

First secondary case of Ebola outside Africa: epidemiological characteristics and contact monitoring, Spain, September to November 2014

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On 6 October 2014, a case of Ebola virus disease (EVD) acquired outside Africa was detected in Madrid in a healthcare worker who had attended to a repatriated Spanish missionary and used proper personal protective equipment. The patient presented with fever $<38.6^{\circ}\text{C}$ without other EVD-compatible symptoms in the days before diagnosis. No case of EVD was identified in the 232 contacts investigated. The experience has led to the modification of national protocols.

Introduction

The current Ebola virus disease (EVD) epidemic affecting countries in West Africa is the largest ever registered outbreak of this disease [1]. Ongoing intensive transmission in the community and in healthcare facilities associated with weak health systems including limited human and material resources hinder adequate outbreak control and case management. Healthcare workers (HCW) in these areas have been significantly affected during this epidemic [2-5].

On 7 August 2014, the Spanish government decided to repatriate a Spanish missionary healthcare worker at the St. Joseph's hospital in Monrovia (Liberia) who had tested positive for Ebola virus. On arrival, the person was admitted to the infectious diseases isolation unit at the reference hospital (La Paz-Carlos III Hospital Complex in Madrid). The patient remained hospitalised until his death on 12 August. On 22 September, a second Spanish missionary healthcare worker who had worked at a hospital in Lunsar (Sierra Leone) and who was also suffering from Ebola virus infection was repatriated under the same procedure. This patient was admitted to the same reference hospital where he died on 25 September. One of the HCW who was caring

for the second repatriated Ebola case was diagnosed with EVD on 6 October. This was the first secondary case of this disease outside Africa.

In this paper we describe the epidemiological characteristics and public health control measures adopted after the identification of this first transmission outside the epidemic area. The information and lessons learnt in Spain may contribute to improving preparedness and response guidelines and protocols in non-affected countries. The risk of transmission of Ebola virus to healthcare professionals associated with repatriated patients needs to be reassessed and considered for future surveillance and control measures in these settings [5-7].

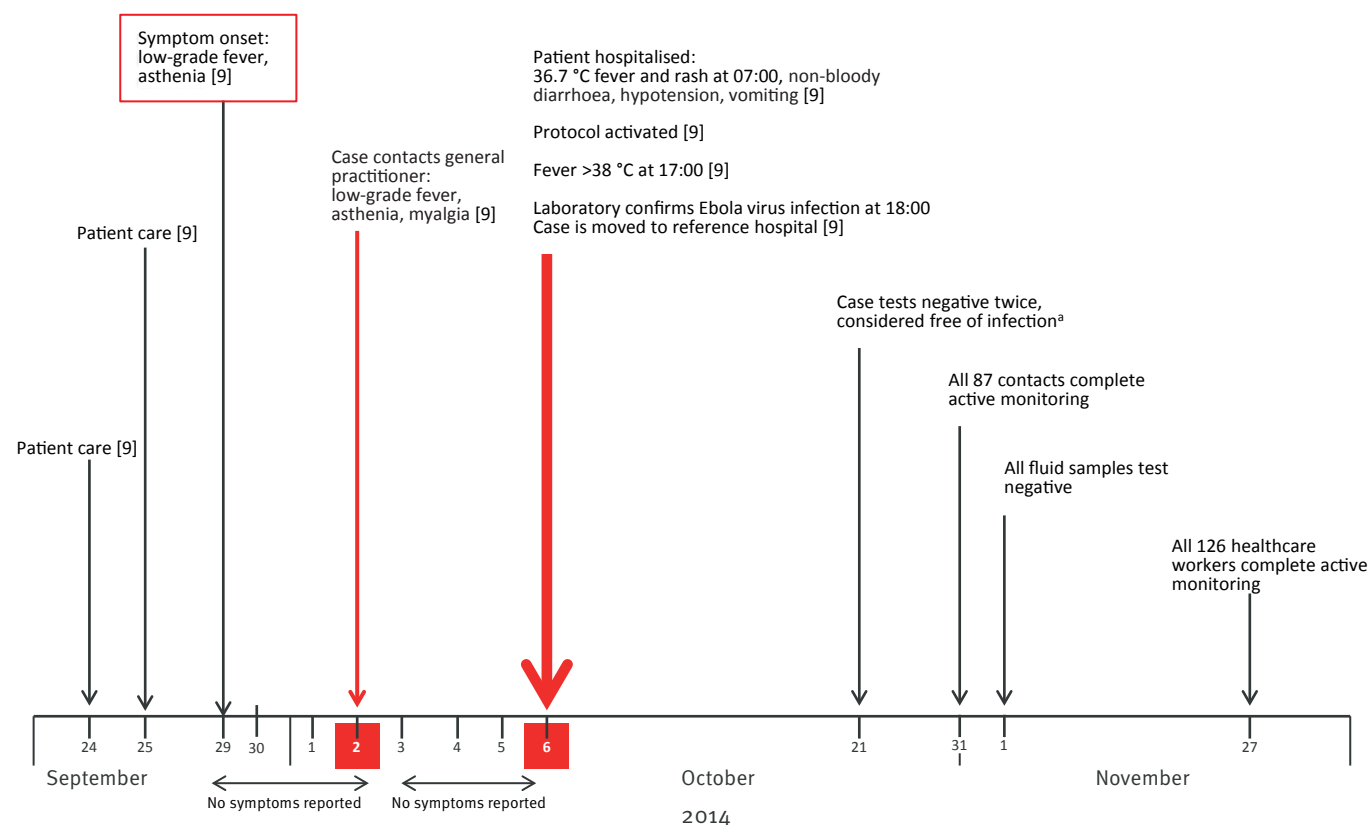
Epidemiological investigation and contact monitoring

