

INTRODUCTION

The mission of the European Centre for Disease Prevention and Control (ECDC) is to identify, assess and communicate current and emerging threats to human health caused by infectious diseases. To achieve this goal, the ECDC works closely with the public health agencies of the member states of the European Union (EU) and the European Economic Area (EEA), with networks of professionals and experts in Europe and around the world (1).

Vector-borne diseases constitute one of the main challenges for the preparedness and response plans in ECDC and the Member States of the EU/EEA. In recent years, the ECDC has published a large number of Rapid Risk Assessments (RRA) related to vector-borne diseases (Dengue, Malaria, Chikungunya, Yellow Fever, Crimea Congo...) and has carried out emergency interventions in response to outbreaks of vector borne diseases both in the context of the European Union (Dengue in Madeira, Malaria in Greece, Crimea Congo in Spain) and internationally (Yellow Fever in Angola, Plague in Madagascar).

The European Surveillance System (TESSy) of ECDC, includes a total of 65 entities regularly reported by the 27 countries of the European Union and the three of the European Economic Area (EEA). Of this set of diseases and entities, around 40% are vector-borne, explaining its relevance to human health. Information available in TESSy is complemented by the monitoring sources of information carried out daily by the epidemic intelligence team, identifying unusual phenomena, epidemic outbreaks and health threats caused by vector borne and emerging diseases.

Complementary to surveillance, preparedness and response activities, the ECDC's emerging and vector-borne diseases program develops guides, maps, tools, technical documents, projects, technical meetings and networking initiatives to support Member States and the European Union to face the challenges posed by emerging and vector borne diseases.

We summarize the activities and results of three interventions performed by ECDC experts and one that counted on the participation of one EPIET/EUPHEM fellow.

MATERIALS AND METHODS

Dengue outbreak in Madeira (Portugal), 2012

On 3 October 2012, Portugal reported two cases of autochthonous dengue virus infection in the Autonomous Region of Madeira (Portugal) (2). By 10 October, when the Institute of Health and Social Affairs (Instituto de Administração da

Saúde e Assuntos Sociais, IASAUDE) reported 18 confirmed and 191 probable cases, it had become clear that this constituted a noteworthy outbreak of dengue in Madeira. Confirmatory tests by the National Institute of Health in Lisbon identified dengue virus serotype 1 (DENV-1). An ECDC Rapid Risk Assessment published on 10 October concluded that this was the first documented outbreak of dengue in Madeira. The *Aedes aegypti* mosquito, the most effective vector for dengue virus, was present on Madeira since at least 2005. Although the introduction of the virus to the island was not an unexpected event, given the dramatic expansion of endemic dengue transmission globally over the last 20–30 years, the outbreak constituted a public health event with regards to the local population and the large number of visitors to the archipelago of Madeira.

Following those events, the authorities of the Autonomous Region of Madeira (RAM) in Portugal and the Ministry of Health in Portugal requested ECDC technical support to improve prevention and control measures and the implementation of actions for vector control.

The objective of the mission was to support Madeira in the investigation of the outbreak of dengue fever detected in one of the islands of the archipelago with special emphasis on:

- Support and development of an epidemiological surveillance system to characterize the outbreak, monitor its evolution and try to identify measures of control
- To define standards and outputs for epidemiological analysis of human cases of dengue, compiling the existing information an defining a systematic process of data collection and data analysis
- Support surveillance for mosquitoes, identifying priority actions according to the evolution of the outbreak
- Contributing to define an operational plan for vector control activities in the affected areas with presence of *Aedes aegypty*

The main tasks regarding the organization and definition of the strategy of this mission consisted on:

- Obtaining a global view of the situation of the outbreak,
- Identifying the main needs and areas of cooperation requested by the RAM,
- Identification and contact the different counterparts and stakeholders involved and potentially
    - involved on the control of the outbreak
- Defining an action plan to develop the objectives of the mission
- Distribution of tasks and activities of the technical team displaced at the area by ECDC.

