



Ebola Outbreak Response; Experience and Development of Screening Tools for Viral Haemorrhagic Fever (VHF) in a HIV Center of Excellence Near to VHF Epicentres

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Abstract

Introduction: There have been 3 outbreaks of viral hemorrhagic fever (VHF) in Uganda in the last 2 years. VHF often starts with non-specific symptoms prior to the onset of haemorrhagic signs. HIV clinics in VHF outbreak countries such as Uganda see large numbers of patients with HIV 1/2 infection presenting with non-specific symptoms every day. Whilst there are good screening tools for general health care facilities expecting VHF suspects, we were unable to find tools for use in HIV or other non-acute clinics.

Methods: We designed tools to help with communication to staff, infection control and screening of HIV patients with non-specific symptoms in a large HIV clinic during the outbreaks in Uganda. We describe our experiences in using these tools in 2 Ebola Virus Disease outbreaks in Uganda.

Results: During the Ebola Virus Disease (EVD) outbreaks, enhanced infection control and communication procedures were implemented within 24 hours of the WHO/Ministry of Health announcement of the outbreaks. During course of these outbreaks the clinic saw 12,544 patients with HIV 1/2 infection, of whom 3,713 attended without an appointment, suggesting new symptoms. Of these 4 were considered at risk of EVD and seen with full infection procedures; 3 were sent home after further investigation. One patient was referred to the National Referral Hospital VHF unit, but discharged on the same day. One additional VHF suspect was identified outside of a VHF outbreak; he was transferred to the National Referral Hospital and placed in isolation within 2 hours of arriving at the HIV clinic.

Discussion: Use of simple screening tools can be helpful in managing large numbers of symptomatic patients attending for routine and non-routine medical care (including HIV care) within a country experiencing a VHF outbreak, and can raise medical staff awareness of VHF outside of the epidemics.

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Data Availability: The authors confirm that, for approved reasons, some access restrictions apply to the data underlying the findings. This paper is an observational study which took place in our HIV clinic. The outcomes are a case series of Ebola Virus Disease suspect patients. Relevant data on the cases are presented in Table 1. This data was extracted from a hard copy of the clinic attendance register and directly from the hard copies of patients clinical files. It is not ethically or legally possible to upload copies of the patients clinical files, or clinical details of other patients attending the clinic. If any reader requires further data about the patients, we would consider a request sent to myself as corresponding author; Rosalind Parkes-Ratanshi at rratanshi@idi.co.ug. Any reasonable request that is relevant to this paper and will not breach patient confidentiality will be considered.

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Introduction

Viral hemorrhagic fevers (VHFs) refer to a group of illnesses that are caused by viruses of diverse families, including Lassa fever, Rift Valley Fever, marburg viruses, and ebola viruses [1,2]. VHF's characteristically lead to overall vascular system damage and often accompanied by hemorrhage (bleeding). VHF have high case fatality rate (between 25–100% [3]) and spread easily (in an outbreak in Zaire up to 25% of cases were health care workers [4]). Providing care to VHF suspects without adequate infection control processes can cause extreme anxiety [5]. Exposure to VHF

patients often results in health care workers being quarantined, which can be frightening and unpleasant [6]. VHF outbreaks provoke widespread national and international interest, often with dramatic media reporting [7]. Therefore, health care workers in VHF areas are usually very aware of health professional fatalities in previous outbreaks, through both media reports and peer to peer communication [8,9]. Therefore providing medical care in any setting near to a VHF outbreak is stressful for health care workers [10–12]. Consequently, managing this anxiety and stress in health care workers, whilst continuing to provide a compre-

hensive service is essential in maintaining an effective health care service during a VHF outbreak.

The initial symptoms and signs of VHF are often non-specific, including fever, rash and vomiting, prior to emergence of a more haemorrhagic pattern [13–16]. In Sub-Saharan African countries, where there is a high burden of infectious disease, non-specific symptoms are commonly seen in many patients without VHF attending health care facilities, especially in those presenting with malaria [17,18] and complications of HIV [19]. This means that during a VHF outbreak there are many people attending health care facilities near to the epicenter who may have similar symptoms to those with VHF, but who are not exposed or infected. In Uganda there are about 438,000 people who regularly access care and treatment for HIV1/2 infection, and many of them attend clinic every month [20]. Therefore, up to 20,000 patients attend for HIV 1/2 related care every day across the country. Missed appointments and especially HIV drug treatment interruptions may adversely affect the health of HIV infected patients. Health centres distant from a VHF epicenter in Angola saw reduced attendance of patients for other causes during the VHF outbreak [21], suggesting that patients also suffer from anxiety during VHF outbreaks and have been found to exhibit altered health seeking behaviours. Ensuring that patients attend for their HIV appointments is vital for good HIV care and treatment, and therefore reassurance to patients during a VHF outbreak is another priority for maintaining good clinical services.