Case description

The secondary case of EVD diagnosed in Spain on 6 October was one of the 117 HCW who had participated in the care of the two repatriated EVD cases. The HCW completed the 21-day monitoring period after caring for the first case on 30 August. On 21 and 25 September, she was exposed to the second patient and presumably contaminated fomites. She was classified as a low-risk contact and was therefore self-monitoring for symptoms, in accordance with the protocol [8]. The HCW had used appropriate personal protective equipment (PPE), i.e. waterproof long-sleeved clothing covering the feet, waterproof footwear, hood, face mask or goggles, double layer of gloves, and FP3 respirator [8], and she did not recall any incident during its use.

FIGURE 1

Timeline of events for secondary Ebola case, Madrid, 24 September–27 November 2014



^a Culture results for all body fluids taken on 21 October were negative

Following the established procedures for HCW caring for EVD patients [8], the hospital recommended self-monitoring for 21 days from 25 September onwards. According to these procedures, the HCW was supposed to inform the monitoring official at the hospital in case of fever >38.6 °C and any of the symptoms of the disease: severe headache, vomiting, diarrhoea, abdominal pain or bleeding. On the following day, 26 September, she was off duty. She contacted the monitoring official for the first time on 2 October.

Symptoms started on 29 September. She presented malaise and low-grade fever <38 °C. The grade fever remained at this level for three days and increased to 38 °C in the three following days [9]. Figure 1 shows the evolution and timeline of events.

On 6 October at 04:00, she called the public health officials to report a temperature of 37.3°C, general malaise, nausea and cough. These symptoms led the public health officer to request medical evaluation at home and to refer her to the closest hospital. On admission at 07:00, she had a temperature of 36.7 °C, blood pressure of 90/60 mm Hg, 95% oxygen saturation measured by means of pulse oximetry, and a maculopapular rash. She reported that she had not

received antipyretic agents [9]. At 08:00 on 6 October, the hospital contacted the public health services and they decided to classify the case as under investigation for EVD and send blood samples to the national reference laboratory. The patient's condition worsened in the following hours [9] and at 18:00, the reference laboratory confirmed the diagnosis of EVD. The patient was transferred to the reference hospital under strict isolation measures. The patient received antiviral treatment and convalescent serum from a recovered Ebola patient. On 21 October, the case tested EVD-negative in two samples taken 48 hours apart and, according to protocols, was considered free of Ebola virus infection on 1 November when a PCR test of all body fluid samples yielded negative results. The isolation measures were suspended on the same day, and the patient was finally discharged on 5 November 2014.

Contact monitoring

The epidemiological investigation began at the time of diagnosis. Information on the patient's possible exposure was requested and contact identification, risk classification and monitoring began at the same time. A committee of experts was established for the classification of contacts. High- and low-risk classification criteria and the action taken for each group are

TABLE 1

Classification of contacts and public health measures adopted for the secondary Ebola case, Madrid, 6 October–27 November 2014