An action plan was designed in cooperation with Portugal (*Direcção*-Geral da *Saúde*) Regional Health Authorities in Madeira and ECDC mission team to deal and set up the investigation and prevention and control measures for the outbreak, with particular focus in four different areas:

- Epidemiologic management of the outbreak, including clinical, lab and geo - reference aspects.
    - The outbreak was appropriately monitored from the clinical side, hospital and primary health care, and public health. Data was compiled and monitored in close cooperation between health care, public health, laboratory and demographics.
    - The ECDC team supported the local surveillance team in Madeira to merge the information of the different available data bases, to get a real dimension of the number of affected cases.
    - Human cases were geo referenced to better identify the source of the outbreak and vector control measures.
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Yellow Fever Angola, 2016

In 2016 an epidemic of yellow fever affected the Republic of Angola (3). The first yellow fever cases, reported in the province of Luanda, had onset of symptoms in December 2015. Since then, all provinces reported cases. Cases were also imported into other countries in the region, raising concern about the international spread of the epidemic. In this context, the European Commission, in close cooperation with ECDC, deployed a team of public health and humanitarian experts in Angola. The mission team reviewed the epidemiological situation of yellow fever in Angola, assessed the implemented control measures (to later advise the Angolan health authorities), evaluated the risk of importation of yellow fever to the EU, assessed the risk for EU citizens, and provided advice to the European Commission. The mission was organised with the Government of Angola and in coordination with the World Health Organization (WHO). The mission was conducted in the framework of the European Union Civil Protection Mechanism (https://ec.europa.eu/echo/index_es) and employed the newly established European Medical Corps.

Since the beginning of the epidemic and as of 25 May 2016, 736 yellow fever cases were laboratory confirmed. Eighty-eight of these confirmed cases were fatal (Case Fatality Ratio (CFR) of 12%). The first suspected case presented with yellow fever symptoms to a private clinic on 5 December 2015 (Figure 1). The patient – from Viana,

Luanda province, a densely populated outskirt municipality of Luanda – was confirmed on 21 January 2016. Since then, cases were reported in all 18 provinces of Angola; confirmed cases were reported in 14 provinces.

As of 15 May 2016, the Angolan Ministry of Health (MoH) notified 2420 suspected yellow fever cases, 298 of which were fatal (CFR of 12%). The epidemic curve showed that the highest number of suspected and confirmed cases was reported in February and March 2016, with a peak of notification at the end of February, when more than 80 confirmed cases per week were reported. Since April, the number of new cases declined in Angola. In the two most affected provinces of Luanda and Huambo, it has decreased to an average of 30 cases per week. However, transmission of yellow fever spread to new areas and increased in Benguela province. Overall, 70% of cases were in males, with a large proportion of men between 15 and 30 years of age.

Crimea Congo Haemorrhagic Fever, Spain 2016

In August–September 2016, the first autochthonous clinical cases of Crimean-Congo Haemorrhagic Fever (CCHF) CCHF in south-western Europe were detected in Spain (4). Following this experience, ECDC in cooperation with Spanish health authorities developed a case study project to identify good practices related to community preparedness for tick-borne diseases.

Specifically, the study aimed at:

- Identifying good practices and patterns of cooperation between affected communities and the official institutions mandated to address tick-borne diseases such as CCHF;
- Identifying inter-sectoral collaboration between health and non-health-related sectors with regard to tickborne diseases, such as CCHF;
- Identifying actions that could be taken by other EU countries.

The case study approach based on three qualitative sources of evidence: documents; interviews with a range of technical experts working at national and autonomous community level; and focus group discussions with community representatives. The latter included people at risk of tick bites (such as hunters, farmers, hikers, veterinarians, and national park workers) and people at risk of nosocomial transmission in healthcare settings. Nine interviews involving a total of 13 individual experts (some interviews included two people) and three focus group discussions involving a total of 15 people were conducted during a visit to Spain by the research team 13–17 November 2017. The data were subjected to thematic analysis in NVivo software and within the framework of a theoretical preparedness cycle that includes the pre-incident, incident, and post-incident phases.

The index case was an adult male who had been hiking on 14 August 2016 in Ávila province, Castilla y León Autonomous Community (AC), which is where he most likely became infected through contact with a tick. He fell ill on 16 August and was admitted to hospital on 18 August in Madrid; he died on 25 August. Since he died without a diagnosis of CCHF, (the disease had not been reported in Spain before and the infected man did not have a travel history to endemic areas), no specific infection control measures were taken, beyond standard procedures, to protect the family members, health workers and laboratory technicians with whom he or his biological samples could have had contact prior to his death.

The second CCHF case was a female health worker who had taken care of the index case while he was in the intensive care unit between 19 and 23 August 2016. She developed symptoms herself on 27 August, recognised that she had the same condition as the index case, and was diagnosed on 31 August, the same day that as the retrospective diagnosis of the index case. She survived and was released from hospital in good health on 19 September 2016.