In 2012 Uganda experienced 3 separate outbreaks of viral haemorrhagic fever; two Ebola Virus Disease (EVD) outbreaks [22] and one Marburg Virus Disease (MVD) outbreak. The Adult Infectious Disease clinic (AIDC) at the Infectious Diseases Institute (IDI) in Kampala sees up to 500 patients with HIV 1/2 infection per day. During the recent VHF outbreaks in Uganda it was essential to protect and reassure both the health care workers and patients as much as possible, whilst maintaining routine clinical services for all patients. However, whilst good tools were available for VHF treatment centres [1,23], we were unable to find any readily available tools or literature that would assist us to deal with a large and often symptomatic HIV clinic population during a VHF outbreak. Therefore, the IDI team developed 3 tools; an action plan for staff and management, a screening tool for symptomatic patients, and a laboratory information leaflet to assist guide and assist health care workers to continue routine clinic activities as safely as possible. In this article we present these tools and our experience with using them.

Methods

The Adult Infectious Disease Clinic (AIDC) at the Infectious Diseases Institute is located within the Mulago National Referral Hospital Complex, Kampala. Between July –September 2012 there were 9925 patients infected with HIV 1/2 registered at the clinic and there were an average of 465 patients seen per day. Patients are seen on appointment (scheduled) or if they are unwell (unscheduled). Between 29th July and 4th October 2012 in Kibale District Western Uganda and 17th November and 30th November 2012 in Luweero District, Central Uganda, there were 2 outbreaks of EVD virus. Between 22nd October and 23rd November 2012 there was a MVD outbreak in South West Uganda. The AIDC clinic is located approximately 206 km, 64 km and 404 km miles respectively from these 3 VHF outbreaks (figure 1). 41% of the AIDC patients live outside of Kampala, and many travel from across the country for their HIV care in the AIDC clinic. During each VHF outbreak both suspected and confirmed VHF patients travelled to Kampala and sought care at the National Referral

Hospital and from other health care providers. Therefore, there was a credible risk of VHF suspects attending for care at the AIDC.

As details of the first outbreak emerged, the clinic management team looked for tools which we could use for information and patient screening in our clinic. The CDC/WHO Infection Control document for VHF in African settings was used as a reference, but this was not specific for an HIV out-patient setting [23]. Therefore we produced and distributed our own tools on 30th July 2012. The first tool (figure 2) was an action plan developed to establish the process of our response to the epidemic, and was circulated to all staff and IDI senior management, along with the CDC Ebola leaflet for background information [24]. As per the action plan, we met to discuss with situation with all staff, and to give them concise and scientific information on the virus.

During each outbreak we identified an infection control nurse to be stationed at the clinic entrance. Her role was to perform triage of patients and to encourage standard infection control procedures such as hand-washing. She was responsible for ensuring that there were adequate hand washing facilities and supplies. All staff and patients were requested to wash their hands before and after entering the clinic. At entrances where soap and water were not available, alcohol gel was used. All staff were reminded to wash hands or use alcohol gel in between patients. The infection control nurse also gave twice daily health talks to patients in the waiting area, and answered questions related to VHF. This nurse also performed a basic triage of unwell patients with respect to haemorrhagic symptoms, and discussed all potential cases with a senior staff member before they were allowed to enter the main clinical unit. Any VHF suspects were directly referred to the National Referral Hospital Ebola unit and not admitted to the AIDC clinic. These activities were continued until Ministry of Health announcements stating the end of the outbreak.

Symptomatic patients are seen and managed in a designated ‘urgent care’ area of the clinic. This is an isolated area, where patients can be seen and can wait apart from other patients. During the VHF outbreaks the staff working in this area were provided with additional protective clothing. All clinic doctors were provided with screening tool (figure 3) for use for all patients who had attended for an unscheduled visit, and any patients with scheduled appointments who reported symptoms suggestive of VHF not identified by the infection control nurse. The tool was reproduced and made available in all clinical rooms. The tool was mainly based on symptoms, and included a points system, where 2 or more symptoms or any sign, or one symptom in a patient having been to an outbreak area highlighted the patient as a possible VHF suspect. These were then discussed with a senior doctor for advice on referral to the VHF unit at the National Hospital. Cardinal signs of haemorrhagic necessitated an immediate referral to the National Hospital. A senior doctor visits the urgent care team frequently to provide support and advice, and this support was increased during the outbreaks. For this study we have reviewed the screening tools filled and the urgent care admissions list to find those considered to be possible VHF suspects during the study period.

The internationally accredited IDI Core laboratory processes an average of 600 samples a day from over 40 sites around the country. The third tool was an information leaflet distributed to all lab staff and to all staff who were taking and dealing with blood and other samples (Figure 4).