CLASSIFICATION OF CONTACTS	PUBLIC HEALTH MEASURES FOR CONTACTS
Low-risk contact	
A person who, with appropriate PPE and without incidences in the use of PPE, had direct contact with a confirmed case, with his/her body fluids or any material that has potentially been contaminated in the course of healthcare;	Active monitoring: professionals responsible for monitoring contacts have daily contact with the monitored individual, measure his/her axillary temperature twice a day and record the presence of any symptom;
A person who has stayed in a closed physical space in which there could have been fomites with biological remains from the case and who does not comply with high-risk contact criteria (e.g. seats in the waiting room, the same surgery, the same ambulance, etc)	The identity of contacts for monitoring is sent to health centres and hospitals (alerts in electronic clinical records) for early detection in case they consult for Ebola-related symptoms. The Blood Donors Centres of the Madrid Region also receive electronic alerts in the clinical records to avoid any incident related to possible blood donations by these individuals.
High-risk contact	
Close contact (distance <1 m), without appropriate PPE or with incidences in the use of PPE, with a confirmed case who was coughing, vomiting, bleeding or had diarrhoea;	Quarantine is indicated. In order to facilitate the compliance with the quarantine, hospital quarantine is offered to these contacts. All contacts included in this group (15 people) agreed to be admitted voluntarily.
Unprotected sexual relation with a confirmed case three months after the onset of symptoms;	
Direct contact with clothing, bedclothes or fomites contaminated with the blood, urine or body fluids of a confirmed case, without appropriate PPE or with incidences in the use of PPE;	
Percutaneous wound (e.g. needle-stick injury) or mucosal exposure to body fluids, tissues or laboratory samples of a confirmed case;	
Healthcare given to a case or handling of his/her samples, without the appropriate PPE or with incidences in the use of PPE.	

TABLE 2

Number of contacts of the secondary Ebola case by exposure place, relationship with case and risk category (high risk contacts in brackets), Madrid, Spain, 29 September–27 November 2014 (n=232)

Relation with case/ place of exposure	Cleaner	Patient/ patient's aid	Spouse	HCW	Dog sacrifice	Ambulance technicians	Other	Total
Transport by ambulance ^a	4	12	0	3	0	10	0	29
Primary care	2 (1)	22	0	4 (1)	0	0	0	28 (2)
Home	8 ^b	0	1 (1)	1 (1)	6	0	1	17 (2)
Hospital	2	0	0	7 (7)	0	0	3 (1)	12 (8)
Other activities	0	0	0	2	0	0	7 (3)	9 (3)
Subtotal	16 (1)	34	1 (1)	17 (9)	6	10	11 (4)	95 (15)
HCW at reference hospital	11	0	0	113	0	0	2	126
Reference laboratory	0	0	0	0	0	0	11	11
Total contacts	27 (1)	34	1 (1)	130 (9)	6	10	24 (4)	232 (15)

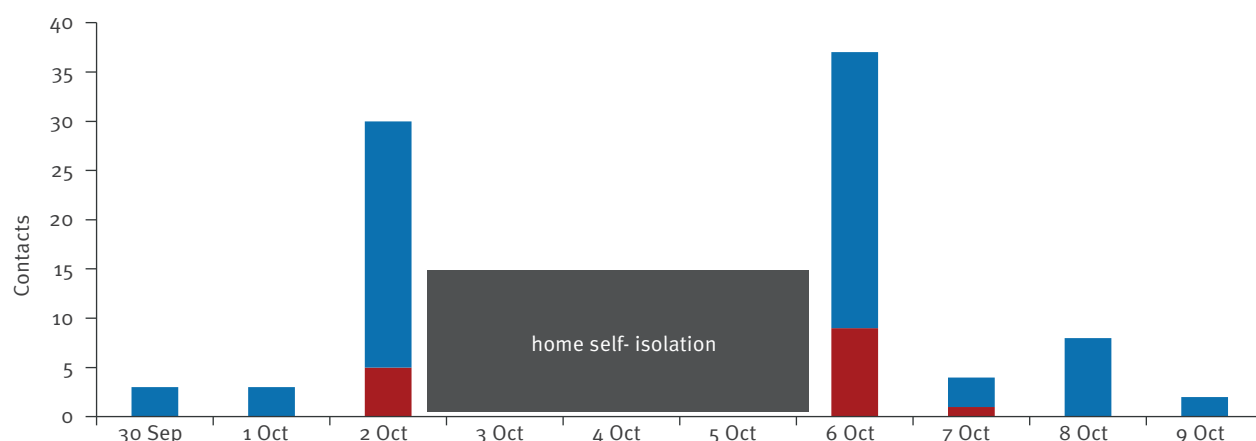
HCW: healthcare worker who attended to the secondary case.

^a Two ambulances: from home to first hospital and from first hospital to reference hospital.

^b The home cleaning was performed on the day after the patient was discharged from hospital.

