Canadian Critical Care Society

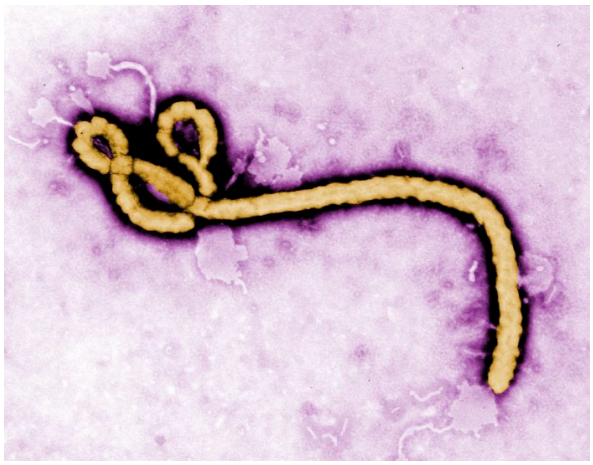
Canadian Assoc. of Emergency Physicians

Assoc. of Medical Microbiology & Infectious Diseases Canada

Ebola Clinical Care Guidelines

A guide for clinicians in Canada

Report #2 – Updated: October 28, 2014



Organized by the Public Health Agency of Canada

Ebola Virus Photo

Courtesy of CDC/ Frederick A. Murphy

Forward

Over the weeks following the interim report from this working group the outbreak of Ebola in West Africa has unfortunately continued essentially unabated, despite mounting efforts from the global community. In addition, exported cases have occurred unfortunately with local transmission to contacts, including health care workers. To date, Public Health measures and the appropriate use of personal protective equipment (PPE) appear to have largely contained and significantly limit transmission from the exported cases. Nonetheless, these events have further increased the need for hospitals within Canada to be prepared for the potential of needing to manage a patient with Ebola Virus Disease (EVD). In addition to planning, at this stage it is important for hospitals and the clinicians who work within them to further prepare, beginning with educating their staff regarding their plans, developing and delivering training on the appropriate use of PPE as well as testing their plans with exercises or simulations.

From a more positive perspective, the events of the past month have also provided us with more information regarding the management of patients with EVD in a Western medical context, particularly the experiences of those at Emory University Hospital in the USA[1]. Additionally, as many hospitals have been developing their plans, we are able to share some of the lessons learned from those experiences. In this updated report we are including that information where available in addition to correcting any gaps noted in the interim report.

Forward to the Interim Report – August 28, 2014

In response to the WHO declaration of the Ebola outbreak in West Africa as a Public Health Emergency of International Concern (PHEIC), the Public Health Agency of Canada (PHAC) invited the Canadian Critical Care Society (CCCS) and the Association of Medical Microbiology and Infectious Disease Canada (AMMI) to consider embarking upon a collaboration to develop clinical care guidelines to support clinicians in Canada who may be required to treat a patient suffering from the Ebola Virus Disease (EVD or "Ebola"). Both the CCCS and AMMI were fully supportive of collaborating on this important initiative. In order to ensure that the guidance developed was applicable to clinicians in all of the areas of hospitals most likely to be required to provide care, the CCCS and AMMI requested that the Canadian Association of Emergency Physicians (CAEP) also be invited by PHAC to participate in the development of the guidelines. As a result the current guidelines have been produced via a collaboration of efforts from all three of the societies.

The current iteration of these guidelines is intended to focus on the management of isolated cases of Ebola in persons arriving in or returning to Canada having been exposed to the virus during travel outside of Canada, Future updates of these guidelines will be developed as information evolves or if there is a need for clinical guidance regarding the management of larger volumes of cases of Ebola in Canadian hospitals. The focus of this document is on clinical care and patient management (e.g. processes & patient flow, bedside care, etc.). With the exception of Inter-facility transport, this document will not discuss the specifics of infection prevention and control (IPAC) and EVD diagnostic testing, as these are covered in separate guidelines from PHAC. Although the specific guidance regarding IPAC will not be provided by this group, the clinical societies which represent those working on the front lines of patient management are uniquely positioned to provide insight on the human factors associated with applying IPAC guidelines in the delivery of patient care.

It must be recognized that much of the guidance within this document derives from expert opinion. There is scant high-grade evidence regarding the either the pathophysiology or optimal specific clinical management of EVD. The aim of this collaborative was to develop a simple, easy-to-use guide for the clinicians who face treating their first case of EVD. Having the luxury of time for contemplation and debate over some of the issues at present, rather than in the heat of the moment, we hope that by articulating our rationale and discussing the pros and cons of various options clinicians will find our 'expert opinion' beneficial.

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Contributions

Each of the societies contributed participants for the working group who could provide particular knowledge, skills, and/or experience relevant to the management of patients with Ebola. Among the working group members there is representation from a variety of clinical backgrounds, including both adult and paediatric providers as well as members of the group who have experience in treating patients with Ebola in Africa during the current outbreak as well as prior outbreaks. In addition to the core working group members, many other members of the societies and other clinical experts contributed content and comments during the development process. This trilateral collaboration was facilitated by PHAC (Dr. Thomas Wong, Dominique Baker, Margie Lauzon, Althea House, Eva Wong and Shamir Nizar Mukhi).

A complete list of society contributors can be found at the end of the document.

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Overview of Ebola Virus Disease

Epidemiology

Ebola virus is member of the filoviridae, enveloped non-segmented, negative stranded RNA viruses. Ebolavirus is a viral genus, which contains 5 species: Bundibugyo ebolavirus, Reston ebolavirus, Sudan ebolavirus, Taï Forest ebolavirus (originally Côte d'Ivoire ebolavirus), and Zaire ebolavirus. The species Zaire ebolavirus contains a single virus known as Ebola virus, the cause of the current outbreak. The reservoir of Ebola virus is most likely to be fruit bats in Central Africa but no human cases have been contracted directly from bats. In the wild, Ebola virus likely spreads from fruit bats to other animals such as rodents, monkeys and chimpanzees, following which humans acquire the infection from eating poorly cooked animals or handling raw animal meat (Bushmeat).

The first case of Ebola virus disease (EVD) was detected in 1976 in a large outbreak in southern Sudan and northern Democratic Republic of Congo (DRC). Twenty subsequent outbreaks have been recorded in Africa with a total of fewer than 1000 deaths until the current 2014 outbreak. The case fatality rate from EVD varies from 30 to 90% depending on the subtype of the virus; the highest mortality is seen from Ebola Zaire (which is the cause of the 2014 West African outbreak) and the lowest from Ebola Bundibugyo infections. The current outbreak began in December 2013 and is the largest on record with more than 8,000 cases and over 4,000 deaths (~50% case fatality rate). As of October 17, 2014, the World Health Organization (WHO) reports the total number of probable, confirmed, and suspected cases in the current Ebola outbreak as 9,216 with 4,555 deaths, primarily in Guinea, Sierra Leone, and Liberia with prior localized transmission or single cases in Senegal, Nigeria, Spain and United States. Please refer to the WHO website for the latest epidemiology.[1]

Transmission

Most human infections occur by direct contact with secretions and excretions of infected (blood, urine, vomit, stool, endotracheal secretions, semen and sweat[1]) from patients or cadavers but **not routinely** by aerosol spread. The virus enters the host through mucosal surfaces, breaks and abrasions in the skin or by the parenteral route. Health care workers are frequently infected from needle sticks or breaks in personal protection techniques. Asymptomatic individuals in the incubation period have not, to date, been documented to transmit the infection. Additionally, persons with a very low viral load (minimally symptomatic) early in the course of their illness are also less likely to transmit the virus.

[1] *http://www.who.int/csr/disease/ebola/en/*

Clinical

The clinical picture of Ebola virus disease (EVD) begins with an abrupt onset of fever following an incubation period of 2 to 21 (mean 4-10 days) and is characterized initially by a nonspecific flu-like illness with fever, headache, malaise, myalgia, sore throat and gastrointestinal symptoms such as nausea vomiting, diarrhoea and abdominal pain. Electrolyte derangements are mostly secondary to the diarrhoea and vomiting. Severe hypokalemia along with moderate degrees of hypocalcaemia and hypomagnesaemia have been reported.[1] In addition, capillary leak combined with intravenous volume resuscitation commonly result in significant third spacing and peripheral oedema. Although cough can occur, it is not a primary feature of this illness. Hiccups and dysphagia are often present, with severe associated discomfort. A maculopapular rash and conjuctival injection may occur. Postural hypotension, confusion and coma precede death. Haemorrhagic manifestations, occurring in fewer than 10 % of clinical cases, arise toward the end of the first week of illness and include petechiae, blood loss from venipuncture sites, bruising and gastrointestinal bleeding. Primary causes of death are typically hypovolemic shock due to orogastric losses and third spacing (not haemorrhagic) and related severe electrolyte abnormalities. Renal failure is frequent in the late phase of severe disease.

Diagnosis

Laboratory abnormalities associated with EVD include early leukopenia, lymphopenia and atypical lymphocytosis. AST and ALP are often elevated. Prothrombin and partial thromboplastin times are increased, and fibrin split products are detectable indicating disseminated intravascular coagulation. Patients who die often do so between the sixth and 16th day in hypovolemic shock and multi-organ failure. The definitive diagnosis of EVD is made by RT-PCR or antigen detection in blood (early or late) or body fluids (late).

Treatment

The mainstay of treatment is supportive care, which includes careful attention to intravascular volume status and oral or intravenous fluid therapy, correction of electrolyte and metabolic abnormalities, correction of coagulation abnormalities, nutritional support, and antibiotics for secondary bacterial infections. Although robust data are still lacking, anecdotal experience from EVD patients treated both Africa and 'Western' health care systems during the current outbreak suggests that the mortality rate associated with EVD can be significantly reduced through the provision of supportive care, and in particular critical care.

Experimental therapies, including monoclonal antibody administration, small inhibitory RNA molecules, Ebola virus-specific convalescent plasma therapy and hyper-immune globulin, pre- and post-exposure immunization, are still experimental. Although some of these treatments have recently been used in a small number of individuals, the available data remain insufficient to determine their clinical efficacy and safety in humans. Efforts to launch clinical trials are rapidly underway and the World Health Organization has issued ethical guidance on use of such agents[2].

[2] *http://www.who.int/csr/resources/publications/ebola/ethical-considerations/en/*

Clinical Leadership

Health facilities leadership should provide direction, be engaged and ensure that the institution has the ability to detect and provide initial appropriate levels of care for all communicable diseases, including those that are:

1. Rare or occur only by importation
2. Have high rates of infectivity
3. Have high mortality

Healthcare Institutions should be alert for the possibility of rare and severe diseases, and the screening of patients for such illness should be routine.

The consequences of these diseases are as follows:

1. For patients – care of an unfamiliar disease may be suboptimal, and fear, even when the diagnosis has not been confirmed, may contribute to patients receiving lower quality of care.
2. For staff regarding their own health and health of their families – they need to have confidence in the medical system that they and their families will be protected from nosocomial transmission during health care.
3. For the entire health system – while the Emergency Department may be the portal of entry to the institution for many patients with infectious diseases, such patients often also receive care from many other services including: medical wards, ICUs, operating rooms, diagnostic imaging, laboratory and pathology services, and pharmacy.
4. Messaging to the media to inform citizens – it is likely that there will be members of the general public who present for assessment ("worried-well") after hearing of certain novel communicable diseases and this has the potential to place additional stress on the capacity of the ED and hospital generally, and hence we need to inform while being prepared for the consequences of increased public concern and attention.

Administrative Leaders within the institution should ensure that they are prepared for these diseases as part of routine care.

Healthcare organization administration and senior leaders should ensure that resources are available such as personal protective equipment (PPE) and experts in patient management, PPE training and utilization,

infection prevention and control to help guide processes of care delivery, general staffing, equipment, medical supplies, etc..

Clinical Leaders should ensure that a team is in place to coordinate the overall response.
The team may vary from institution to institution but should include a senior nurse, senior physician, infection prevention and control (IPAC) officer, and employee safety officer as well as a communications officer. Using the Incident Management System to organize and coordinate the hospitals response is strongly suggested and facilitates easy as well as orderly escalation of the response in the event a suspect case presents.[2] Should there be the possibility of a EVD case identified in the ED, or other area of the hospital, the staff of that clinical area should promptly notify appropriate personnel through their usual reporting channels who will then activate the hospital-specific team through predefined protocols and prepared messaging that will need to be deployed on short notice.