Staff taking blood samples and working in the lab received sensitization on how to take samples, to manage samples and to dispose of samples in a safe manner.

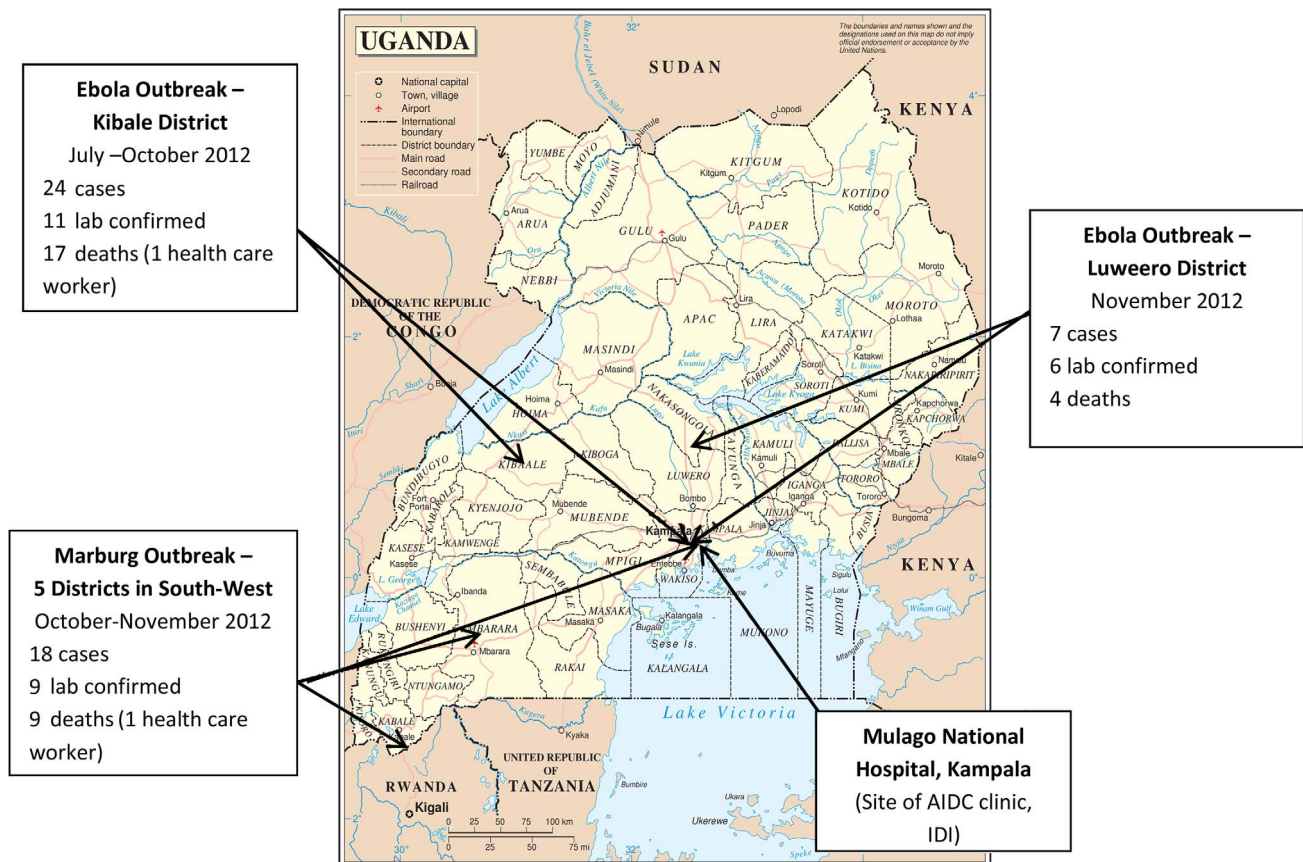


Figure 1. Map of VHF outbreaks in Uganda July 2012–June 2013.
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Ethical considerations

This process was approved by the Institutional Review Board. The study and use of data was reviewed and approved by the Scientific Review Board of the Infectious Diseases Institute, the Institutional Review Board of Makerere University and the Uganda National Council of Science and Technology. Individual written patient consent was waived by these ethical and review committees since data was collected for routine clinical care and unique identifiers are removed for operational research purposes.