FIGURE 2

Number of contacts of the secondary Ebola case, by exposure date and risk category^a, Madrid, Spain, 29 September–9 October 2014 (n=87)



	30 Sep	1 Oct	2 Oct	3 Oct	4 Oct	5 Oct	6 Oct	7 Oct	8 Oct	9 Oct
Low risk	3	3	25	0	0	0	28	3	8	2
High risk	0	0	5	0	0	0	9	1	0	0

^a Excluded healthcare workers at the reference hospital, laboratory workers and home cleaners.

presented in Table 1. These actions were adapted from those established in the current protocol [8]. The first epidemiological information was provided by a family member of the patient at the hospital and was completed with available health and administrative records and the locations the patient reported to have visited from onset of symptoms until hospitalisation.

A total of 232 contacts were identified, of whom 15 were classified as high-risk and 217 as low-risk (Table 2). Most contacts, excluding HCW at reference hospital, occurred on the day of diagnosis at the hospital where the diagnosis was established (Figure 2). The 15 contacts classified as high-risk were informed of the risks associated with their contact with the case and were recommended a quarantine, at a hospital facility if possible. All of them voluntarily agreed to undergo hospital quarantine for 21 days after the last exposure day.

One of the low-risk contacts presented fever during the monitoring, but EVD was ruled out.

A total of 126 hospital employees were in contact with the patient during her stay at the hospital. Follow-up ended on 27 November, 21 days after the final exposure of the hospital cleaning staff. By that time, none of the contacts monitored had presented EVD.

Discussion

Action protocols are based on the evidence obtained in the outbreak in Africa [9–11]. Early detection of cases for minimising the probability of transmission is the key aim of contact monitoring. However, when the first

secondary case was diagnosed in Spain, the case definition provided in the existing national protocol and in most international protocols (European Centre for Disease Prevention and Control [12], United States (US) Centers for Disease Control and Prevention [13,14]) required a fever of ≥ 38.6 °C and symptoms compatible with the disease. This definition was not sensitive enough to detect this case in the first stages of disease. The non-specific clinical presentation of Ebola also makes early case detection difficult. This situation was also observed in the two secondary cases diagnosed a few days later in the US [15–17].

We would like to draw attention to the ‘paucisymptomatic’ presentation of EVD in infected contacts closely monitored after exposure to confirmed cases outside of the epidemic area in Africa not described up to now.

The public health measures applied immediately to the contacts of the secondary case in Madrid included active monitoring of low-risk contacts and quarantine for high-risk contacts. All contacts accepted these measures. However, in the future it may be necessary to apply the quarantine to more people or to contacts who refuse to be quarantined. In our opinion, it is necessary to develop procedures and laws which would establish and help apply the quarantine.

The experience with the repatriated cases in several non-epidemic countries and the secondary transmissions identified in Spain and in the US have resulted in proposals to modify existing protocols. These proposals [18] include increased sensitivity of the case

definitions for persons under investigation in order to detect possible cases in the initial phases of the disease, particularly for contacts of confirmed cases, and a revision of contact classification and monitoring measures.

The Spanish experience highlights that the generation of secondary cases among HCW caring for repatriated EVD patients represents the currently main risk for Europe as has happened also in US [8,13-15]. The risk is very low, however it can not be excluded [19].

Despite the existence of preparedness and response plans, trained professional teams, 24/7 alert systems and contingency plans for control and response of communicable diseases in both hospitals, the number of exposed contacts among HCW was high. After the secondary case was diagnosed, training and assessment was reinforced for all healthcare professionals involved in the treatment and care of EVD and a committee was set up to classify incidents. This alert shows the need for constant updating and training of professionals in the use of PPE and strict application of donning and doffing procedures in order to minimise the risks. Hence it is necessary to provide adequate risk communication and create awareness in HCW who care for these patients.

Despite the rapid activation of the protocols and control measures, this first case of secondary transmission of EVD outside Africa has represented an unprecedented challenge for the health services and public health authorities in Spain [9,12-14] and has highlighted the need to strengthen continuous preparation and training in order to respond properly to this type of emergency.

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Conflict of interest

None declared.

Authors' contributions

Jenaro Astray and M^a Ángeles López wrote the first draft of the manuscript. M^a Ángeles López managed the Ebola outbreak alert system, Jenaro Astray coordinated the Ebola response team of the Community of Madrid and acted as a liaison to the reference hospital, Maria Ordobás was responsible for contact monitoring, Felicitas Dominguez managed the alert information system, Carmen Álvarez and Manuel Martínez led the Ebola Crisis Committee. Carmen Amela, M^a José Sierra and Fernando Simón coordinated the Ebola response at the national level, and Carmen Amela also participated in the regional Ebola response team. Josep Jansa and Diamantis Plachouras participated in the contact classification and assessment. The working group participated in the fieldwork, conducting epidemiological survey, classifying

cases and contact monitoring. All authors critically read and revised the drafts of the manuscripts.

Members of the working group of the Ebola outbreak investigation team of Madrid

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