Point of First Contact – Emergency Department

Preparedness

It is crucial for hospitals and Emergency Departments (EDs) to prepare for responding to a potential patient with EVD before their first possible case presents to their department. This involves developing plans to screen patients and to respond should a patient screen positive. Strategies should be implemented to mitigate ED overcrowding by ensuring outflow from the ED is prompt and wait time targets are met. Ideally, EDs will have a single process which allows them to screen for and appropriately respond to any patient presentation suggesting a highly infectious disease be it EVD, MERS CoV, H7N9, or any other emerging pathogen. However, this document will focus solely on issues related to EVD.

Risk Factors in ED

Overcrowded emergency departments and prolonged wait times make the ED Waiting Room and triage area high-risk areas for patients and family to come in contact with a potential Ebola patient. Although the risk of transmission is relatively low in this setting, it can lead to high numbers of patients having to be traced and followed by public health. To mitigate, the ED should start by having high visibility signs at the entrance telling persons with risk factors for Ebola to immediately report to the Triage Nurse so they can be isolated. It is also imperative for hospitals to routinely support timely throughput of other patients through the ED by ensuring patients requiring hospital admission are quickly moved out of the ED to inpatient units once the decision has been made to admit, thus avoiding ED "access block" (the condition where undifferentiated incoming patients are unable to access appropriate ED care spaces due to admitted patients being boarded in the ED), and by providing adequate numbers of HCW to assess and treat the volume of incoming patients. Freeing up care spaces for newly presenting ED patients, and meeting wait time targets are critical to mitigate overcrowding and the resulting inability to provide adequate infection control measures in the waiting room and Triage area.

Appendix 1 provides examples of the type of approach recommended within the ED to screen for and respond to a potential patient with EVD. Below a brief description of the key aspects of case identification, infection control and testing in the ED is provided however HCWs should refer to the most up-to-date guidance for these areas provided on-line by the National and Provincial public health agencies[3].

[3] http://www.phac-aspc.gc.ca/id-mi/vhf-fvh/ebola-ipc-pci-eng.php

In addition, EMS in Canada should screen patients, as should tele-health and outpatient clinics. If any fail the screen they should consult or advise the ED before sending the patient in order for the department to prepare to isolate the patient. Each region may have its own way to arrange transfer to the ED utilizing a designated EMS vehicle and crew wearing proper PPE. Regions may choose to designate specific hospitals or care units for Ebola patients.

Triaging the Patient with Risk Factors for Ebola

It is important to remember that most patients presenting to the ED will be relatively well i.e. no vomiting, diarrhoea or haemorrhagic signs, and the risk of transmission is low at this stage.

The first responsibility of the Triage Nurse is to take protective action. Keeping a distance of 1-2 m and not touching the patient provide the first protection. Once a potential EVD patient is suspected, the nurse will then don his/her institution's recommendations for personal protection. This can vary and may consist of mask, gloves, gown and face shield.

The Triage RN should not examine the patient or ask detailed questions; rather he/she should focus on isolating the patient. Ideally the ED will have a designated isolation room(s) available. These rooms do not have to be negative pressure for initial screening or routine care. They should ideally have a bathroom or at least be large enough for a commode. If the patient must wait for the room to be prepared, e.g. another patient has to be moved out, then the patient should be isolated at the triage area or another area in the ED where access can be controlled. An area where HCW are able to doff the contaminated PPE needs to be prepared.

Once the patient is moved to the isolation room the areas at triage they contacted should be cleaned according to the recommendations for environmental cleaning.[4]

Examining the Possible Ebola Case in an ED Isolation Room

It is at this point the level of personal protection must be carefully considered. If the patient is relatively well the risk of transmission is low. Hospitals may vary in guidance but simple droplet and contact precautions and good hygiene may be sufficient for the well looking patient.

[4] http://www.phac-aspc.gc.ca/id-mi/vhf-fvh/ebola-ipc-pci-eng.php

However if the patient has or develops vomiting, diarrhoea or haemorrhagic signs in the ED the risk climbs significantly and higher levels of personal protection are required. These levels of protection necessitate that staff have been trained in the donning and doffing of this equipment in order to use it safely. Scrubs only, should be worn into these patient's rooms. No charts should be taken in and designated medical equipment should remain in the room. Vitals should be done with a cleanable monitor that displays or transmits the information and contact should be limited to the minimum number of essential personnel.

Limited staff only should examine this patient. No learners, families or friends should be allowed in with the patient. If children are involved, hospitals will have to determine the risk of allowing parents in and consult public health. Staff and visitors should consider the use of phones or intercom systems for communicating with the patient in order to minimize exposure. Much of the history can be obtained in this manner.

The patient should be given treatment as needed.

The Staff MD should perform a detailed Epi-Link screen (see case identification below). If the screen is positive thus indicating the patient is potential suspect case, consultation with an infectious disease or tropical disease specialist is strongly recommended and IPAC should be notified immediately.

Labs to be drawn consist of routine CBC, electrolytes, venous blood gases, urea, creatinine, blood glucose, liver function tests, INR, PTT, malaria tests, EVD viral studies and 2 sets of blood cultures. The laboratories must be informed about **ALL** specimens that may contain Ebola virus so that appropriate transport and handling can be arranged. Specimens should be carried by hand in appropriate containers. They should NOT be sent by pneumatic tube or similar systems.

Chest xrays should be only if absolutely essential, as this poses risk to additional staff and may require additional decontamination of equipment and space.

Appropriate signs indicating restricted access should obviously be placed on the patient's door.

Case Identification

Early identification of potential Ebola cases is based on: A) clinical presentation, AND B) epidemiologic risk. Please refer to the PHAC website for the most up-to-date case definition[5]. Case definitions can evolve over

[5] http://www.phac-aspc.gc.ca/id-mi/vhf-fvh/national-case-definition-nationale-cas-eng.php

time based upon the changing epidemiology of an outbreak in addition to advancements in our scientific understanding.

Case identification requires a high index of suspicion, routine screening of all patients, knowledge of clinical features of EVD, and frequently updated knowledge of relevant exposure risks for EVD. The recent case in Texas[6] of a patient returning from an endemic area presenting to an ED with symptoms and then being released, highlights both the importance of case recognition as well as the challenges that can be faced in effectively implementing screening.

Established EVD is almost always associated with high fever – usually at least 38.0 degrees Celsius. Although a single temperature taken at triage may be normal, a history of fever or feverishness will be present. However, the use of antipyretics may prevent or weaken this response. Fever may also be milder earlier in the illness. Prostration and headache may be useful very early indicators. Rash, conjunctival injection, loss of appetite, nausea and vomiting usually start several days into illness. Because these symptoms are non-specific, knowledge of and screening for travel history and other exposures is critical.

EVD should be considered in a febrile patient whose onset of symptoms is within 2 to 21* days of:

- residence in or travel to an area where EVD transmission is active[7]
- directly or indirectly caring for a probable or confirmed case of EVD (e.g. direct patient care or contact with environment or fomites of a case)
- contact with someone who is symptomatic and is known to have recently travelled to the effected areas or cared for an EVD infected patient
- spending time in a healthcare facility where EVD patients are being treated
- household exposure to a confirmed or probable EVD patient
- processing laboratory specimens from a confirmed or probably EVD patient, or in a hospital in an area where EVD transmission is active
- Direct exposure to human remains (e.g. through participation in funeral rites) in an area where EVD transmission is active
- Contact with bats or primates from EVD-affected country

**note: some authorities are now using 30 days as the upper limit, clinicians should refer to their local public health guidance for the most up-to-date case definitions*

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[6] *http://dfw.cbslocal.com/2014/10/10/ebola-patient-arrived-at-er-with-103-degree-fever/*

[7] *As of August 17, 2014, EVD transmission is active in Guinea, Liberia, Sierra Leone, and Nigeria. Refer to the World Health Organizations's Ebola Virus Disease (EVD) website for updated information on affected areas: http://www.who.int/csr/disease/ebola/en/*

Preparation for Potential EVD Cases

Preparing to manage the first recognition of a patient ***potentially*** infected with EVD requires a specific plan and procedure that is unique to each hospital. This plan needs to focus on as rapidly as possible protecting the hospital staff as well as other patients and visitors.

Staff should be trained and experienced with both the use of the appropriate PPE as well as the process to be followed immediately upon recognition of a suspect case as well as the subsequent evaluation of that patient. This requires practice for the staff as well as exercising the systems/processes. Simulation can be particularly useful in assisting in these preparedness activities. A brief review of the steps in the plan should be done at the beginning of each shift. This may take only 5-10 minutes and if done on a regular basis the plan will become common knowledge.

Small posters with guidelines should be posted and key areas, triage and desk areas where staff work etc. Online material should also be available.

The training in selection of personal protective equipment, donning, doffing, and self-decontamination is critical to staff. The details of this are beyond the scope of the document. It is suggested hospitals, especially in the ED and Critical Care Unit, train small teams well rather than attempting to train all employees, in advanced PPE. At least 1-2 members of the advanced PPE teams should be present on each shift, to assist staff as needed, and call for the full team if necessary. If the number of patients with Ebola should rise in Canada, then these teams will train additional staff.

It must be recognized by the hospital leadership that it is **insufficient** to simply have a plan in place. Once a suspect case has been identified and isolated a 'buddy system' should be in place to ensure 'cross-checks' of PPE use as well as potential risk procedures such phlebotomy. Infection control considerations commonly include the following items listed however; HCWs should consult their local IPAC policies and National/Provincial Public Health guidelines[8].

An ED's plan must include the logistics as to how PPE will be rapidly accessed in response to a suspect case. Many hospitals have developed EVD kits and have pre-positioned them in or close to their ED so that they are easily accessible if required. In addition, given the dynamic nature of most EDs and the volume of patients typically seen, hospitals must ensure plans for isolating patients contain multiple contingencies in the event that the preferred location for isolating a suspect EVD patient is not immediately available when required.

[8] http://www.phac-aspc.gc.ca/id-mi/vhf-fvh/ebola-ipc-pci-eng.php

Where To Provide Care For An Admitted Patient With Suspected or Confirmed Ebola

Selection of the appropriate clinical area to manage a patient with Ebola, or a suspect case with a high index of suspicion) once he or she has entered a health care facility will be dependent upon a number of factors. Every institution will have to make an individual decision about what is best for their particular circumstance. Some institutions with adequate space and isolation facilities in their ED have elected to hold a suspect case in the ED until the diagnosis of EVD has been either confirmed or ruled out. However, for many institutions this would lead to grid lock in the ED therefore many institutions will choose to move suspect cases to an in-patient bed or to a designated facility outside of the hospital. Adhering to the basic principles that apply in emergency preparedness[2], hospitals should undertake an inventory of their facilities and identify potential areas for managing highly infectious patients such as those with Ebola **well before** they are faced with their first potential case.

When assessing potential areas to care for an Ebola patient, consideration should be given to the following factors:

- Single Patient Room with a private bathroom, door and anteroom (or space to create one)
    - Negative pressure isolation is only essential if aerosol generating procedures are to be conducted
- Ability to dispose of body fluids safely within the patient's room
- Infrastructure for patients to communicate to staff/visitors outside of the room
- Ability to restrict access to the area as well as to the patient's room
- Ability to provide dedicated patient care equipment (preferably disposable)
- Ability to provide critical care without having to move the patient should he/she deteriorate
    - Suction
    - Monitors
    - Sink (with dialysis connections if needed)
    - Electrical outlets (including emergency power supply)
    - Medical Gas (Oxygen & Medical Air) connections
    - Space for life support equipment

- If facility resources permit, overhead hoists to facilitate patient movement with minimal staff involved
- Sufficient space for providers to don and doff PPE, ideally with a separate 'clean' entrance and 'dirty' exit
- Storage for medical supplies and PPE outside of the room
- Appropriate facilities outside of the room to clean or dispose of contaminated medical equipment and supplies, including space for storage of waste until it can be removed safely.
- Potential for access to or placement of point-of-care testing equipment
- Work area outside of the room for staff
- Necessary IT & communications connections for both staff and patient use
- Ability to bring portable x-ray machines into room to minimize patient transport
- Physically separated from other non-EVD patients
- Close access to elevators or diagnostic suites to minimize transportation times

When a Canadian hospital is faced with the need to care for a single patient with Ebola, for many hospitals the most practical place to provide this care may be in an Intensive Care Unit (ICU). ICUs in many hospitals are the most likely locations to possess the factors ideal for caring for an Ebola patient. In addition to the physical and logistic issues, ICU provides 1:1 (or higher) nurse to patient ratios, which will in part mitigate the negative impact on patient care due to the burden associated with the PPE requirements[3]. Further, patients suffering from EVD require close attention to fluid management and volume resuscitation, skills that critical care clinicians possess as a primary expertise. Finally, ICU staff typically represent a contained audience to target for education and training related to the provision of care to patients with EBV. They should already be well practiced in the use of appropriate PPE, and in performing aerosol-generating procedures if necessary, for these situations.