Results

Outbreak 1 – Ebola Virus Disease Outbreak, Kibale (29th July 2012 to 4th October 2012)

We developed the first draft of the tools within 24 hours of the WHO and Uganda Ministry of Health (MoH) announcements. The action plan was initiated and the screening tool was first distributed to staff on 30th July 2012. The screening tool was then refined and re-circulated on 31st July 2012. Over the 67 days of this outbreak, we saw 9458 patients in the clinic and of these 3077 were unscheduled appointments. The laboratory processed about 38,000 samples. The AIDC clinical team identified 2 possible suspects. Case 1 was female patient identified by the infection control nurse. She reported to the infection control nurse with a history of haematuria and diarrhea. She had not travelled to the VHF epicenter area and had not cared for patients from that area. The patient was seen in the urgent care isolation zone, with barrier nursing. Detailed further history revealed dysuria and diarrhea. She was afebrile and urine analysis was normal. She received

ciprofloxacin and paracetamol and was discharged home. Case 2 was a female patient with fecal blood who had not been identified by the infection control nurse or the doctor, but reported bloody diarrhea to a counsellor, in the clinic. The counsellor requested she see a doctor but the patient absconded from the clinic. She was contacted by telephone by a clinic doctor later that day and gave a 3 month history of altered bowel habit, with some per rectal bleeding, not consistent with an acute infection. This was worse after taking her ART. She had not travelled to the epicenter area and had not cared for patients from that area. VHF was ruled out on clinical history and was encouraged to come back for further investigations of her chronic problem. Case 3 had fever, headache, abdominal pain, and an itchy skin rash. She was afebrile, and she was treated for a non-specific rash with prurigo. She was treated with cetirizine, hydrocortisone cream and magnesium suspension for gastritis. She was discharged home that day.

Outbreak 2 - Ebola Virus Disease (EVD) Outbreak, Luweero (17th November and 30th November 2012)

We instigated the process 24 hours before the WHO and MoH announcements (due to information received from Mulago Hospital) and an updated screening form were circulated to staff on 16th November 2012 (figure 2 shows the response times in this outbreak). Over the 13 days of this outbreak we saw 3086 patients with HIV 1/2 infection in the clinic, and 636 had unscheduled appointments. The lab processed about 7,200 samples. We identified one possible suspect (case 4) who had a rash, fever, and diarrhea and was from Luweero district. This patient was

Plan for infection control at AIDC in case of major or potentially severe communicable disease outbreaks

Background

The purpose of this document is to plan activities in the case of a communicable disease outbreak (including but not limited to Ebola Virus Disease, Marburg Virus Disease) in Uganda.

Strategy

The strategy in this situation is to protect staff and patients as much as possible and safely refer possible cases, without causing undue panic.

Objectives

The specific objectives are;

- 1) To ensure general infection control practices are in place
- 2) To add disease specific infection control policies if necessary
- 3) To identify and refer possible cases to the National centre as swiftly and calmly as possible
- 4) To keep all staff and SMT aware of the situation regularly
- 5) To liaise with Mulago National Referral Hospital, Ministry of Health, CDC, WHO and other partners as necessary

Abbreviations

HOD – Head of Department	AIDC- Adult infectious diseases clinic
PCT – Prevention, Care and Treatment program	SMT- Senior Management team
PNO- Principle Nursing Officer	SMO- Senior Medical Officer
ED – Executive Director	MOH – Ministry of Health
MO – Medical officer	CDC – Centres for Disease Control
PMO – Principle Medical Officer	WHO – World Health Organisation
Mulago – National Referral Hospital, Mulago Complex	BOD – Board of Directors

Specific Activities

Activity	Person responsible	Timeline	Dates Completed during second outbreak
1. Sensitize staff on issue and current situation	Deputy HOD PCT	Daily if necessary	16.11.12
2. Identify lead nurse and SMO to take these activities forward	PNO, Clinic manager	Day 1	
3. Ensure infection control measures in place <ol style="list-style-type: none"> a. Soap, water and hand towels (disposable) in each clinic room b. Soap, water and hand towels (disposable) at clinic entrance c. Gloves and disposable aprons in each clinic room d. Full gown and mask available in urgent care in case of high suspicion who needs transfer to Mulago 	Head of nursing	Daily	16.11.12
4. Sensitization of staff and friends without causing undue panic <ul style="list-style-type: none"> • Posters on hand washing in each room/ waiting area • Health talks to friends • Distribution of info leaflet to staff • No hand shaking policy 	Clinic manager / head of counseling	Ongoing	16.11.12
5. Liaise with MOH/Mulago staff to see where to refer patients and offer support	HOD PCT	Day 1 and ongoing	19.11.12
6. Stop all unnecessary field visits of IDI staff (research and outreach) to epidemic areas	Head of research/ Head of outreach	Ongoing	NA at present
7. To liaise with CDC/ WHO to seek advice and offer support where appropriate	ED /HOD PCT	Day 1 and ongoing	
8. Enhanced surveillance at AIDC <ol style="list-style-type: none"> a. Nurse at entrance to encourage hand washing and look for sentinel signs b. Doctors to fill proforma for all urgent care patients to screen for those infected c. Named SMO or higher to be consulted on all suspected cases 	Clinic manager/PMO	Daily	16.11.12
9. Liaise with Outreach team to discuss procedures at other sites where IDI work	HOD PCT and HOD outreach	As necessary	19.11.12
10. SMT members to be informed of procedures / plans. (IDI BOD to be informed at discretion of ED)	HOD PCT	As necessary	19.11.12

References

1. Infection Control for Viral Haemorrhagic Fevers in the African Health care setting CDC WHO 1998
2. Ebola Hemorrhagic Fever Information Packet. CDC. 2009
3. www.cdc.gov/ncidod/dvrd/spb/mnpages/dispages/ebola.htm

Figure 2. Plan for infection control at AIDC in case of major or potentially severe communicable disease outbreaks.

