Ebola Clinical Care Guidelines
UW Health

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BACKGROUND:

Ebola virus disease (EVD) is caused by infection with a virus of the family Filoviridae, genus Ebolavirus. The subtype causing the current outbreak in West Africa is Ebola Zaire. The natural reservoir for the virus is unknown; however, fruit bats are thought to be the most likely source. Based on past epidemics, the mortality of EVD ranges from 60 to 90%; there is no approved vaccine or previously identified specific treatment. Information on the current and past Ebola outbreaks can be found on the CDC website, http://www.cdc.gov/vhf/ebola/resources/outbreaks.html

Transmission of Ebola virus is via direct contact with bodily fluids of an infected individual. Spread from an asymptomatic individual in the incubation period has not been documented. Healthcare workers are at high risk for contracting infection because of potential contact with patient blood or bodily secretions. Every effort should be made to prevent transmission of Ebola within healthcare facilities.

The clinical course of EVD generally begins with non-specific symptoms and later gastrointestinal symptoms. Progression to severe disease and death can occur. Non-fatal cases typically improve 6-11 days after symptom onset.\(^1\) An excellent clinical overview of EVD can be found at: http://www.cdc.gov/vhf/ebola/hcp/clinician-information-us-healthcare-settings.html

PRESENTATION:

Although screening mechanisms in the US may identify patients early in the course, a patient could present at any stage of disease. Early symptoms are non-specific (fever, chills, myalgias, malaise, and anorexia) and generally manifest 8-10 days (range 2-21 days) after exposure. Approximately five days after symptoms onset, patients may develop gastrointestinal signs/symptoms such as nausea, vomiting, watery diarrhea, and abdominal pain. Significant volume losses are common. Cases may progress to hypovolemic shock, hemorrhagic manifestations, coma, and death.\(^1\)

Based on data from the current EVD outbreak\(^2\), the most common symptoms during the course of EVD are listed in Table 1.

Table 1. Frequency of Symptoms During EVD Course

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Frequency</th>
<th>Symptom</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>87%</td>
<td>Any Unexplained Bleeding</td>
<td>18%</td>
</tr>
<tr>
<td>Fatigue</td>
<td>76%</td>
<td>Confusion</td>
<td>13%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>68%</td>
<td>Hiccups</td>
<td>11%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>66%</td>
<td>Jaundice</td>
<td>10%</td>
</tr>
<tr>
<td>Anorexia</td>
<td>65%</td>
<td>Eye Pain</td>
<td>8%</td>
</tr>
<tr>
<td>Headache</td>
<td>53%</td>
<td>Coma</td>
<td>6%</td>
</tr>
<tr>
<td>Abdominal Pain</td>
<td>44%</td>
<td>Rash</td>
<td>6%</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>39%</td>
<td>Melena/Hematochezia</td>
<td>6%</td>
</tr>
<tr>
<td>Myalgia</td>
<td>37%</td>
<td>Hematemesis</td>
<td>4%</td>
</tr>
<tr>
<td>Chest pain</td>
<td>37%</td>
<td>Vaginal Bleeding</td>
<td>3%</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>33%</td>
<td>Gingival Bleeding</td>
<td>2%</td>
</tr>
</tbody>
</table>
Information is limited on the presentation and impact of EVD on children. Previous outbreaks have occurred in settings with limited resources, and information about pediatric cases has not been routinely collected. The data available suggest that children are more prone to fever and respiratory or gastrointestinal symptoms and less likely to experience hemorrhage or central nervous system signs. Although reasons are unknown, children may be less prone to EVD than adults based on data from previous outbreaks. However, in one outbreak in which large numbers of children were affected, school-age children and adolescents had increased survival compared to children less than 5 years of age and to adults. Children are more likely to become rapidly dehydrated from vomiting or diarrhea because they have less body fluid reserve than adults. Children also have smaller circulating blood volumes than adults, so relatively small amounts of volume loss can become dangerous more quickly.