General Considerations for Clinical Care

A number of key considerations should guide the clinical care of confirmed or suspected EVD patients:

- Safety: patient safety, HCW safety, community safety.
- The overarching philosophy should be to minimize the number of people who have contact (exposures) with the patient. Adhering to this philosophy requires restricting the staff who enter a patients room to only a small number of core physicians and nurses (and potentially respiratory therapists for an intubated patient). This requires a significant alteration in how care for patients is typically managed in most modern hospitals. In the situation of managing an EVD patient all tests or procedures conducted, all care provided, and even all cleaning of the room whilst the patient is present, should be conducted by core nurse and physician team. Support staff can continue to help with other aspects of care such as the preparation of medications etc., but these staff should not enter the patient's room. Unfortunately this also applies to visitors and family.
- The amount of time HCWs are exposed to a patient should be minimized. HCWs should only enter the patient's room when essential. Many aspects of care such as history taking and routine communication can be modified to occur from outside the patient's room via telephone or intercom if the patient is awake and alert. Alternatively, an awake patient can be provided with a white board to communicate with staff. Arrangements should be made to allow family members to communicate from outside the unit (or hospital) with the patient. Internet based video chat technologies can be very useful for this.
- Despite the need to minimize the amount of time spent in a patient's room, a HCW must always be at the ready to quickly enter the patient's room. Given the significant length of time to don PPE in a safe and controlled manner this means that a HCW must always be dressed in PPE sitting in the warm zone and ready to enter into the hot zone at a moment's notice if the patient requires assistance to get to the commode or is severely/critically ill.
- The high dependency of EVD patients in particular due to the implications of the required PPE and necessary safety precautions such as utilizing a buddy care system or safety officer requires a RN to patient ratio of at least 2:1. Increasing the staffing ratio however, must be balance by the first principle of minimizing the number of people who have contact with the patient. The buddy system must be in place for all HCWs who enter the room, not only nursing.

Personal Protective Equipment Considerations

Guidelines for the minimum standard of PPE required are provided elsewhere and are beyond the scope of this clinical guideline.[9] However, there are a number of lessons from the experience of clinicians who have been providing care for patients that may be useful for clinicians to consider.

- Although IPAC professionals posses the expertise to recommend the appropriate PPE to mitigate infection based upon the primary route of transmission, selecting the appropriate PPE based upon the clinical tasks that need to be performed and determining the most appropriate process for donning and doffing requires input from both IPAC professionals and the clinicians who are going to use the PPE. Not only will this result in the best plans and safest care, it will also significantly boost the clinician's confidence in caring for patients.
- Selection of the appropriate PPE should be geared to the risk of exposure involved. For example, the risk associated with a suspect case of EVD or an early presentation of EVD where the patient is minimally symptomatic poses a lower potential risk for infection then a patient confirmed to have EVD in the later stages who is experiencing significant vomiting, diarrhoea or other leaking of body fluids into the environment. Therefore HCWs should expect that the PPE used in these two situations will likely be somewhat different.
- Individual pieces of PPE (e.g. face shields, gowns, gloves, etc.) must be combined together to provide a package of protection for the HCW. However, not all pieces of PPE are identical between various manufacturers. Designing the overall PPE package to provide the appropriate protection for the HCW is somewhat akin to assembling a puzzle and all the pieces must ultimately fit together. Therefore, HCWs should expect that if different hospitals are using different pieces of PPE from different manufacturers some variations in the design and use of the PPE package are going to occur between different institutions. This should not cause HCWs to be alarmed. Instead HCWs should work with their IPAC colleagues to ensure that the PPE package designed in their institution will work for them in their context to provide the required level of protection.
- The ability of PPE to protect the HCW is an important but not the sole factor to be considered when making decisions regarding PPE. The HCW must also be able to provide care to the patient in a manner that is both effective and safe for both parties. Heat stress in the PPE used for caring for EVD patients has been a significant issue for HCWs. In the situation where the patient is relatively well (e.g. a suspect case or minimally symptomatic patient) where the patient is unlikely to require urgent assistance, thus allowing for HCWs to remove PPE when they exit the patient's room, and time to don it when they are required to enter the room for short periods of time, heat stress should not be a significant issue. However, in situations where HCWs must remain in PPE for long periods of time, heat stress is a significant issue and has led some institutions to select the use of powered air purifying respirators (PAPRs). It should be stressed however, that these decisions have

[9] http://www.phac-aspc.gc.ca/id-mi/vhf-fvh/ebola-ipc-pci-eng.php

been based primarily on HCW's physical comfort and not due to specific concerns of airborne transmission. Minimizing the impact of heat stress allows PPE to be worn for longer period which in turn means fewer shift changes which in turn means less donning and doffing as well as fewer people exposed to the patient. All of these factors must be balanced against the increased complexity and potential risk of self-contamination associated with using PAPRs.

- The safety officer or 'buddy' who will be overseeing the donning and doffing of PPE should play an active role, directing the donning and doffing process following a checklist, not simply observing. The doffing and donning process should be deliberate and controlled. Particularly during the doffing process when the HCW doffing is hot, fatigued and anxious to remove their PPE.
- Specific training is required for those who are going to act as a safety officer ('buddy') to direct the donning and doffing of PPE.

Waste Management

We will not delve into the specific technical details regarding the infection control issues related to the handling of waste from a suspect or confirmed EVD case, as that information is well described elsewhere[10] [11] [12]. However, this section has been included simply to highlight for clinicians and the hospital leadership that this waste management may present several logistical challenges and potentially significant risk[1]. Plans and processes must be in place to address how waste will be managed in the patient's room, transport from the patient's room to a holding area, and ultimately transported for disposal in a safe manner. Restrictions on the transport and disposal of EVD waste can result from regulations and legislation existing from the Municipal through to Federal jurisdictions and therefore each hospital must tailor their policy to address these.

[10] *http://www.albertahealthservices.ca/assets/info/hp/ipc/if-hp-dis-ebola-waste-management.pdf*
[11] *https://www.tc.gc.ca/eng/tdg/safety-menu.htm*
[12] *http://www.publichealthontario.ca/en/BrowseByTopic/InfectiousDiseases/Pages/EVD_FAQ.aspx#EnvironmentalCleaning,WasteDisposalandLinens*

Care of the Suspect Ebola Patient

This is most likely the most challenging situation currently faced by clinicians in Canada, in relation to the current outbreak of Ebola. At the present time, the chance of a even a 'high-risk' suspect patient actually having EVD is most likely a fraction of one percent (one in a thousand or one in a million), nonetheless, given the need to protect the safety of the public and HCWs, appropriate precautions must be taken until they are confirmed to be free of the virus. At present, the turnaround time for EVD testing in many parts of the country can be 6 to 24+ hours, therefore it is not feasible to await these results before proceeding to investigate and treat the suspect patient. This however, leads to a significant number of logistical and ethical challenges for the clinicians caring for these patients.

First it must be recognized that although a 'suspect' patient is unlikely to have EVD, they are essentially certain to have some other medical illness (including potentially life threatening illnesses) otherwise they would not be 'symptomatic' and therefore would not meet the case definition for a suspect case. As a result, this creates the common, but uneasy, ethical dilemma faced in public health where the needs of the population at large are pitted against the needs of the individual. It has been stated with regard to the outbreak in Africa that Ebola will kill more people who have never contracted the virus then those who have due to the impact on health care delivery for other conditions. This statement holds an even greater potential to be true in Canada. In an effort to prevent this prediction from coming to fruition it is essential that clinicians aggressively seek out and treat any alternative diagnoses in suspect EVD cases. Failure to do so is likely to result in preventable morbidity and mortality among this population. A balance must be struck between the need to protect others and the need to provide appropriate medical treatment for the patient.

Investigations in Suspect EVD Patients

The infection control practices for laboratory investigations in suspected EVD cases result in a very limited menu of blood tests that are available for clinicians caring for these patients. This menu of options is even further curtailed if the hospital's laboratory is only able to provide limited point of care testing in these cases. Unfortunately, point of care testing is insufficient to appropriately evaluate many illnesses. As a result it is essential that processes are in place that will allow smaller community facilities to access a broader range of laboratory investigations that can be safely offered in EVD patients but which are only available at large academic centers. However, many of the same principles should apply in the management of suspect cases as in confirmed cases including the need to minimize lab tests. Therefore appropriate tests should be sent once

during the initial evaluation of the patient and follow-up testing should be limited to that which is essential. For example it is not necessary to repeat a patient's CBC every 12 hours if they appear clinically well and have no clinical evidence to suggest bleeding.

In addition to laboratory investigations, it may be necessary and helpful to obtain radiological investigations in suspect cases. Given that these patients are in isolation and their movement within the facility should be strictly minimized, portable investigations will be the most appropriate forms of investigation. Portable x-ray and ultrasound are the most feasible in this situation. Patients with suspected EVD will often have gastrointestinal complaints and therefore may require investigations to rule out diagnoses such as appendicitis or a perforated viscus. The index of suspicion for EVD versus other alternative diagnoses informed by the history, epidemiological factors, clinical findings and laboratory investigations should inform the degree to which radiological investigations are pursued. For example a patient with low risk epidemiologic links but peritoneal findings on clinical exam would certainly warrant a portable chest xray to rule out free air.

Empiric Therapies

Given the limited diagnostic capabilities, it may be necessary to consider more liberal use of empiric therapies than is typical. In particular the two conditions in this group that must be considered and may warrant early empiric therapy if clinical risk factors exist and diagnostic investigations are delayed are: a) malaria, and b) systemic bacterial infections. Both of these are potentially life threatening, and there is evidence to support the benefit of early initiation of therapy. Given the complexities in making decisions regarding empiric therapy in these cases early consultation with an Infectious Disease specialist should be sought to guide decision-making.

Life Support and Resuscitation

Given that most suspect cases of EVD currently presenting in Canada will NOT end up having EVD, life support and resuscitation should be considered if medically indicated in this group, particularly since even if the patient does have EVD they will most likely be in the early stage of the illness, free of multi-organ failure. In situations where cardiopulmonary resuscitation is attempted, the number of people participating in the resuscitation should be strictly limited (4 or less people). They should all be wearing PPE to protect against aerosols, and interventions should be limited to those that are of high clinical yield for mitigating readily reversible aetiologies.

Having said this, resuscitation in this group presents significant logistical challenges. The degree of PPE required will create significant delay in the response as providers don the equipment. This delay has the potential to significantly decrease the effectiveness of any resuscitation effort. Therefore the primary approach to mitigate this should be for early identification of any patient showing signs of deterioration and the institution of appropriate interventions prior to mitigate this prior to a crisis occurring. The literature demonstrates clearly that in the vast majority of cases, warning signs are present up to eight hours before a cardiac arrest occurs in a hospitalized patient.[4]

Given that it is not possible to predict and prevent all acute deteriorations in patients' conditions, hospitals should develop and exercise a protocol for responding to a code blue situation with a suspect EVD patient. The following should be key considerations when developing this plan:

- Focus on key interventions such as rapid automatic external defibrillation that can be easily initiated and have high efficacy with a plan to initiate this in a staged and prioritized fashion as team resources increase.
- Limiting the number of people involved in the resuscitation (3-4 people maximum)
- Meticulous attention to the use of appropriate PPE including its application in a rapid but safe manner
- Team leadership and the effective use of crisis resource management during the resuscitation to optimize the effectiveness and safety of the resuscitation.
- Packaging of limited essential kit to bring into the room.
- The presence of an organized team outside the room to support those within the room e.g. prepare medications, manage logistical issues, monitor team safety inside the room, etc

Clinical Care of Confirmed Ebola Infected Patients

Clinical Examination & Assessment

The discussion of this section will be brief and focus primarily on the identification of common complications associated with EVD and to provide a guide to the expected natural history of the illness. Clinical examination of the patient should occur at least twice daily (once per nursing shift) in patients who are not severely ill. Patients who are severely ill require more intense monitoring, similar to other critically ill patients. Monitoring should follow the usual approach to patient assessment with an additional focus on vital signs and their variability (discussed further below under 'Monitoring').

The natural history of Ebola is typically divided into three phases: early, late, and terminal or recovery[5-7]. Understanding the common findings during each of these phases will allow the clinician to identify both expected and unexpected complications should they occur.

The following features may be seen in the early phase of Ebola infection:

- Fatigue & malaise
- Generalized weakness
- Fever (sudden onset)
- Headache
- Myalgia & arthralgia
- Pharyngeal erythema
- Lymphadenopathy
- Nausea & anorexia
- Vomiting
- Diarrhoea (non-bloody) described as 'cholera like' in its volume

The following features tend to develop during the later phase of disease. It should be noted that often the features overlap and there is not a clear distinction between the phases. Additionally, despite the classification of Ebola as a "haemorrhagic fever" and the discussion of haemorrhagic symptoms below, bleeding is a predominant symptom in a minority of patients with Ebola.