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given metronidazole and ciprofloxacin and transferred to the VHF unit at Mulago Hospital. Full infection control procedures were followed by staff handling the patient, and in handling laboratory samples. The patient was discharged from the VHF unit later in the day with no definite diagnosis. Laboratory samples were disposed of as per the protocol. Staff received counseling, but were not quarantined as they had no direct contact with body fluids. During the second outbreak we were contacted by another HIV

service provider and research clinic working within the Mulago Hospital Complex, who requested our tools for use in their clinic.

Outbreak 3 - Marburg Virus Disease Outbreak, South West Uganda (22nd October-23rd November 2012)

The process was not fully implemented as there were no reported suspects reaching Kampala, and the outbreak was mainly confined to the South West of Uganda.

Form for assessment in urgent care for haemorrhagic fevers

Name of Patient _____ AIDC number _____ DOB _____

Symptoms

Does the patient have fever? Yes/No

Does the patient have a headache? Yes/No

Does the patient have joint pain or muscle aches? Yes/No

Does the patient have a sore throat? Yes/No

Does the patient have diarrhoea/ vomiting or stomach pain? Yes/No

How long has the patient had these symptoms? _____

How many symptoms? _____

Signs

Does the patient have red eyes? Yes/No

Does the patient have a rash? Yes/No

Does the patient have hiccups? Yes/No

High suspicion signs

Does the patient have bleeding eyes or mouth or other bleeding? Yes/No

If yes send directly to National Referral Hospital Mulago A &E (regardless of other symptoms/geography)

Geography

Has the patient been to Luweero in the last 3 weeks? Yes/No

If yes, where and when _____

Has the friend worked or been in Mulago hospital in the last 3 weeks? Yes/No

Please discuss with PNO, HOD PCT, HOD research, or Team leader doctors if

- 1) Patient has 2 or more symptoms
- 2) Patient has ANY sign
- 3) Patient has 1 symptom and has been to W Uganda or Mulago

Decision _____ Senior Clinician name _____

Figure 3. Form for assessment in urgent care for haemorrhagic fevers.

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EBOLA TESTING IN UGANDA

Diagnostic specimens should be handled with extreme caution and can be sent for Ebola Testing to the CDC/IVRI in Entebbe-suspected samples must be well packed before sending to the CDC/IVRI Laboratory AND LABELLED AS HAZARDOUS

HISTORY OF EBOLA RELATED LABORATORY EXPOSURE

One reported near-fatal case following a minute finger prick in an English laboratory (1976). A Swiss zoologist contracted Ebola virus after performing an autopsy on a chimpanzee in 1994. An incident in Germany in 2009 when a laboratory scientist pricked herself with a needle that had just been used to infect a mouse with Ebola, however infection has not been confirmed. In a Level 4 lab in the US a non-fatal incident was recorded in 2004, and a fatal case in Russia in 2004 as well.

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PRIMARY LABORATORY HAZARDS: Accidental parenteral inoculation, respiratory exposure to infectious aerosols and droplets, and/or direct contact with broken skin or mucous membranes.

LABORATORY PROTECTIVE CLOTHING: Laboratory Personnel working on Ebola suspected specimens must wear appropriate protective laboratory clothing, a barrier-proof lab coat/gown with tight fitting sleeves, gloves, and respiratory protection (for routine operation may just wear a laboratory face shield). If no face shield is available Eye protection must be used where there is a known or potential risk of exposure to splashes

HANDLING of SPILLS: Allow aerosols to settle, wearing protective clothing, gently cover spill with paper towels and apply suitable disinfectant starting at the perimeter and working towards the centre. Allow sufficient contact time before clean up (at least 20min).

STORAGE: Only in Level 4 laboratory (doesn't Exist in Uganda) in sealed, leak-proof containers that are appropriately labeled.