**DIAGNOSIS:**

**Screening:**

All patients accessing UW Health, hospital or ambulatory care centers should be screened for EVD risk as follows:

1. Identification of travel in the last 21 days to a country where Ebola transmission is active (currently Liberia, Sierra Leone, and Guinea) OR contact with an individual with known EVD

   **AND**

2. Fever (≥99.5°F) or any compatible Ebola symptom including headache, weakness, muscle pain, vomiting, diarrhea, abdominal pain, or hemorrhage

Please see the UW Infection Control *Ebola Identification and Control Plan* for location-specific steps to take if an individual screens positive for both items above. If there is any suspicion for EVD, immediately isolate the patient and page the Emerging Pathogens Physician, pager 4400 by calling 608-262-2122

**Differential Diagnosis/Other diseases to consider:**

Malaria, typhoid fever, meningococemia, other bacterial infections, Lassa fever, and influenza are common illnesses in geographical regions where EVD is most prevalent that may initially present in a fashion similar to EVD. In children, additional considerations include viruses that can cause systemic syndromes similar to EVD such as adenovirus, enteroviruses, norovirus, rotavirus, and specific bacterial infections like pneumococcal disease and H.influenzae.
Testing:

RT-PCR is the recommended test for diagnosis of acute EVD and is highly sensitive and specific. Serology is not predictable in early disease and is therefore of less use. Testing for the Ebola virus must be approved by the CDC. Once testing is approved, UWHC will send a specimen to the CDC or designated State Health Laboratory. All laboratory staff volunteers for the Emerging Pathogen (EP) Point of Care (POC) laboratory are trained and certified to package and ship Category A agents. Please see the UW Laboratory protocol for Ebola testing for detailed information on collection and the process of sending out the sample: [http://blogs.uwhealth.org/ebola/clinical-laboratories/](http://blogs.uwhealth.org/ebola/clinical-laboratories/) Time from collection to result will depend on the location of the laboratory performing the test and the method of transportation of the specimen to the laboratory.

Managing Results of Ebola virus RT-PCR:

If positive - treat as confirmed EVD

If negative – If symptoms started ≥72 hours before a negative result, EVD is unlikely, and alternative diagnoses should be considered. Infection control precautions for EVD can only be discontinued after a discussion with the Infection Control physicians. If symptoms started less than 72 hours before the negative RT-PCR result, the result is not definitive and the test must be repeated ≥72 hours after the onset of symptoms. The patient must remain in isolation as a suspected case until a repeat RT-PCR ≥72 hours after symptom onset is negative. For all suspected cases of Ebola, infection control consultation must occur.

TREATMENT:

General Considerations: While there is no proven treatment specifically for EVD, several experimental therapies have been used.6 Aggressive supportive care remains the mainstay of therapy. For intravenous access in all suspected or confirmed EVD cases, UW would prefer early placement of a triple-lumen PICC (peripherally inserted central catheter) upon patient arrival to the F6/5 isolation unit as soon as is possible/feasible. This would allow for needleless daily blood sample collection as well as the capability to deliver fluids, electrolytes, and possibly vasoactive medication centrally. If PICC placement is not possible, large bore peripheral IVs or a central venous catheter could be placed, depending on the availability of individuals able to place such lines and on the severity of illness at presentation. For pediatric patients, size and age will determine whether single or multi-lumen PICC or other venous access is appropriate. Specific adult and pediatric order sets will be available for basic and recommended orders pertaining to EVD patient care.

Specific Issues:

Hypovolemia – Diarrhea and vomiting can result in fluid losses of 5-10L/day in adults and substantial volume losses in children. Careful monitoring of urine output, daily weights, and possibly central venous pressures are critically important. There should be a low threshold for placement of a
urinary catheter, which allows for accurate output measurements and minimizes caregiver exposure to urine. Patients with diarrhea who are able to ambulate should use the toilet; those unable to ambulate may have a stool collection bag placed. Use of a bedpan or bedside commode is discouraged due to the risk of spillage. For children who are not toilet trained, diapers should be used and weighed to track output. Aggressive volume repletion is vital. Oral rehydration options will be available and should be used as much as possible in addition to IV fluids. The selection of IV fluids will be determined by the provider, but based on studies in Dengue hemorrhagic fever Lactated Ringer’s solution may be the preferred intravenous fluid.7

**Electrolyte disturbances** – Due to fluid losses/shocks resulting in hyponatremia, hypokalemia, hypocalcemia, hypomagnesemia, and hypophosphatemia, patients with EVD need close electrolyte monitoring and aggressive repletion. Of particular concern are potassium and calcium. Daily labs will be automatically completed each morning, and point of care testing of an abbreviated panel including electrolytes can be done on an as-needed basis. Children who are clinically stable may not require automatic daily labs.