- Abdominal pain (RUQ tenderness on palpation +/- hepatomegaly)
- Profuse diarrhoea
- Severe vomiting
- Hiccups
- Conjunctivitis
- Confusion, agitation, delirium, prostration, seizures, coma
- Maculopapular rash with erythema and desquamation
- Shock
- Chest Pain
- Icterus or jaundice
- Respiratory distress (rarely primary, more commonly in response to metabolic acidosis, volume overload, etc.)
- Miscarriage in pregnant women
- Capillary leak and peripheral oedema/third spacing
- Haemorrhagic manifestations
    - Ecchymosis & petechiae
    - Oozing from intravenous and venipuncture sites
    - Melena or hematochezia
    - Conjunctival haemorrhage
    - Epistaxis
    - Hematemesis
    - Hemoptysis
    - Vaginal bleeding
    - Hematuria

Patients who enter the terminal phase of the illness are often obtunded and hypotensive prior to cardiorespiratory failure.

Should the patient enter the recovery phase, it can occur over days, weeks or months [7]. Many symptoms may persist during this phase including weakness, weight loss, headache, migratory arthralgias, desquamation, hair loss, confusion, and anaemia. Additionally, late occurrences of acute orchitis and uveitis have been reported[7].

Monitoring (Invasive/Non-invasive)

As previously mentioned, the care of patients with EVD is primarily supportive.[6] Patients with probable or confirmed EVD should be monitored in a setting that is capable of intensive and frequent monitoring of vital signs, fluid balance, and neurologic status. Ideally all patient monitors should be visible from outside of the patient's room either via a window or satellite monitoring station and alarms must be audible from outside of the patient's room with the doors closed. Video monitoring of the room can also enhance the effectiveness of patient monitoring. Finally, the patient should have a mechanism to signal for assistance and communicate with staff outside of the room. In addition to monitoring, nursing staff caring for the patient should have well prescribed parameters for alerting the patient's attending physician if there is deterioration in the patient's status.

Non-invasive cardiorespiratory monitoring

Non-invasive cardiorespiratory monitoring including heart rate (EKG), respiratory rate, oxygen saturation (pulse oximetry) and non-invasive blood pressure (NIBP) should be available for all patients with Ebola, although the frequency of monitoring should be determined by the patient's clinical condition. The use and frequency, in particular, of NIBP monitoring of patients will have to be assessed on an individual basis, depending upon the patient's severity of illness, type of NIBP monitor and degree of capillary leak (ecchymosis & petechiae) as significant bruising may result particularly from older generation NIBP monitors that use repeat high cuff pressures. Newer generation of monitors and manual BP monitoring may be less traumatic.

Urine Output

Hydration and volume status are particularly important factors in patients with Ebola given both their gastrointestinal losses and the potential for capillary leak or haemorrhage. Therefore, close monitoring of urine output is an essential tool for detecting volume depletion, particularly since accurate documentation of fluid balance ("in's and out's") is often difficult in the setting of vomiting and diarrhoea. In less severely ill patients the measurement of voided urine is appropriate. However, if the patient is having significant

diarrhoea or is seriously/critically ill, the preferred method of monitoring urine output will be with a Foley catheter and urometer. This should be recorded on an hourly basis.

Sequential weight assessment may also be a useful index for fluid management particularly if the patient is exhibiting substantial unmeasured fluid losses due to diarrhoea or insensible losses.

Invasive arterial blood pressure monitoring

Invasive arterial blood pressure monitoring should be considered in select cases with hemodynamic instability requiring vasoactive agents and frequent blood-work monitoring. The potential benefits must be balanced against the risk of blood exposure and the potential for arterial spray of blood in the event of a circuit disconnect or leak. In most circumstances radial arterial access would be preferable over femoral access particularly given the frequency of soiling of the groin area, and for the possibility of coagulopathy among some patients. If the patient has central venous access in place and NIBP monitoring is effective, the additional benefit of arterial monitoring is minimal and may be outweighed by the associated risks to the patient, or of blood exposure to staff.

Central line access and central venous pressure (CVP) monitoring

The current literature on the utility of CVP monitoring is mixed. Given the lack of strong evidence to support the utility of CVP monitoring we would not recommend the establishment of central venous access for the purpose of monitoring alone. In such circumstances, assessment of volume status based upon clinical examination of the jugular venous pressure (JVP) or other clinical indicators is most appropriate. However, if central venous access has been established for an alternative indication, (difficult peripheral access, requirement for vasopressors, or electrolyte replacement) the use of CVP monitoring can be considered. Central venous access has been required in the management of the majority of EVD patients treated in 'Western' health care systems due to a) the requirement for aggressive potassium replacement and b) difficulty in obtaining peripheral venous access due to oedema. The use of central venous oxygen saturation as a measure of adequacy of forward flow may be useful if intravascular volume or cardiac function is uncertain and clinical examination is not adequately revealing.

End-tidal carbon dioxide ($ETCO_2$) monitoring

$ETCO_2$ should be considered in patients who are receiving mechanical ventilation. The combination of $ETCO_2$ monitoring and pulse oximetry may decrease the need for arterial blood gas analysis, potentially eliminating the need for an arterial catheter or for repeated arterial punctures and thus the risk of needle stick injuries to staff.

Other invasive monitoring

In general, it is best to minimize any forms of invasive monitoring due to risks associated with coagulopathy, sharps exposure during insertion and body fluid exposure. It is unlikely that any forms of invasive monitoring aside from those listed above would be necessary for the management of a patient with EVD.

Body Fluid Control

Given that Ebola is primarily transmitted through body fluids (blood, urine, diarrhoea, emesis, saliva, and other fluids) control of these substances is vital in preventing transmission and protecting health care workers. If the patient is continent of faeces and urine, access to a private washroom or bedside commode should be ensured. The experience at Emory reveals that many of the patients were too weak to walk to the bathroom and therefore a bedside commode was the preferred option. However, given the 'cholera like' volumes of diarrhoea the traditional bedpans used in commodes have been too small to accommodate the volumes of diarrhoea experienced. A convenient solution to this problem has been to replace the commode bedpan with a 10 gallon bucket. The use of a 10 gallon bucket not only accommodates the volumes of stool experienced but also allows a lid to be secured on the bucket before it is moved therefore decreasing the splash risk to staff.

If the patient is incontinent of urine or faeces the use of a Foley catheter and/or faecal collection system should be considered, especially in children. Nasogastric tubes with gastric suctioning or drainage may be useful in preventing or minimizing vomiting. If body fluids are spilled in the patient care environment, the appropriate containment and environmental cleaning guidelines should be followed[13]. Consider the use of products that absorb urine, vomit, stool and make them non-liquid, thus decreasing the risk of splash exposure to staff. Additionally, prior to adding the solidifying solution, some centers add a disinfectant to deactivate the virus.

[13] http://www.phac-aspc.gc.ca/id-mi/vhf-fvh/ebola-ipc-pci-eng.php

Airway Management & Ventilation

Pulmonary involvement of Ebola is not a common feature of the disease, however respiratory failure may occur in these patients requiring mechanical ventilation. Secondary causes of respiratory failure may include (but are not limited to) shock, fatigue from prolonged compensation of metabolic acidosis and iatrogenic complications (e.g. transfusion-related lung injury). Airway management may be required independent of respiratory failure for airway protection purposes, with situational examples including decreased level of consciousness or massive upper GI bleeding.

Non-invasive ventilation

Non-invasive ventilation (NIV) may be considered for support of patients with EVD having rapidly reversible causes of respiratory failure; however, there are significant concerns that warrant caution and likely outweigh any potential benefits of NIV in this patient population. First, many patients with EVD have frequent vomiting which will increase the risk of aspiration. Second, NIV will cause prolonged risk of aerosolization, and therefore must be performed in a negative pressure isolation room. All staff managing a patient on NIV must wear the PPE required during aerosol generating procedures while in the patient room. Third, should the patient fail NIV and require immediate intubation, there is higher risk to staff by rushing to don PPE leading to a breach of infection control and possible transmission. Therefore, should a trial of NIV be performed, close and frequent monitoring must be performed to identify need for intubation as early as possible to allow sufficient time for staff to carefully prepare equipment and institute appropriate infection control practices. Fourth, the risk of oropharyngeal bleeding and hematemesis with an NIV mask in place may create significant risk to the patient for aspiration, with a significant delay in staff response to assist due to need to don PPE when entering the patient room. In general, it is safer to manage a patient with EVD and respiratory failure using a strategy including elective intubation, traditional mechanical ventilation including filtration of exhaled gases, and frequent monitoring of improvement in clinical status leading to a controlled attempt at extubation as the patient responds to therapy.

Endotracheal intubation

The need for endotracheal intubation should ideally be recognized early enough to allow a non-emergent procedure, thus avoiding a potential rush leading to mistakes in use of personal protective equipment (PPE) and other infection control precautions. In addition to the usual clinical indicators suggesting the potential for a difficult intubation, patients with EVD may have nasopharyngeal or oropharyngeal bleeding impairing

visualization of the vocal cords during intubation. An exhalation filter should be attached to the bag ventilation device.

Appropriate PPE must be worn when preparing for high-risk aerosol generating medical procedures, such as airway management. As per Infection Prevention and Control guidelines[14], this must include protective fluid resistant or impermeable clothing that provides facial/eye protection including goggles or face shield, and a respirator mask with protection at least equivalent to meet N95 standards with appropriate fit testing for the specific respirator. For those properly trained in their use with meticulous attention paid to avoid self-contamination upon doffing, clinicians may also consider using full hood powered air purifying respirators (PAPR) as a more comfortable option that provides better protection against sprayed body fluids while at the head of the bed, along with fluid-impermeable clothing preventing any skin exposure such as a full body suit. Current infection control recommendations include having patients in negative pressure isolation rooms during performance of any aerosol generating medical procedures. Although the airborne spread of Ebola is not a usually recognized mechanism of transmission in humans, the potential for aerosol generation of other primarily droplet transmitted viruses has been demonstrated during some procedures such as intubation[8, 9], and the presence of an anteroom in typical negative pressure patient isolation rooms allows safer donning and doffing of PPE.

The patient should be intubated by a clinician highly experienced in airway management (e.g. staff anaesthetist or intensivist). Some adjunctive strategies beyond the use of direct laryngoscopy may be helpful. Video/optical laryngoscopy should be considered to allow better visualization of the vocal cords in anticipated or unanticipated difficult airway, and will increase the distance between the patient and the clinician during the intubation, which may reduce the likelihood of aerosolization exposure or inadvertent dislodgment of PPE.

Rapid sequence intubation, including the use of rapid-acting neuromuscular blockade, should be considered. Given the potential for hemodynamic instability in patients with EVD, the medication regimen for sedation should consider use of agents that are less likely to drop the blood pressure, such as ketamine, or use of agents to mitigate or prevent hypotension to due direct side-effects or sedatives, or loss of intrinsic sympathetic activation. Good intravenous access must be present to allow rapid fluid resuscitation in case the blood pressure drops during the intubation process, and vasopressors (e.g. phenylephrine or ephedrine) should be immediately available to administer as a bolus if required.

[14] http://www.phac-aspc.gc.ca/id-mi/vhf-fvh/ebola-ipc-pci-eng.php

Mechanical ventilation

Usual practices regarding invasive mechanical ventilation should be followed, including avoidance of excessive tidal volumes (keeping Vt < 6 ml/kg if possible), avoidance of excessive plateau pressures (keeping less than 30 cm H20), appropriate positive end expiratory pressure (PEEP) to avoid recurrent atelectrauma. Ventilators must have capability for HEPA filtration of exhaled gases. Given the potential risk for unexpected aerosol generating medical procedures (i.e., accidental extubation requiring immediate re-intubation), the patient should be maintained in a negative pressure isolation room. Ideally, an interface between the mechanical ventilator and the patient monitoring system will allow easier monitoring of ventilation parameters without frequent re-entry into the patient room. An emergency plan must always be in place as to how self-extubation, ventilator disconnect will be managed and the necessary equipment is in the room. The ventilator will have to be disinfected at the end, currently Emory keeps all non-disposable equipment in the patient's room until discharge at which time they have a company disinfect it with vaporized hydrogen peroxide prior to being returned to general circulation.