MANAGEMENT OF ACCIDENTS

- Laboratory personnel accidentally exposed to potentially infected material (e.g. through injections, cuts or abrasions on the hands) should:
 - Immediately wash the exposed part with soap and water and
 - Apply a disinfectant solution e.g. 70% alcohol or Betadine.
 - If infected material is accidentally splashed into the eyes, wash thoroughly with eye wash solution provided. Do not use any other disinfectants.
 - In case of heavy contamination of clothing, the contaminated clothing must be discarded in the laboratory and the person should shower immediately.
 - The staff member should be assessed and counseled by an Infectious Diseases Physician as soon as possible.
 - An incident report must be completed.
 - The person should be considered as a high-risk contact and placed under surveillance.
 - Further details may be obtained from the Infectious Diseases Physician at the site of the designated isolation hospital.
- Accidental spills of potentially contaminated material should be:
 - Covered with an incontinence pad saturated with 1% hypochlorite, left to soak 30 minutes, and then wiped up with absorbent material soaked in 1% hypochlorite

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solution.

- The waste should be placed in a biohazard bag. With the help of an assistant, this bag should be placed inside another biohazard bag and sealed with tape for disposal.
- If accidental spills of potentially contaminated material result in aerosol formation (e.g. major spills outside a class 1, 2 or 3 BSC), evacuate the laboratory for at least 1 hour.

HOW IS EBOLA VIRUS DIAGNOSED IN THE LABORATORY?

Diagnostic specimens should be handled with extreme caution and sent to an **appropriate laboratory**, using approved shipping containers and import permits. The diagnosis depends on detecting the infectious agent during the acute phase of the disease or measuring the host's specific immunological response during illness and convalescence. Several approaches have been developed for the diagnosis of Ebola, using standard diagnostic methods on acute sera or post-mortem tissue specimens from infected humans and animals, as well as materials gathered during ecological investigations on possible reservoir hosts, namely fruit bats.

Sensitive tests are already available to measure the degree of infection during the acute phase of illness. The four tests described below are species-independent.

- ELISA** techniques have been developed to allow the **detection of the viral antigen** on inactivated specimens, such as blood, serum, or tissue suspensions.
- Nucleic acid detection (reverse transcriptase polymerase chain reaction, RT-PCR; or real-time RT-PCR, also known by the trade name TaqMan)** on inactivated material is rapid, more sensitive than antigen detection ELISA, and provides specific genetic identification of genetic fragments of the virus, allowing identification of the virus species.
- Virus isolation** is relatively simple but requires a Biosafety Level-4 laboratory and can take several days.
- ELISA IgM and IgG antibody:** allow the detection of the viral antibody at the acute-phase and post recovery
- On dead animals and collected tissues, **immunohistochemical staining and histopathology** can localize viral antigen within formalin-fixed tissues and assist in elucidating the pathogenesis of the disease.

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References

- Ayato Takada, A., Kawaoka, Y.B., (2001). The Pathogenesis of Ebola Hemorrhagic Fever. Trends in Microbiology 2001, 9:506-511
- Australian Government- Department of Health and Ageing Retrieved on 04 Aug 2012 from <http://www.health.gov.au/internet/main/publishing.nsf/Content/cda-phn-vhf-parta.htm>
- Joshua Pozos – online Ebola article- Retrieved on 04 Aug 2012 from <http://www.austinc.edu/microbio/2704w/ev.htm>
- National Center for Infectious Diseases/Centers for Disease Control and Prevention- Retrieved on 05 Aug 2012 from <http://www.cdc.gov/ncidod/dvrd/spb/outbreaks/qaEbolaRestonPhilippines.htm>
- Public Health Agency of Canada - Retrieved on 04 Aug 2012 from <http://www.phac.aspc.gc.ca/lab-bio/res/psds-ftss/ebola-eng.php>
- Public Health Agency of Canada- Retrieved on 05 Aug 2012 from <http://www.phac.aspc.gc.ca/lab-bio/res/psds-ftss/ebola-eng.php>

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Figure 4. Laboratory Information –Ebola.
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Post outbreak experiences (1st December 2012–1st July 2013)

During the 6 months following the outbreaks in Uganda, 10306 patients visited IDI (6032 unscheduled appointments). Clinic staff identified one VHF suspect (case 5) outside of a known outbreak in mid-2013. The patient presented with headache, fever, and diarrhea. He had epistaxis, hematemesis and bloody diarrhea. On examination he had hyperemic conjunctiva. He was found to have a thrombocytopenia with a platelet count of $114 \times 10^3/\mu\text{L}$. This patient was admitted to the National Referral Hospital within 2 hours of being seen in the clinic. The patient was isolated on the ward, and hospital staff treated the patient as VHF suspect. Senior clinic staff were notified immediately. No staff member was exposed to patient fluids. Urgent communication to lab staff ensured that blood samples taken by staff were handled safely. The MOH national VHF response team was notified and he was tested by the MOH team for VHF within 24 hours of admission. The case was VHF serology negative. No definite diagnosis was found. (Table 1 summarizes clinical information on all suspects seen)

Discussion

The VHF outbreaks in Uganda have caused a considerable amount of anxiety for both patients and staff in our large HIV clinic. In order to manage this anxiety and reduce the risk of occupational exposure in our clinic while providing an uninterrupted service we have designed and implemented easy to use tools in our clinic for use in VHF outbreaks. The action plan enabled us to communicate with staff within the clinic and in outreach projects around the country, as quickly and early as possible, in order to provide valuable information and to reduce anxiety. In both outbreaks we managed to communicate important information to staff within 48 hours of the announcements.