Plague - Madagascar 2017

An outbreak of plague in Madagascar started in August 2017, and was notified to WHO in September (5). Soon after, WHO classified the event as a Grade 2 emergency, and GOARN issued a request for assistance from international partners. An EPIET-EUPHEM (ECDC field epidemiology path and public health microbiology path) fellow was deployed as an epidemiologist to provide direct assistance to Madagascar health authorities on October 10th. The deployment was part of a GOARN (Global Outbreak Alert and Response Network) mission

The fellow was part of the WHO team integrated in the health Cluster, which involved all partners in contributing to the response: Direction of Health Monitoring and Disease Surveillance, WHO, UNICEF, the Red Cross, and major NGOs, including Médecins du Monde, and Médecins Sans Frontières.

As a specific task, the fellow joined the surveillance platform, and worked with national and international colleagues to identify and break the transmission chains, by developing tools for contact tracing, and training the healthcare and community workers as quickly as possible.

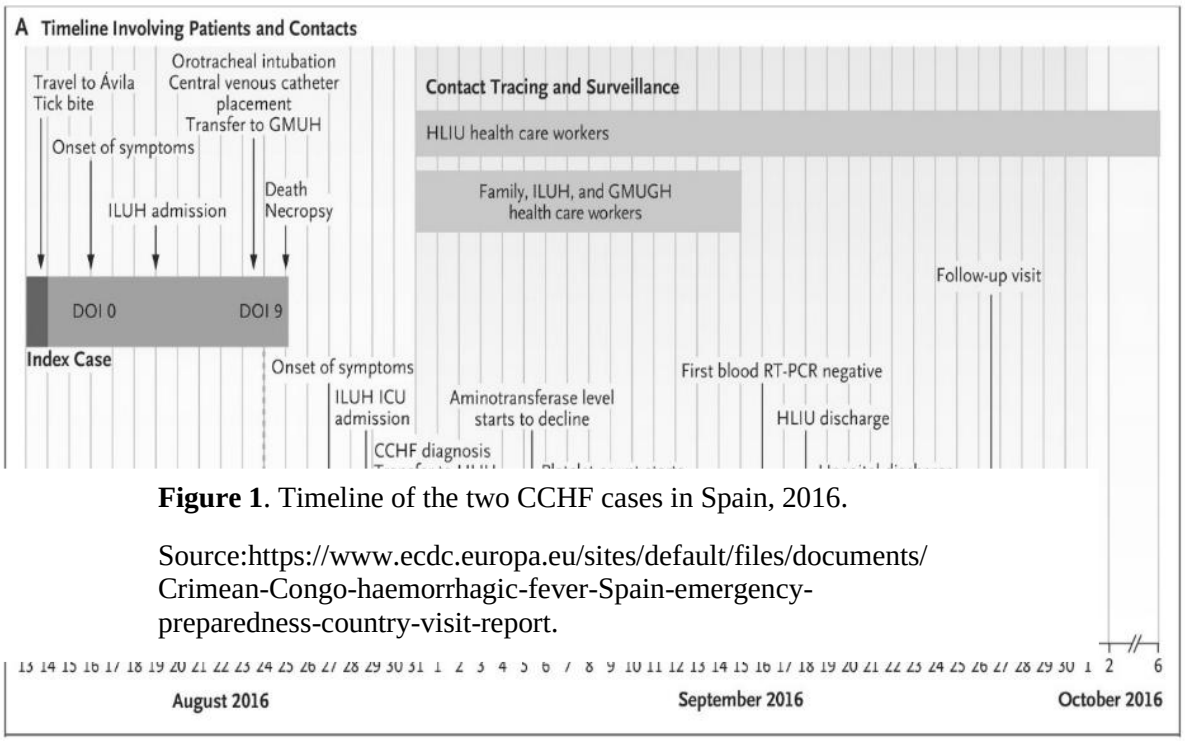

Figure 1. Timeline of the two CCHF cases in Spain, 2016.

Source:https://www.ecdc.europa.eu/sites/default/files/documents/Crimean-Congo-haemorrhagic-fever-Spain-emergency-preparedness-country-visit-report.

Note: Dark blue denotes the day of infection for each patient; DOI denotes day of illness; GMUGH denotes Gregorio Marañón University General Hospital; HLIU denotes high-level isolation unit; ICU denotes intensive care unit; ILUH denotes Infanta Leonor University Hospital.

One of the first tasks was to work with the healthcare representatives from Antananarivo health districts and from the other cities affected by the outbreak, to organize training sessions for the next 2 days. The team spent the evenings rapidly developing and adapting tools for contact tracing and case investigation, and preparing the communication medium, while the training sessions continued on during the day. At that point in an outbreak response, the urgency and necessity outweigh the exhaustion! The team also had to prepare communications on prevention, and transmission risks. Plague is still a terrifying disease, and the population, including healthcare professionals, were scared.