Fluid Resuscitation & Electrolytes

With critically ill EVD patients, hypovolemia is the most common and predictable anomaly. Accordingly, administration of fluids and electrolytes constitutes the first step in a series of supportive care interventions. Persistent fluid loss, potentially compounded by shock due to other causes, often requires on-going fluid replacement. There are no studies specific to the treatment of patients with EVD to guide fluid management strategies in these patients. The suggestions below are largely extrapolated from other literature such as the management of Dengue Haemorrhagic Fever or septic shock.

Oral fluid and electrolyte replacement

Oral fluid and electrolyte replacement is preferred in patients who are not critically ill, who are able to drink and not suffering from significant nausea and vomiting. Purpose designed oral rehydration solutions will provide the most effective volume replacement and electrolyte replacement in those with significant diarrhoea. Anecdotal observations made during the West African outbreak suggest, however, that many cases may be associated with an inability to eat and drink adequately thereby limiting the utility of the oral route for rehydration and electrolyte replacement. Early NG tube insertion for fluid and electrolyte repletion may be considered, especially for children.

Intravenous access

Intravenous (IV) access will be required for those patients who are unable to tolerate oral fluids or hemodynamically unstable. In the early stages of EVD and for those with milder manifestations of the illness

peripheral IV access is suitable for fluid management. Large bore IVs (14-18 gauge, for adults, and age-appropriate for children) are preferred to allow large volume fluid resuscitation in the event the patient deteriorates. Central or peripherally inserted central venous access should be considered for patients who require intravenous electrolyte replacement (particularly potassium), vasopressors, or where vascular collapse limits peripheral IV access and increases the multiple attempts at IV insertion with the associated needle stick injuries and potential bleeding complications for the patient and blood exposure to staff. In the event that central venous access must be obtained, the risk of injury to either the patient or staff can be minimized by having an experienced physician conduct the procedure under direct ultrasound visualization with the patient calm or sedated. At all times, caregivers should adhere to recommended barrier precautions and personal protective equipment. Consideration should be given to using non-suture securing devices to minimize skin punctures as well as the risk of needle stick injuries. For both peripheral and central IV lines needle-less systems should be used to avoid sharps injuries.

Intravenous fluid replacement and resuscitation

The amount of intravenous fluid administration required will depend upon the specific patient's symptoms and should be guided by the degree of overt volume loss (diarrhoea, vomiting, and urination) as well as factors suggesting volume contraction: decreased skin turgor, dry mucous membranes, tachycardia, decreased urine output, and hypotension. We suggest that Ringer's lactate (LR) should be the fluid of choice for volume replacement. This is based upon evidence extrapolated from the management of patients with Dengue Haemorrhagic Fever[10] and the management of septic shock[11-13]. There is evidence to suggest that compared with Normal Saline, Ringer's Lactate may be associated with lower rates of mortality[13], renal failure[12], acidosis[14-16], and haemorrhage[17-19]. For patients that are hypotensive initial boluses of Ringer's Lactate in the order of 20ml/kg should be considered and repeated as required until the heart rate, blood pressure and parameters of end-organ perfusion are within the desired range. Pulmonary oedema has been noted after excessive fluid resuscitation from the Emory experience, requiring mechanical ventilation. In the event where large volumes of crystalloid solutions are being administered, consideration may be given to the use of albumin[20]. Artificial colloids (e.g. pentastarch or hydroxyethyl starch) should be avoided given their associated risks of renal injury[21], bleeding[22] and mortality[23]. In the event the patient is haemorrhaging and/or coagulopathic consideration should be given to the administration of packed red blood cells, platelets, fibrinogen and plasma as required based upon their hematologic laboratory values and clinical findings. A target haemoglobin of greater than 70 g/L is recommended. There is no evidence to support the transfusion of platelets and coagulation factors in patients with DIC who are not bleeding or who are not at high risk of bleeding. However, treatment is justified in patients who have serious bleeding, or are at high risk

for bleeding, or require invasive procedures. Platelets should be administered to patients with a platelet count of less than 20 x 10^9/L or if less than 50 x 10^9/L and associated with serious bleeding. If serious bleeding is occurring and the INR is greater than 2, fresh frozen plasma (FFP) should be administered. Similarly if the fibrinogen is low in the face of significant haemorrhage cryoprecipitate should be transfused. When managing a patient with EVD who is experiencing DIC and haemorrhage clinicians should consult a haematologist and/or their blood bank physician. In certain cases the potential efficacy of multiple transfusions must be weighed against the availability of resources.

Blood Products

It is very likely that EVD patients (both confirmed or suspected) may require blood products as part of their clinical management. However, the provision of blood products to these patients presents significant technical and patient safety challenges given that no samples from any suspected or confirmed Ebola patients should be sent to the blood bank given that blood bank testing is "open" and therefore not allowed (or safe), until Ebola results come back negative.

Each blood bank therefore must have a protocol and process in place to manage blood product transfusion issues for this group of patients. At present many hospitals are not doing phenotyping – but are providing phenotyped units based upon the following approach:

- *Unknown to the hospital and never been seen by a blood bank elsewhere:* – issue O neg, Kell neg (so E,C,K neg = 85% of antibodies mitigated)
- *Unknown to the hospital but seen elsewhere* – get info from all other hospitals – issue O neg, kell neg as above + any antibodies matched (eg. jka, etc.)
- *Known to the hospital* – same as above
- *Sickle cell patients* – give phenotyped matched based on CBS registry + matched for any antibodies

When the transfusion is provided it is recommended that a very cautious 15 min test dose be undertaken at the beginning of the transfusion as essentially the final crossmatch will be done in the patient.

This approach will work if the incidence of Ebola cases (confirmed or suspect) remains rare. However, this strategy will have to be revised if Ebola becomes common as there will not be enough O neg blood available to sustain the approach.

Electrolyte replacement

Clinicians should expect and monitor for significant electrolyte deficiencies (particularly hypokalemia and metabolic acidosis secondary to bicarbonate loss from vomiting and diarrhoea respectively) to occur in those patients suffering vomiting and/or high volume diarrhoea. As stated earlier, if tolerated, oral replacement of electrolytes is the preferred method. Consideration should be given to adding potassium and bicarbonate to appropriate maintenance IV fluids early for patients with diarrhoea to prevent severe hypokalemia (assuming there is no evidence of renal failure) and metabolic acidosis. Hypocalcemia is often observed, and will frequently require aggressive replacement. In the event that concentrated intravenous electrolyte replacements are necessary, central venous access will be required in addition to ensuring appropriate cardiac monitoring is in place. Electrolyte replacement protocols that adhere to the ISMP[15] or WHO[16] best practices for concentrated electrolyte replacements should be used. Given the importance of electrolyte management in this patient population, central laboratory or point-of-care testing should include the ability to measure serum sodium, potassium, sodium, bicarbonate, creatinine, glucose, lactate, calcium, magnesium and phosphate.

Vasopressors

Hypotensive patients failing to respond to volume resuscitation, or while volume resuscitation is in progress, should be supported with vasopressor therapy in accordance with the guidelines for the management of septic shock[11]. Prescribing and monitoring of vasopressor agents should adhere to the recommendations for safe practice from the ISMP[17]. The guidelines for vasopressor use in septic shock are:

- A mean arterial blood pressure (MAP) target of 65-70 mmHg (or median for age in children) is a reasonable initial target in adults [24] but should be re-assessed based upon individual patient factors such as a history of hypertension and indicators or whether or not satisfactory end-organ perfusion is being achieved.
- Norepinephrine infusion (up to 1.0 µg/kg/min) is the preferred first-line agent for managing hypotension.
    - In the event norepinephrine is administered via a peripheral IV the maximum concentration used should be no more than 4mg/250 ml ('single strength'); a large bore IV should be used

[15] *https://www.ismp.org/tools/institutionalhighAlert.asp*
[16] *http://www.who.int/patientsafety/solutions/patientsafety/PS-Solution5.pdf*
[17] *http://www.ismp-canada.org/download/safetyBulletins/2014/ISMPCSB2014-1_ImprovingVasopressorSafety.pdf*

preferably in the antecubital or other large vein with good flow and it should be closely monitored for signs of extravasation.

  - Centrally administered norepinephrine can be mixed in concentrations of 8mg/250ml ('double strength') or 16mg/250ml ('quad strength').

- Vasopressin 0.03µg/min or 0.04µg/min may be used to minimize the dose of norepinephrine required
- Epinephrine can be added as a second line therapy
- Except in the instance of bradycardia and potentially paediatric patients, dopamine should generally be avoided given its association with increased rates of cardiac arrhythmias and mortality[11, 25].
- Dobutamine (0-20 µg/kg/min) can be considered if there is evidence of myocardial dysfunction or on-going hypoperfusion following adequate volume resuscitation.

Antibiotics & Antivirals

The clinical manifestations of severe Ebola disease may overlap with symptoms and signs observed in septic shock of bacterial origin. The published literature is generally silent on the incidence of bacterial superinfection in the context of Ebola. Almost all published data from previous case series were derived from settings where bacterial cultures were unavailable. Post mortem pathology has been described in a limited number of cases. Extensive necrosis of a variety of organs, especially liver, spleen, kidneys, and gonads is associated with direct viral cellular invasion, although the gut appears to be relatively spared. Alveolar damage with interstitial oedema is common on pathology of deceased patients but not a common clinical syndrome. A dysregulated highly pro-inflammatory and procoagulant state is typical of EVD.

It appears that bacterial infection or sepsis is an uncommon manifestation or complication of Ebola. Despite this, the use of appropriate antibiotics to those with manifestations of possible bacterial sepsis is reasonable early in the course of the disease where GI symptoms predominate and the risk of bacterial translocation is present. However, it is important to discontinue antibiotics in those where the diagnosis of EVD has been confirmed and particularly when cultures and other relevant investigations do not reveal a bacterial infection. There is no evidence-based guidance on the choice of specific antibiotics; however, patients frequently will manifest severe gastro-intestinal symptoms and antibiotic choice should cover potential enteric pathogens, among others. Broad-spectrum antibiotics should be used sparingly to avoid the potential for bacterial superinfection with CDI and/or multi-drug resistant pathogens, which might contribute to added morbidity and mortality from the medical management of EVD.

Organ Support (IHD, CRRT, ECMO)

A small subset of patients with severe EVD will progress to organ failure requiring extracorporeal supports during the course of their illness. Any decision to use extracorporeal support must incorporate any baseline coagulopathy present.

Renal failure is common in severe cases and renal replacement therapy has been used in recent cases to good effect in the appropriate setting. In appropriate settings, dialysis should be considered in the patient with EVD and renal failure. The mode of dialysis, whether intermittent hemodialysis or continuous renal replacement therapy (CRRT), should be individualized based upon the patients status and the treating clinician. However, the use of CRRT will minimize the need for additional staff to enter the patient's room as CRRT is typically managed by critical care nurses. It is reassuring to note that investigations conducted at Emory the Ebola virus was NOT detected in the dialysate fluid of EVD patients receiving dialysis.[1] Recently the CDC has provided a guidance document on the provision of CRRT based upon the experience at Emory.[18] We suggest any hospital considering providing CRRT to a patient with EVD review the CDC document and develop their own internal SOP's based upon the guidance provided.

Liver dysfunction progressing to liver failure is a major consideration for severe EVD, with hepatocellular necrosis found in the few autopsies performed in severe EVD.[26] Extracorporeal liver support is not recommended in severe EVD, given the scant evidence base, and therapy for liver failure should be supportive, including correcting metabolic abnormalities, monitoring (clinical or non-invasive) for cerebral oedema, and correcting coagulopathies.

Extracorporeal membrane oxygenation (ECMO) for cardiorespiratory failure has not been reported in severe EVD. The initial presentation of severe EVD very uncommonly includes severe respiratory or myocardial failure, with the nature of the shock typically being hypovolemic or distributive in nature.[7] The limited potential benefit of ECMO in this setting must be weighed against the potential for significant blood exposure to staff during cannulation and bleeding complications from the sites of cannulation due to the coagulopathy that can accompany EVD, particularly in severe and refractory cases. Further, the close monitoring and care demands associated with patients on ECMO would result in significant exposure time for staff. Therefore we do not recommend ECMO in patients with EVD.