The use of an objective point based screened tool enabled us to continue to see a high number of HIV patients, often with vague symptoms, in a safe and effective manner in an out-patient HIV clinic which was not a VHF receiving centre. Our main objective was to provide a sensitive tool for identifying possible VHF suspects within a population of patients with HIV in order to refer them to a designated VHF clinic. Therefore, our tool was purposefully less specific than the WHO screening tools to be used in VHF centres, for instance, whilst we asked about symptoms, the questions we asked about exposure were limited to being in the

geographical area, and did not go into details about contact with patients/attendance at burials etc. This did increase the number of “possible” suspects that were highlighted to a senior doctor, but our experience was that this was manageable number and that it was important to have a more sensitive tool that could be a primary screening, prior to more intensive screening by the VHF receiving centre.

The lessons learnt from the development of these tools included that having access to tools to follow also helped to reduce stress of the staff, as they were able to perform their normal duties with reassurance that not every patient they encountered might have VHF. During the second outbreak we were able to update the existing screening form very quickly and our response was more rapid and coordinated. Additionally the use of these tools has sensitized our staff on the symptoms and signs of VHF, and how to identify a possible suspect quickly. This was highlighted by the identification and rapid management of a possible suspect outside of a known outbreak. Whilst the IDI laboratory employs universal precautions at all times, management of suspected VHF samples requires a higher level of caution. The laboratory document enabled laboratory staff to understand what additional precautions they needed to take, and consequently to reduce anxiety by providing a procedure for management of samples.

Whilst our tool is “ideal” for our clinical environment, it does have to be adapted to each outbreak. What is “ideal” for us may not work in other clinics with different models of care e.g. nurse led services, services without an “urgent care” area. Perhaps the WHO or local Ministries of Health in countries at risk of outbreak could consider making these tools or adapted versions of these tools available for other out-patient clinic settings with high patient loads. Whilst our experience suggests that the action plan and the screening tools are easily understandable to staff, we did find that with multiple experiences we became quicker at implementing our response. Therefore, we think that health facilities may consider simple training programme or staff sensitization prior to an outbreak, which might also help health care workers to become familiar with the tools and to implement them quickly if an outbreak occurs.

Conclusions

We believe that these tools/response aids may serve an unmet need in countries which suffer relatively frequent VHF outbreaks

Table 1. Summary of VHF suspect characteristics.

Patient	Age and Sex	Cd4 count	ART regimen	Symptoms	Possible exposure	Outcome
Case 1	46, F	592 (21%)	TDF/3TC/LPR-RIT	Dysuria, haematuria, diarrhea. No fever	Nil known	Treated for bacterial gastro-enteritis/UTI as outpatient with Ciprofloxacin
Case 2	42, F	196 (8%)	AZT/3TC/Nevirapine	Abdominal pain and diarrhoea after taking drugs	Nil known	Drug side effect – monitored as out patient
Case 3	35, F	492 (23%)	AZT/3TC/Nevirapine	Headache, Abdominal pain, Rash	Nil known	PPE and gastritis – treated with cetirizine, hydrocortisone and magnesium suspension
Case 4	42, M	139 (13%)	TDF/3TC/EFV	Fever, joint pain, sore throat, diarrhoea	From district containing epicentre (Luweero)	Given treatment for bacterial gastroenteritis with ciprofloxacin/metronidazole. Transferred to National Referral Hospital VHF unit for investigation but discharged
Case -5	35, M	237 (17%)	Nil	Fever, headache, bloody diarrhoea, epistaxis, hematemesis	Outside of known outbreak	Transferred to National Referral Hospital VHF unit

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and have a high HIV prevalence. We would encourage other HIV clinics or clinics with a high turnover of patients, who work in areas of potential VHF outbreaks to consider a risk management strategy, with readily available and objective assessment tools, which can be activated quickly during a similar emergence outbreak situation.

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Author Contributions

Conceived and designed the experiments: RPR CM FM BM AE. Performed the experiments: RPR FM BM. Analyzed the data: RPR. Contributed reagents/materials/analysis tools: CM AE. Wrote the paper: RPR FM AE AC CM BM.