Soon after her arrival, the fellow was requested to support the laboratory response to evaluate the capacity for plague diagnosis in the context of the outbreak, to identify how WHO could support improvements, and to implement our recommendations once validated by the incident leader and response manager. Human resources, equipment, reagents, logistics, needs for training, sensitivity and specificity of the diagnostic methods, SOPs, national regulations… The team had to consider each step in the process, from the sampling of a suspected case to getting laboratory results back to the clinicians in the designated plague health centers.

Working in lab support feels like the central hub of the public health network: an efficient laboratory can rapidly confirm or discount a clinical suspicion of plague. Rapid laboratory diagnosis with good performance is essential, particularly because the clinical picture for pneumonic plague is not specific at early stages of the disease. Laboratory confirmation is essential for the field epidemiologists to monitor the evolution of the outbreak, but also for the clinicians who take care of suspected cases.

The mission was not limited to the short-term response to the emergency, but also aimed at developing longer term solutions that will be helpful to tackle the next outbreak. knowing that plague is endemic in Madagascar, one of the objectives of this mission was preparing for the future, providing the country with the resources to face it.

RESULTS AND DISCUSSION

Dengue Outbreak In Madeira

- Entomological situation and vector control activities. At the time of the intervention, there was an absence of a global strategy for vector control activities leaded by the public sector. There is absence of specific equipment (vehicles, sprayers…) dedicated to vector control owned by the public sector and no expertise too. The larvae source reduction in areas affected by dengue outbreak (breeding sites reduction during door-to-door visit) was ongoing but no adulticide has been employed around/within the households within an affected area. Three private companies worked in place for disinfection, insect elimination and mice control
- Planning technical, logistic and normative aspects. Case definitions were updated and a common source of information for cases was set up. ECDC was working under a general plan overview for the control, of the outbreak
- Cross-sector approach with other stakeholders in Madeira. The Regional Secretary of Social Affairs, in charge of the health system requested applied the commitment of the different Departments and Public organizations to actively commit in the vector control measures. A contingency plan was developed with the contributions of tourism, transports, environment education and health and social affairs.

In March 2013, ECDC conducted a second mission to Madeira to retrospectively assess outbreak epidemiology as well as the public health measures and activities implemented between September 2012 and February 2013 and to discuss with the local health authorities response and preparedness planning with regard to future scenarios. Upon request from the Portuguese Directorate-General of Health, the team conducted a SWOT analysis (strengths, weaknesses, opportunities, and threats) of main activities related to dengue prevention and control in Madeira.

Yellow Fever In Angola

The ECDC team identified the following actions that could contribute to strengthening the efficiency of control measures in Angola:

- The provision of standardised protocols for the clinical management of suspected yellow fever cases at the provincial and national levels and the development of standardised algorithms for case ascertainment at the emergency department level.
- The consistent application of case definitions at all levels, combined with improved reporting of suspected cases, particularly in areas such as Cabinda province, from where several cases were exported. All cases meeting the case definition, including those reporting a history of vaccination and those testing positive for malaria infection, should be reported, regardless of severity.
- Laboratory capacities for differential diagnosis of flavivirus IgM-positive samples should be strengthened.
- Accelerating vaccination campaigns in areas at increased risk for the spread of the disease:
- Densely populated urban areas
- Municipalities with a highly mobile population such as Lubango (Huíla)
- Areas along international borders with presence of Aedes mosquitoes and suitable for vector transmission – even during the dry season – such as Cabinda province
- Municipalities surrounding areas of local transmission should be prioritised in order to create a vaccinated buffer zone and prevent the further spread of yellow fever.
- Implementation of mop-up campaigns in local transmission areas with low vaccination coverage and new cases. This can prevent transmission in areas that had already been targeted by vaccination campaigns, e.g. in Luanda province. Understanding the reasons for not getting vaccinated can help public health authorities to implement interventions to increase vaccine acceptance. Additional vaccine supplies should be made available by the international community to allow vaccination campaigns in additional municipalities where local transmission is not yet confirmed. The international community and local authorities should also ensure that a sufficient stock of yellow fever vaccine for routine childhood vaccinations remains available.
- Vector control activities in areas with local transmission should be performed as soon as a suspected case were detected.

At the end of the mission, the team concluded that the difficulties in controlling the outbreak were partly due to the delayed vaccination and vector control measures, which were only implemented after case detection and confirmation

of local transmission. The spread of the disease could only be halted through proactive vaccination in urban areas characterised by high population density and intensive human movement, and in areas where the vector is present. The lack of background information on Aedes infestation levels and the most productive breeding sites in Angola complicated the planning for vaccination campaigns and efficient proactive vector control. The restricted availability of yellow fever vaccine hampered the possibility of preventing the spread of transmission by vaccinating individuals who live in areas with spots of local transmission.