[18] *http://www.cdc.gov/vhf/ebola/hcp/guidance-dialysis.html*

Cardiopulmonary Resuscitation

Data, and clinical experience, with cardiopulmonary resuscitation (CPR) in patients suffering from EVD is completely lacking. However, when considering the role of CPR four primary issues should be considered:

I. Medical indication and utility of CPR in that context

II. Ability to provide effective CPR

III. Safety of those providing care

IV. Patient's preferences

As with any medical treatment, the first step in the decision to offer a therapy is whether it is medically indicated, is it likely to improve the physiological issue. At baseline the likelihood of survival with a good outcome from cardiac arrest in intensive care units is poor, approximately 3%[27, 28], and is likely lower in adult patients with multi-organ failure. Patients with late stage EVD who experience an un-witnessed cardiac arrest in the context of multi-organ failure (MOF) have minimal expectation of survival. Similarly, patients with multi-organ failure being supported with artificial life support in a critical care environment who deteriorate to cardiac arrest despite full support, are also highly unlikely to survive. A very select group of patients with EVD who are experiencing clinical conditions that are potentially associated with better outcome from cardiac arrest, such as hypovolemia or electrolyte abnormalities, an acute coronary syndrome associated with ventricular arrhythmias, may benefit from therapies including defibrillation and anti-dysrhythmic drugs for witnessed cardiac arrest.

If medically indicated, the feasibility of providing effective CPR in this context can be a significant challenge for a number of reasons. As critical care clinicians are aware, the time to initiate CPR in a patient suffering a cardiac arrest is critical in order to prevent ischemic organ damage. The time required for the resuscitation team to arrive and don PPE often will take on the order of 10-15 minutes or more, which is beyond the window of preventing organ damage. Additionally, performing effective chest compressions is very physically demanding and can only be sustained for a short period requiring frequent change of providers. This also presents a challenge with a very limited team size of 3-4 people wearing PPE.

HCW safety in rescue and resuscitation is always a primary consideration but particularly in patients with serious infections which have previously been implicated in HCW transmission in other outbreaks[9]. There is a significant risk of body fluid exposure, needle stick injuries, and other exposures during resuscitation. Despite the instinctive urge to rush into a patient isolation room to help, staff **must not** take shortcuts in

donning appropriate PPE, which should meet the standards required for management of aerosol generating medical procedures.

Taking all of the above issues into consideration, in the majority of situations CPR will not be able to be offered to patients with EVD. The responsible physician (ideally in conjunction with the clinical team and hospital) need to decide on their approach to offering CPR in advance and be sure to communicate their decision to offer CPR to the patient and/or family. If a hospital and the clinical team felt they were able to identify a process to provide safe and effective resuscitation that would be associated with a high likelihood of survival and return to a good QOL, our recommendations should not preclude their decision to offer CPR. If offered, as for any therapy the patient or their substitute decision maker may choose to accept or decline the therapy.

A child who suffers cardiac arrest due to severe EVD and multi-organ disease also has a very small likelihood of survival, and similar to adults, not initiating CPR is appropriate in this circumstance. If a clear reversible cause is present, however, this should be promptly treated.

Medical management of cardiac arrest in a patient with Ebola, if attempted, should follow current BCLS and PALS/ACLS guidelines.

Symptom Management

Given that the overall management of EVD is supportive, effective symptom management composes a significant component of the therapies clinicians may offer their patients.

Symptom	Aetiology & Implications	Management
Seizure or Coma	Aetiology unclear, potentially related to liver failure or direct viral CNS invasion. Typically an ominous sign, seen typically shortly before death.	Airway management as required Benzodiazepines +/- dilantin to control seizures Laboratory investigations (e.g. Na+, glucose) CT head if lateralizing features
Hypotension & Shock	Frequently an early manifestation of severe cases. Also a common manifestation of illness severity and plausible lethal pathway. Initially, hypovolemia from profound GI losses. A component of early distributive shock remains a possibility but has not been confirmed. Secondary sepsis remains a possibility but has not been confirmed.	Close monitoring of fluid balance Aggressive repletion of fluid and electrolyte losses (potassium, bicarbonate) Consider vasopressor therapy if hypotension continues despite adequate fluid resuscitation.
Dyspnea or Respiratory failure	Respiratory involvement not a cardinal feature. Polypnea seen at all stages of illness in the context of shock and profound metabolic acidosis, or with pulmonary oedema following fluid resuscitation.	Oxygen therapy +/- mechanical ventilation
Severe diarrhoea and vomiting	Frequent early presentation, the aetiology of which remains unclear.	NG tube insertion & suction Ondansetron ≤40 kg: 0.1 mg/kg iv or >40 kg: 4 mg as a single dose over 2 to 5 minutes Haloperidol 1mg PO/IV/SC q8h standing. (0.25-0.5 mg in children) Metoclopramide 10mg PO/IV/SC q6h standing (0.1 mg/kg/dose in children)

Intolerant to oral intake	Common in severe cases. Associated with chest pains so esophagitis is a plausible mechanism but unproven.	Consider enteral nutrition if tolerated If enteral nutrition are poorly tolerated, consider TPN after 8 days of unsuccessful enteral nutrition
Hiccups	Common in severe cases.	Consider enteral nutrition via NG tube. Symptomatic management with chlorpromazine.
RUQ pain and hepatomegaly	Common in severe cases Unproven but hepatitis plausible	Monitoring of liver biochemistry, consideration of vitamin K for early signs of INR elevation, watch for hypoglycaemia
Haemorrhage (GI & puncture sites)	Ominous sign, seen typically shortly before death Aetiology most likely DIC	Complete haematology and liver laboratory workup Consider platelet transfusions is low, FFP if INR elevated, cryoprecipitate if fibrinogen low
Fever, chills, headache and myalgias	Common Aetiology associated to viremia	Acetaminophen 650mg PO q4h PRN (maximum 4g in 24h) (Paediatrics 10-15 mg/kg/dose Q4H to in children, max of 5 doses per 75 mg/kg/day). Lower doses may need to be used in patients experiencing hepatic dysfunction. Non-steroidal anti-inflammatory medications should be strictly avoided due to their platelet-inhibiting effects, which could exacerbate haemorrhage
Pain	Common, often involving abdomen, chest wall, headache and joint pain that are not adequately managed with acetaminophen alone.	Narcotics, morphine, fentanyl, hydromorphone if renal impairment

Prophylaxis and Preventative Measures for the Critically Ill

Patients with severe EVD have multi-organ disease and avoidance of secondary infections and complications is vital, given the associated immune dysregulation with acute EVD.[29] Standard protocols for the avoidance of nosocomial infections should include maintaining the head-of-bed at 30° for ventilated patients and limiting indwelling urinary catheter and central venous line days, where applicable. Specifically, strategies to avoid ventilator associated pneumonia, such as keeping the head of the bed elevated and chlorhexidine mouth care, should be followed. GI bleeds are frequent in severe EVD, and stress ulcer prophylaxis with either a histamine-2 receptor antagonist or a proton-pump inhibitor is recommended for patients who are mechanically ventilated. If patients develop coagulopathies they should not receive deep-venous thrombosis prophylaxis.

Nutrition

In less severely ill patients with Ebola, oral rehydration fluid should be provided to maintain intravascular volume and normal electrolytes. Smaller volume, more frequent eating may be better tolerated. Prophylactic antiemetic medication may be helpful to encourage oral intake. Oral nutritional supplements could be considered for those patients with suboptimal intake. In patients too unwell to safely swallow, placement of a nasogastric tube may be considered to allow provision of enteral feeds to meet nutritional and fluid needs. Similarly, intubated patients should have early placement of an orogastric tube and initiation of enteral feeds. Use extreme caution in placing a nasogastric tube in patients already experiencing mucosal bleeding due to haematological complications of Ebola infection. Patients already experiencing diarrhoea may

note worsening of their symptoms with enteral feeds, and therefore consideration of feeds with lower osmolality or semi-elemental feeds may help avoid worsening of diarrhoea. Enteral feeds are highly preferred to parenteral nutrition, and there are no data describing the risks and benefits of using parenteral nutrition in patients with Ebola infection. Early consultation with a dietician is strongly recommended to assist with choosing appropriate enteral feeds, and ensuring that adequate caloric, protein and other nutrient needs are being met.

Experimental Antiviral Medications & Vaccinations

The information regarding various experimental medications continues to evolve rapidly. Each institution should have in place a mechanism for rapid informed consent should utilization of such medications be contemplated. It is likely that clinical trials involving some of these medications will become available, and institutions should consider expedited review of these protocols as they are developed, so that they can be implemented in a timely fashion. Experimental vaccines are available in limited quantities at present and may be accessible for post-exposure prophylaxis (PEP) as part of a clinical trial. If a hospital is treating a confirmed EVD patient they would be prudent to discuss in advance with their Public Health Agency whether or not it is possible to access vaccine for PEP in the event of a detected high risk breach in PPE. Given the time to administration of PEP in these circumstances is very short, it would likely be necessary to have the discussions ahead of time and vaccine available on site.

Discharge Decisions

Once a patient with EVD has recovered, discharge from the hospital can be considered once they are physically well enough to leave hospital and their infectious risk is minimal. Establishing precisely when to discharge the patient must be made on a case-by-case basis and the decision should be made in conjunction with Infectious Disease and Public Health consultants. In general current criteria that have been used for guiding discharge decisions are:

- The patient has been symptom free for greater then 72 hours
- Two consecutive blood samples at least 24 hours apart have been negative for the Ebola virus by PCR

Given evidence that suggests the Filoviruses may persist for prolonged periods in some body fluids[7], patients should be given instructions on discharge regarding issues such as use of condoms for sexual activities.[19]

Palliative Care

Key Messages:

- Symptom management is important for patients, and should be provided early even for patients who are expected to survive.
- Honest communication allows the patient and family to participate in good decision-making, and receive support during their grief and bereavement.

Patients may present *in extremis*, or they may deteriorate after receiving aggressive medical care for some time. Healthcare providers (HCP) have an obligation to provide appropriate symptom management for their patients.

Sudden Terminal Events (Massive hemoptysis, asphyxiation)

- Midazolam 5-10mg IV/SC q5min PRN
- Deliberate terminal sedation may be important to avoid severe suffering at the time of death. This would be standard practice for such events in palliative care units. It may be necessary to keep this medication near the bedside so that it can be given in a timely fashion.

Communication is another important component of palliative care. Patients dying of viral haemorrhagic fevers such as Ebola are different from our classical model of Palliative Care because the patients are often young and previously healthy. In such situations, physicians may hesitate to communicate dire prognoses. It is important to communicate honestly and openly with family members, so that they can participate effectively in care decisions, and be supported through their grief and bereavement.

Pregnancy & Obstetrics

Ebola virus disease may affect women of child-bearing age, and it is possible that pregnant women may present with this infection. Literature regarding EVD in pregnancy is limited but includes a single case-series of

[19] *http://www.phac-aspc.gc.ca/id-mi/vhf-fvh/cases-contacts-cas-eng.php*

15 women[30], which suggests an increased severity of illness, high incidence of spontaneous abortion and risk of severe genital bleeding.

Management should include consideration of alternative diagnoses, particularly those associated with fever and/or coagulopathy, such as puerperal sepsis, TTP, HELLP as well as benign gestational thrombocytopenia. Pregnancy normally is associated with a mild leukocytosis but platelet counts are usually unchanged. Pregnant women have friable upper airway mucosa, increasing the likelihood of bleeding related to tube insertions and manipulation. Clinical management would not be very different to the non-pregnant patient, with a few exceptions. Fever is likely harmful to the foetus and should be avoided. Left lateral positioning is important to prevent the supine hypotension syndrome, in the 2nd half of pregnancy. Usual infection control precautions should be supplemented with for planning for management of excessive blood loss, with higher blood loss anticipated post Caesarean section. Planning for spontaneous delivery should include adequate PPE and equipment for obstetric and neonatal teams, as well as an assessment of viability of the foetus (by Obstetrics and Neonatology), to avoid the risks associated with futile neonatal resuscitation.

Paediatric Considerations

All of the above issues are applicable with the child with suspected or proven EVD. Children are especially susceptible to electrolyte abnormalities and hypovolemia; hence early recognition and aggressive treatment should be the standard of care. Given the expertise and infrastructure available, these children should be considered early for transport to the regional paediatric facility for on-going evaluation and care, especially given the challenges in obtaining intravenous and/or intra-arterial access and the availability of PICU beds.

Impact on Health Care Worker's Caring for EVD Patients

It is understandable for HCWs to be concerned about the risk of becoming infected and transmitting infection to their family or friends. However, caring for EVD patients while following recommended infection prevention guidelines, including wearing appropriate PPE, presents a very low risk to HCWs of becoming infected. This being said, the recent infection of HCWs caring for patients in 'Western' health care systems with adequate access to PPE has highlighted the lack of margin for error in the use and removal of PPE.

There are no restrictions (e.g. quarantine) placed upon HCWs who care for EVD patients who have not experienced a noted breach in infection control procedures. However, HCWs caring for EVD patients are

recommended to self-monitor for fever, for the full details on current guidance please refer to[20]. Hospitals should have policies in place that provide necessary supports for HCWs providing care to EVD patients, including protocols for self-monitoring for fever, and for management of blood exposures, in the unlikely event that they occur. Additionally, a process should be in place to manage a HCW who becomes febrile after having cared for an EVD patient, and the HCWs should be informed of the process.