References

- Centers for Disease C Viral hemorrhagic fevers. Available: <http://www.cdc.gov/ncidod/dvrd/spb/mnpages/dispages/vhf.htm>.
- WHO Hemorrhagic Fevers, Viral. Available: http://www.who.int/topics/haemorrhagic_fevers_viral/en/.
- Feldmann H, Geisbert TW (2011) Ebola haemorrhagic fever. *Lancet* 377: 849–862.
- Sanchez AKT, Rollin PE, Peters CJ, Nichol ST, Khan AS, et al. (1995) Reemergence of Ebola virus in Africa. *Emerging Infectious Diseases* 1: 96–97.
- Locsin RC, Matua AG (2002) The lived experience of waiting-to-know: Ebola at Mbarara, Uganda—hoping for life, anticipating death. *J Adv Nurs* 37: 173–181.
- Bitekerezo M, Kyobutungi C, Kizza R, Mugeni J, Munyarugero E, et al. (2002) The outbreak and control of Ebola viral haemorrhagic fever in a Ugandan medical school. *Trop Doct* 32: 10–15.
- Mwesiga A (2011) Reporting epidemics: newspapers, information dissemination and the story of Ebola in the Ugandan district of Luwero. *Pan Afr Med J* 9: 43.
- Green A (2012) Uganda battles Marburg fever outbreak. *Lancet* 380: 1726.
- Kinsman J (2012) “A time of fear”: local, national, and international responses to a large Ebola outbreak in Uganda. *Global Health* 8: 15.
- Hewlett BL, Hewlett BS (2005) Providing care and facing death: nursing during Ebola outbreaks in central Africa. *J Transcult Nurs* 16: 289–297.
- Raabe VN, Mutyaba I, Roddy P, Lutwama JJ, Geissler W, et al. (2010) Infection control during filoviral hemorrhagic fever outbreaks: preferences of community members and health workers in Masindi, Uganda. *Trans R Soc Trop Med Hyg* 104: 48–50.
- Borchert M, Mutyaba I, Van Kerkhove MD, Lutwama J, Luwaga H, et al. (2011) Ebola haemorrhagic fever outbreak in Masindi District, Uganda: outbreak description and lessons learned. *BMC Infect Dis* 11: 357.
- Mupere E, Kaducu OF, Yoti Z (2001) Ebola haemorrhagic fever among hospitalised children and adolescents in northern Uganda: epidemiologic and clinical observations. *Afr Health Sci* 1: 60–65.
- Shoemaker T, MacNeil A, Balinandi S, Campbell S, Wamala JF, et al. (2012) Reemerging Sudan Ebola virus disease in Uganda, 2011. *Emerg Infect Dis* 18: 1480–1483.
- Roddy P, Howard N, Van Kerkhove MD, Lutwama J, Wamala J, et al. (2012) Clinical manifestations and case management of Ebola haemorrhagic fever caused by a newly identified virus strain, Bundibugyo, Uganda, 2007–2008. *PLoS One* 7: e52986.
- Jeffs B (2006) A clinical guide to viral haemorrhagic fevers: Ebola, Marburg and Lassa. *Trop Doct* 36: 1–4.
- Mbonye AK, Magnussen P (2010) Symptom-based diagnosis of malaria and its implication on antimalarial drug use in pregnancy in Central Uganda: results from a community trial. *Int J Adolesc Med Health* 22: 257–262.
- Ndyomugenyi R, Magnussen P, Clarke S (2007) Diagnosis and treatment of malaria in peripheral health facilities in Uganda: findings from an area of low transmission in south-western Uganda. *Malar J* 6: 39.
- Wakeham K, Harding R, Bamukama-Namakoola D, Levin J, Kissa J, et al. (2010) Symptom burden in HIV-infected adults at time of HIV diagnosis in rural Uganda. *J Palliat Med* 13: 375–380.
- UNAIDS (2013) Uganda AIDSinfo. Available: <http://www.unaids.org/en/regionscountries/countries/uganda/>; Accessed 2013 Jul 11.
- Roddy P, Marchiol A, Jeffs B, Palma PP, Bernal O, et al. (2009) Decreased peripheral health service utilisation during an outbreak of Marburg haemorrhagic fever, Uige, Angola, 2005. *Trans R Soc Trop Med Hyg* 103: 200–202.
- (2012) Outbreak news. Ebola haemorrhagic fever, Uganda - update. *Wkly Epidemiol Rec* 37: 493.
- WHO CfDCa (1998) Infection Control for Viral Haemorrhagic Fevers in the African Health care setting. Available: http://www.who.int/csr/resources/publications/ebola/WHO_EM_C_ESR_98_2_EN/en/.
- Control CfD (2009) Ebola Hemorrhagic Fever Information Packet. <http://www.cdc.gov/vhf/ebola/Ebola-FactSheet.pdf>.