Crimea Congo in Spain

This study details a set of 13 good practices for promoting collaboration and synergies between the authorities and the community, as well as four other key lessons learned. In the list below, we have identified the good practices specific to tick-borne diseases (T), other zoonoses (Z), and/or to public health threats more generally (PH). Each of these points was suggested to us by one or more of the informants participating.

- Promoting inter-sectoral collaboration and synergies between the authorities
- Implement a multi-sectoral tick surveillance programme, with activities integrated between the Ministry of Health and the Ministry of Agriculture (T, Z).
- Conduct multi-sectoral simulation exercises, including key stakeholders at national, Autonomous Community and local levels (PH).

Promoting collaboration and synergies within the health sector

- Develop a protocol, in advance of any public health incident, to establish a crisis committee and identify a spokesperson to represent the authorities (PH).
- Ensure efficient and smooth information exchange within and between key health sector institutions, including public health agencies at both national and Autonomous Community levels, healthcare facilities, and laboratories (PH).

Promoting collaboration and synergies between the authorities and the community

- Adopt different approaches as appropriate when following up different categories of potentially exposed contacts in the community (PH).
- Use pre-existing connections with the community and local organisations to effectively disseminate information to people who may be at risk of tick-borne or other zoonotic diseases (T, Z).
- Provide feedback to community members who contribute to surveillance and other preparedness activities by, for example, collecting and sending in ticks (T, Z).
- Ensure that systematic efforts are made to monitor community perceptions of any public health incident (PH).
- Recognise the rural-urban divide in perceptions regarding tick-borne diseases when designing communication strategies and targeting messages (T, Z, PH). Ensure that risk communication messages reach people who could be considered vulnerable to infection, but who may not easily receive or access information about prevention. This could include people who do not speak Spanish and who may therefore need translated materials (PH).
- Use occupational health specialists as a valuable resource for dissemination of information on prevention for specific, at-risk professions, and as a key support for contact tracing and follow-up activities (PH).
- Build trusting relationships with journalists prior to the crisis (PH).
- View the community – including interest group associations that serve people who may be at risk of zoonotic infections – as a resource for optimising preparedness planning and response actions (Z, PH).

Other important lessons learned

- Introduce evaluation activities into standard operating procedures, and establish the practice of sharing experiences and lessons learned between stakeholders in different sectors at various levels (PH).
- Verify that haemorrhagic fever protocols have been updated after the 2014–15 Ebola crisis (PH).
- Establish tracking systems for biological samples in reference laboratories (PH).
- Train triage and primary care nurses to be on the lookout for unexpected and potentially dangerous infectious diseases, for the purposes of rapid diagnosis and initiation of appropriate public health measures (PH).

This study demonstrated the potentially substantial value gained by building collaboration between health and non-health authorities and the community in the prevention and control of zoonotic and other communicable disease threats in Spain. Goodwill and a willingness to work together was apparent from all the stakeholders interviewed, but any successful long-term collaboration will require significant ongoing efforts, planning, and resources.

Consideration could be given to directing future operational research to focus on how best to implement and sustain the good practices identified above, and to develop additional means of bringing about effective community-authority collaborations in preparedness and response to zoonotic diseases. Such work would complement global efforts to implement international conventions such as the 2015 Sendai Framework for Disaster Risk Reduction and the 2005 Bangkok Charter for Health Promotion in a Globalized World, while also building on the principles outlined in the 2005 International Health Regulations as well as EU Decision 1082.

Plague in Madagascar

As part of WHO response team supporting the government, the fellow had the unique opportunity to witness a public health emergency brought under control. She arrived during the peak of the outbreak and left after 5 weeks with a situation much improved. By working with epidemiologists, clinicians, community workers, communications, operations and logistics specialists, IPC specialists, and lab technicians, the field epidemiologist had to consider issues related to clinical management, difficulties in implementing infection control and prevention measures, and how to tackle rumours effectively, so that they don't undermine confidence in the response.

From that experience, the fellow had a good overview on crisis management, emergency response, and coordination with national authorities, political bodies and with representatives from international NGOs, in a setting where resources were limited and team members had to use all their skills and knowledge.

CONCLUSIONS

ECDC's contribution to preparedness and response to outbreaks and epidemics of vector borne diseases represents a valuable support to the affected countries and it comes as a result of the cooperation between experts from emergency and vector borne diseases together with those of preparedness and response. The four examples included in this paper, represent the interventions performed by ECDC teams in close cooperation with the local authorities and WHO and other agencies in case of international outbreaks.

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