Psychological Support (Patients, Families & Providers)

Rare and life threatening infectious diseases can be associated with significant psychological stress for both the patients who are infected with the diseases and their families as well as the providers who care for them.[31-34] The WHO Viral Haemorrhagic Fever handbook states:

> ***"Psychological support for the patient and the family are very important in the management of VHF. Anxiety and fear are normal given the high mortality rate for confirmed VHF. It is important to communicate well with the patient and family, explaining the need for isolation and PPE, and to provide psychological support from the beginning of care."***

Hospitals should plan to provide supports for both patients and their families. This includes ensuring that processes are in place to allow communication and visitation between patients and families. Given the concerns regarding transmission and desire to minimize patient exposure leveraging technologies such as internet video chat should be considered and the necessary IT infrastructure should be provided. Support services including Social Work, Chaplaincy and Psychiatrists should be available to support EVD patients and their families. Additionally, the stresses associated with coping with an EVD infection should be 'normalized' and acknowledged.

Support services for staff should also be provided. Hospitals should have a plan in place to support health care workers caring for EVD patients. If at all possible, resilience training should be provided in advance of staff providing care for EVD patients to potentially protect them from the stress of the situation.[35] Staff caring for EVD patients may face a variety of stressors including: fear of contracting the illness, concern for infecting family members, prolonged periods in PPE, social isolation, and fatigue from long hours of work.

[20] http://www.phac-aspc.gc.ca/id-mi/vhf-fvh/ebola-ipc-pci-eng.php

Inter-facility Transport of Patients with EVD

General Considerations for Aeromedical Evacuation

To date there is very little experience with aeromedical evacuation of patients with EVD, however all of the basic principles of aeromedical evacuation apply[36]. Transport of a high-risk patient should occur on an aircraft dedicated to single patient, without additional patients on board. Crew should be kept to the minimum required to carry out the flight and patient care duties in a safe manner. Those not directly involved in aircraft operation or patient care should not be present on board. A primary caregiver(s) should be assigned to the patient, based on the patient's needs for care. The type and scope of practice should be determined based on the patient's needs prior to transport and allow for medical management of any deterioration in clinical condition that could occur during transport. All patients and equipment must be secured within the aircraft in accordance with Transport Canada regulations. Additionally all equipment used on the aircraft must meet airworthiness testing standards. Finally, flight safety must remain a primary consideration for the aircrew, medical staff and the patient including response to in-flight emergencies and emergency egress.

Aircraft Selection

Cabin airflow characteristics may reduce exposure of occupants to airborne infectious particles. Whenever possible, aircraft used to transport patients with diseases transmitted by airborne spread should have separate air-handling systems for the cockpit and cabin, with cockpit air at positive pressure relative to the cabin.

- Fixed-wing pressurized aircraft:
    - Providers should consult the aircraft manufacturer to identify cabin airflow characteristics, including HEPA filtration and directional airflow capabilities, air outlet location, presence or absence of air mixing between cockpit and patient-care cabin during flight, and time and aircraft configuration required to perform a post- mission airing-out of the aircraft.
    - Aircraft with forward-to-aft cabin air flow and a separate cockpit cabin are preferred. Aft-to-forward cabin air flow may increase the risk of exposure of cabin and flight deck personnel if aerosol generating procedures are conducted. Aircraft that re-circulate cabin and flight-deck air without HEPA filtration ideally should be avoided. Aircraft ventilation should remain on at all times during transport, including during ground delays.
- Rotor-wing and non-pressurized aircraft

- In aircraft with uncontrolled interior air flow, such as rotor-wing and small, non-pressurized fixed-wing aircraft, all personnel should wear disposable N95 or higher-level masks during transport of patients where airborne spread of disease is possible. For cockpit crews, aircraft aviator tight-fitting face pieces capable of delivering air/oxygen that has not mixed with cabin air may be used in lieu of a disposable N95 respirator.

The type and size of aircraft will determine the extent to which optimal capabilities and practices can be carried out. The greatest separation possible between the aircrew and patient is desirable particularly for longer duration flights given that a lack of sufficient separation would require the aircrew to wear PPE, which in turn, could degrade their flying performance.

Logistical Pre-flight Planning and Post-flight Procedures

- Sufficient infection control supplies should be on board the aircraft to support the expected transport duration plus additional time in the event of delays or weather diversions.
- A Flight Surgeon or Air Ambulance Medical Director should validate the patient for medical suitability for aeromedical evacuation. This will involve balancing multiple factors including: the medical stability of the patient, potential for deterioration, benefit of the transfer to the patient's clinical care, and ability to suitably mitigate the infectious risk posed by the patient to the medical staff, aircrew and the aircraft.
- Flight planning should identify locations for potential emergency diversion and coordinate logistical support in the event of an in-flight emergency.
- Upon termination of the transport, the air medical team should include in their patient care report the estimated duration of patient contact, description of PPE used, and any recognized breach(es) in infection control precautions encountered in flight.
- Appropriate cleaning and decontamination of the aircraft (or isolation unit) will be required and should be conducted by appropriately trained staff wearing the necessary PPE.[21]

Emergency procedures

There should be a written plan addressing patient handling during in-flight or ground emergency situations related to the aircraft. All crew and passengers should be briefed on the emergency procedures prior to departure and crew should have been trained in and exercised the procedures. Activities such as donning life vests and emergency patient egress may create special exposure risks. Use of PPE must be weighed against time constraints and on-board emergency conditions such as cabin decompression or smoke in the cabin.

[21] http://www.phac-aspc.gc.ca/id-mi/vhf-fvh/ebola-ipc-pci-eng.php

Waste disposal

All waste should be considered hazardous, handled with the utmost care, and disposed of in accordance with local and regional requirements for regulated medical waste. Personnel handling waste should adhere to the same precautions and PPE use as those providing patient care.

Cleaning and disinfection

- Disinfectants should be available during transport to manage events that result in contamination.
- Compressed air should not be used for aircraft cleaning.
- Non-patient-care areas of the aircraft should be cleaned and maintained according to manufacturer's recommendations.
- Patient care areas and equipment should be cleaned and disinfected with a disinfectant suitable for Ebola as outlined in the PHAC IPAC guidelines that has approved by the aircraft manufacturer.
- Personnel cleaning the aircraft and its equipment should wear PPE that is, at minimum, consistent with precautions for contact and droplet precautions. Additional PPE should be considered for cleaning of heavily contaminated environments or if aerosols could be generated.
- Contaminated seat cushions or webbed seats should be removed, placed in a biohazard bag, labeled, and sent for cleaning and disinfection or disposal.
- Contaminated reusable patient care equipment should be placed in biohazard bags, labeled, and sent for cleaning and disinfection, according to the manufacturer's instructions.

Regional Aeromedical Evacuation

Regional aeromedical evacuation refers to short duration flights, typically less than 3 hours, conducted by provincial air ambulance resources within Canada.

Patient Isolation & PPE

A designated isolation area should be established on the aircraft and patient movement restricted to this designated area. In general, patients should be placed as far away from the flight crew as possible. If available patients should be placed in a portable isolation unit to create the isolation area, however these are rarely available given the type and size of aircraft typically used for regional aeromedical evacuation. Medical staff should wear PPE in accordance with the same recommendations as for health care workers within the hospital setting. However, given the tight quarters, need for greater mobility, lack of ability to exit the patient care environment if there is not an isolation unit, and the variability of settings during the transport environment

more durable, comfortable and modified PPE may be required in the transport setting. Patients should wear a surgical mask to reduce the risk of droplet production.

Patient transfers from bed to stretcher and movement in and out of the aircraft can be particularly high-risk exposure periods given the close contact and physical manipulation of the patient that is often required. Therefore, these transitions should be minimized as much as possible. If the patient cannot be separated from the aircrew by a sufficient distance and/or the use of an isolation unit, the aircrew will also have to wear PPE. Any potential aerosol generating procedures, such as intubation, that are likely to be required during transport should be anticipated and done electively prior to transport while in the sending hospital in a negative pressure isolation room. Alternatives to aerosol generating procedures (e.g. use of metered-dose inhalers instead of nebulizers for inhaled medications) should be sought for essential medical care while in transit.

If an isolation unit is not available, a designated isolation area should be established in which PPE appropriate for airborne and droplet precautions must be maintained. The minimum radius of 2 metres around the patient is recommended for such an area. Surfaces within the isolation area must be smooth, nonporous, and impermeable to permit thorough cleaning and disinfection. Waste receptacles should be placed inside the isolation area. Materials required for patient care must be organized outside the isolation area.

National & International Aeromedical Evacuation

The transportation of patients with EVD over long distances either within a country or between countries or transoceanic, involves many complex medical, logistical, and potentially diplomatic issues. Many of the same basic principles apply as discussed above, however, issues such as the long duration of the transport and potential transoceanic aspects of long distance aeromedical evacuation lead to additions challenges in transporting a patient with Ebola such as:

- Requirement for additional medical staff to allow crew rest out of PPE which must be balanced against the need to minimize the number of crew/staff exposed.
- Need for a containment unit for the patient or some other way to create a separate cold (clean) zone separate from the patient care area (hot zone) in order for medical staff to rest without PPE.
- Toilet facilities for the patient or a process for containing and disposing of patient body fluids.
- Increased risk of patient deterioration to occur over the course of the transport.
- Potential requirement for refuelling stops and therefore clearance to land in additional countries.

- Requirement of a process to occur, on short notice, for a health care facility at an alternate destination to assume care of the patient in the event of a diversion due to weather or mechanical issues, alternatively the ability to for the medical staff to continue to care for the patient for a prolonged period (days) on the aircraft or in a temporary location.
- Logistical issues associated with retrieving a patient from a developing country health care facility including transportation issues, security threats, and lodging for the aircrew and medical staff in a country with a major Ebola outbreak given the limitations of flight duty day and requirement for crew rest.

Patient Isolation & PPE

Given the requirement to create separate environments (Figure 1) within the aircraft during prolonged transport, EVD patients should be transported in an isolation unit. The primary purposes of the isolation unit are to contain body fluids so that:

- Contamination of the aircraft is minimized
- Protection of the aircrew is enhanced and they are not required to wear PPE on the flight deck
- Medical staff are able to have a crew rest area where they do not require PPE

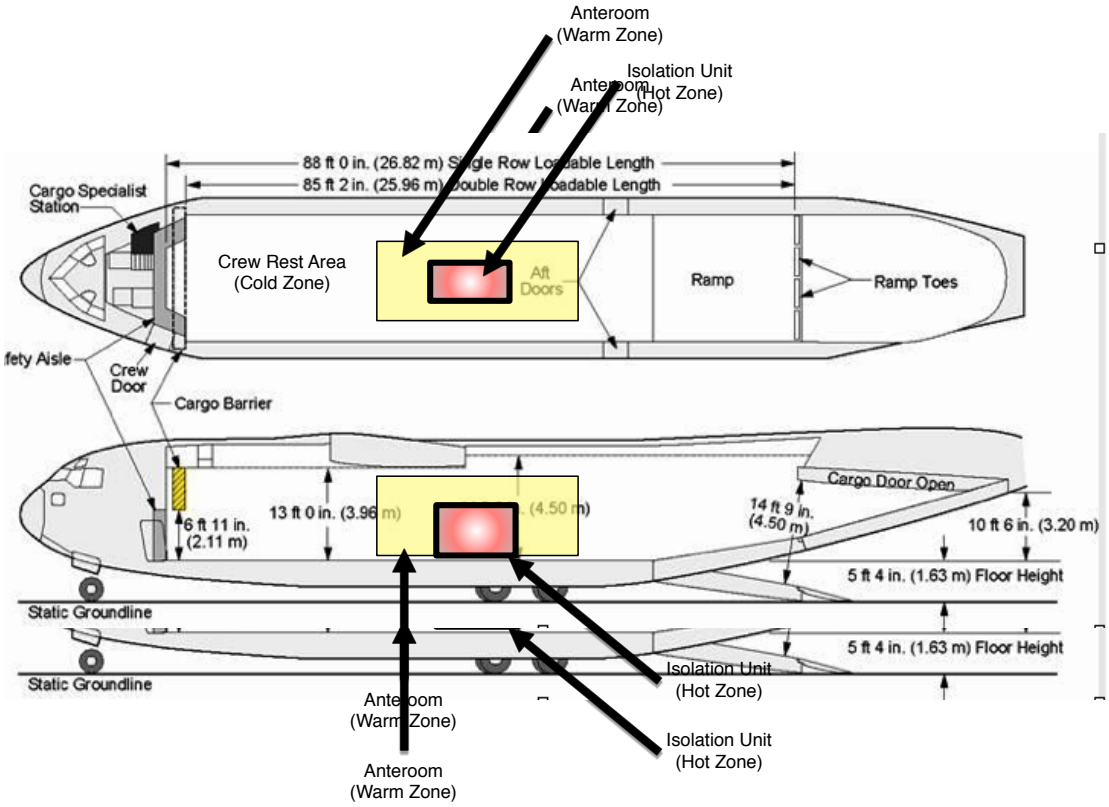

Figure 1: Example of infection control zones for aeromedical evacuation

In addition to the medical and infection control requirements, the flight logistical requirements (range of the aircraft) will also factor into the decision as to which aircraft is most appropriate. The exact nature of the containment unit and the layout of the zones will vary based upon the type and size of the aircraft used. Features of the isolation unit should include:

- Ability to properly secure the isolation unit within the aircraft and the patient within the isolation unit during take-off, landing and turbulence.
- Ability for staff to view and monitor the patient from outside the unit to minimize their exposure.
- Ability for the patient to communicate with the staff from inside the unit and vice versa.
- Sufficient space for staff to provide medical care, including procedures if necessary, storage of essential medical supplies, equipment and monitors properly secured. Most medical supplies and all PPE should be stored outside of the isolation unit.

- Toilet facilities (chemical) or a method to contain and dispose of body fluids as well as medical waste.
- Fluid impermeable to contain body fluids and prevent contamination of the aircraft and crew.
- Negative pressure or HEPA filters in the event that aerosol generating procedures are conducted.
- Capability to be disinfected and/or disposed.

The 'warm zone' includes the area, ideally a contained anteroom, where PPE is donned and doffed. The space must be large enough to allow PPE to be applied and removed without cross-contamination. There should also be a shelf or table upon which to place supplies while putting on PPE before entering the isolation unit. The 'cold zone' is reserved for crew rest and the storage of clean PPE and medical supplies.

In general, patients should be placed as far away from the flight crew as possible but also taking into consideration the pattern of airflow pattern within the aircraft. Medical staff should wear PPE in accordance with the same recommendations as for health care workers within the hospital setting when in the 'hot zone'. As with regional aeromedical evacuation, the tight quarters, need for greater mobility, prolonged duration of the flight and time with patient contact, and the variability of settings during the transport may mandate more durable, comfortable and modified PPE.

Patient transfers from bed to stretcher and movement in and out of the aircraft can be particularly high-risk exposure periods given the close contact and physical manipulation of the patient that is often required. Again, these transitions should be minimized as much as possible. Despite the isolation unit, any potential aerosol generating procedures, such as intubation, that are likely to be required during transport should be anticipated and done electively prior to transport while in the sending hospital in a negative pressure isolation room. Alternatives to aerosol generating procedures (e.g. use of metered-dose inhalers instead of nebulizers for inhaled medications) should be sought for essential medical care while in transit.

Research

The current weighted case fatality rate of nearly 70% for all Ebola virus outbreaks is an unacceptable outcome. In addition to improving local, national and international response with personnel and supportive care, epidemiology, contact tracing and social mobilization in West Africa, we must also consider observational and experimental research as a core component of an EVD outbreak response. While improving the care of infected patients takes precedence, we must concurrently improve our research response by implementing observational studies, biological sampling protocols and interventional studies. Such studies should ideally be previously developed, vetted, funded and then approved in the jurisdictions likely to be affected. If we attempt to initiate clinical research only *during* the outbreak, it rarely occurs. Although the history of critical care therapeutics teaches us that the greatest benefit to patients is likely to emerge from consistent application of a system of critical care focused upon timely recognition, early resuscitation, supportive care and prevention of complications, promising interventions such as vaccination, convalescent plasma or monoclonal antibodies require investigation to determine their value. A lack of history of research acceptance in many jurisdictions is a common challenge; however, not engaging these challenges represents an irresponsible approach to improving medical care.

The World Health Organization has recently released a statement[22] on the role of investigational therapies during this Ebola virus outbreak concluding:

> *In the particular context of the current Ebola outbreak in West Africa, it is ethically acceptable to offer unproven interventions that have shown promising results in the laboratory and in animal models but have not yet been evaluated for safety and efficacy in humans as potential treatment or prevention.*
>
> *Ethical, scientific and pragmatic criteria must guide the provision of such interventions. The ethical criteria include transparency about all aspects of care, so that the maximum information is obtained about the effects of the interventions, fairness, promotion of cosmopolitan solidarity, informed consent, freedom of choice, confidentiality, respect for the person, preservation of dignity, involvement of the community and risk–benefit assessment.*
>
> *If and when unproven interventions that have not yet been evaluated for safety and efficacy in humans but have shown promising results in the laboratory and in animal models are used to treat patients, those involved have a moral obligation to collect and share all the scientifically relevant data generated, including from treatments provided for "compassionate use".*

[22] *World Health Organization. Ethical considerations for use of unregistered interventions for Ebola virus disease (EVD). Available from: http://who.int/csr/resources/publications/ebola/ethical-considerations/en/*

Researchers have a moral duty to evaluate these interventions (for treatment or prevention) in clinical trials that are of the best possible design in the current exceptional circumstances of the West African Ebola outbreak, in order to establish the safety and efficacy of the interventions or to provide evidence to stop their use. Continuous evaluation should guide future interventions.

A number of resources exist to assist with identification of pre-existing observational and experimental research protocols that may be assessed by appropriate research ethics boards, and offered to patients in an accelerated fashion, and may help to improve the understanding of this illness, and improve the care delivery during this and future outbreaks (e.g. ISARIC[23]).

[23] *ISARIC - International Severe Acute Respiratory and Emerging Infection Consortium - https://isaric.tghn.org/*

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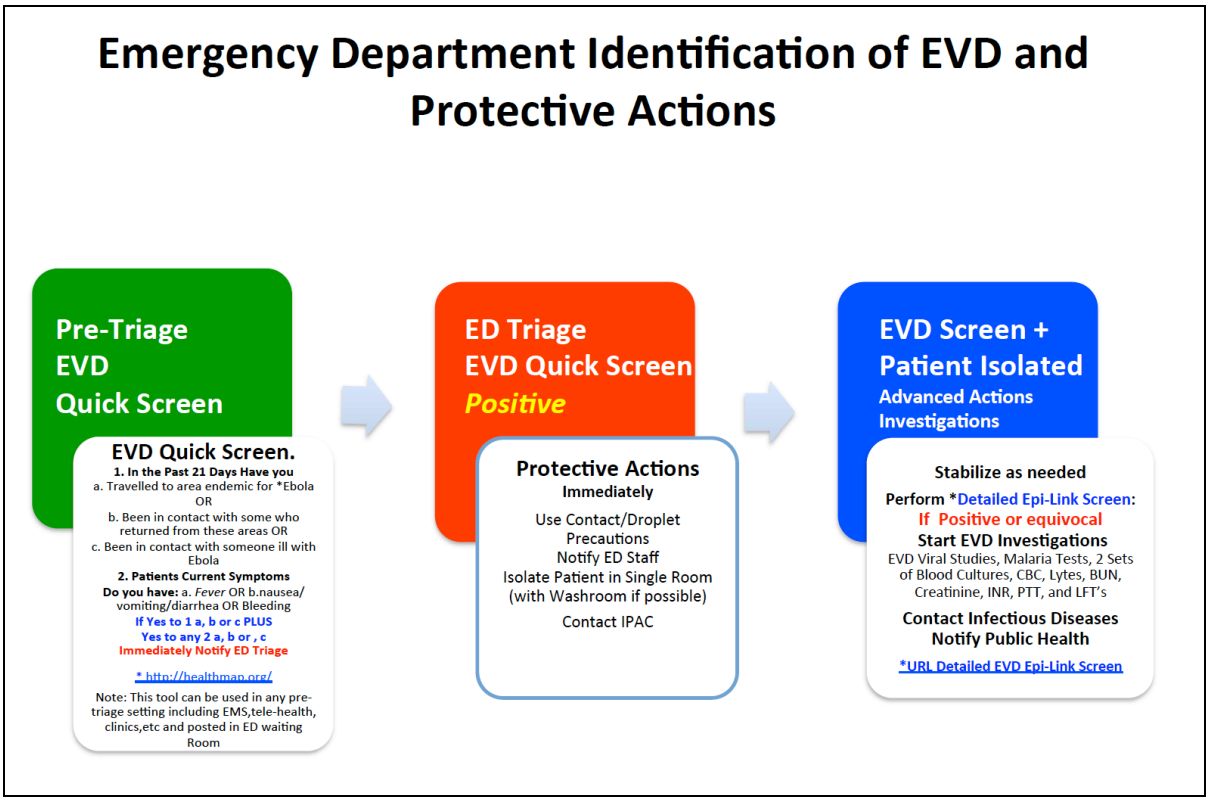
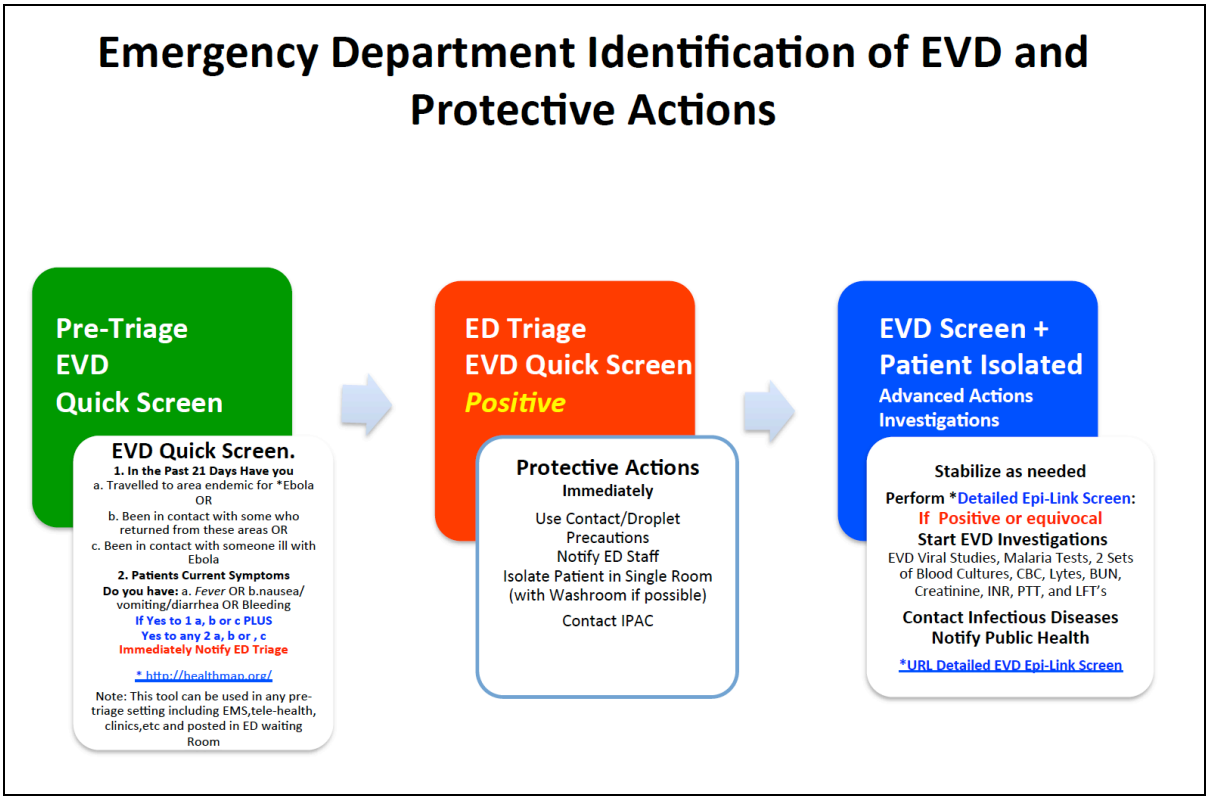
Appendix 1 – ED Screening for & Response to Possible EVD Cases

The figure below provides an example of a general approach to screening and response to EVD patients.





A Detailed EVD Epi-link screen changes as the disease moves and this should be a downloadable from a site that continual updates this information. It should be similarly formatted in a check list manner AS ED will not do it if prolonged-they can't-they are way to busy with sicker patients, and will over investigate and over-consult if this takes to much time. Language and illness may make it impossible to conduct a screen well= equivocal. If the suspicion is even remotely there…ED Should investigate.

Other examples:

UK: http://www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1317135155050