**Sepsis** – Because of limited testing availability and non-specific presenting signs/symptoms in patients who are likely to be at risk for other infectious diseases, empiric antimicrobial coverage should be considered. Consult Infectious Diseases for recommendations on anti-infective treatment. For patients coming from malaria-endemic areas, one should consider empiric arteether/lumefantrine, with support from the Infectious Disease consult service for dosing and IV therapy options. For patients in whom typhoid fever, meningococccemia, or Haemophilus bacteremia is a possibility, empiric ceftriaxone is appropriate (weight-based dosing for children). In patients with suspected pneumococcal invasive disease, vancomycin in addition to ceftriaxone should be considered. If a patient has upper respiratory infection (URI) symptoms or a typical influenza presentation, empiric oseltamavir should be considered. Respiratory virus testing including influenza will not be available during the EVD testing period.

**Hemorrhage** – Although not a major feature of the current EVD outbreak, EVD can certainly result in hemorrhage. Close attention to hemoglobin and platelet count is warranted. If needed, blood product transfusion will be available using universal donor products. No type and screen or cross match testing is planned at this time.

**Symptom management** –

EVD-associated diarrhea – thorough literature review and evaluation indicate no clear contraindications to the use of anti-motility agents including loperamide or diphenoxylate-atropine in adults (APPENDIX 1). Anti-motility agents are generally not used in children due to safety concerns. EVD-associated nausea – no known contraindication for the use of ondansetron, prochlorperazine, or lorazepam in adults. Prochlorperazine is contraindicated in children due to the high risk of extrapyramidal effects.
EVD-associated fever – acetaminophen used as needed is likely to be safe. NSAIDs should be avoided due to risk for hemorrhage and renal injury.

**Prophylaxis** - Chemoprophylaxis against venous thromboembolism will be held, given the risk for hemorrhage and other hematologic complications. Mechanical prophylaxis will be held due to risk to staff due to contamination with infected bodily fluids.

**Laboratory**: For adult patients in Ebola isolation with confirmed or suspected EVD, a full laboratory panel will be performed each day with specimen collection beginning at approximately 8am, independent of specific orders. For stable pediatric patients, the medical team will determine if daily labs are necessary. Laboratory staff will run the labs in a point of care (POC) laboratory facility on the isolation unit. A more limited number of tests can be performed by nursing staff at the patient bedside at the request of physicians. With the exception of the diagnostic specimen packaged for shipping on the isolation unit to be sent for Ebola virus testing, no specimen will leave the unit and no testing will be performed outside of the EP POC laboratory.

First collection after admission: specimen for Ebola virus testing to be sent to CDC or State Health Lab

Initial infectious testing: Blood cultures to be drawn before antibiotics and incubated in the POC lab – further workup plan for blood cultures will be determined based on patient clinical status. Rapid HIV and Malaria point of care test will be done as consent and testing protocols become finalized.

Urine testing – first urine specimen available: UA (dipstick) and urine pregnancy test

Daily panel (collection beginning at approximately 8am):

- CBC with shortened differential (WBC, RBC, Hgb, Hct, MCV, MCH, MCHC, platelet count, Lymphocyte%, Lymphocyte#, Neutrophil%, Neutrophil#)
- Chemistry (Glucose, BUN, Creatinine, Sodium, Potassium, Chloride, CO2, Uric Acid, Calcium, Ionized Calcium, Phosphorus, Magnesium, Albumin, Total protein, ALT, AST, Total bilirubin, GGT, Amylase, Lactate)
- Coagulation (INR)
- Blood gases panel (pH, pCO2, PO2, Bicarbonate, Sodium, Potassium, Ionized Calcium, Hct, Hgb, Glucose, Lactate)

Bedside testing (as needed, via nursing draw)

- pH, pCO2, PO2, Bicarbonate, Sodium, Potassium, Ionized Calcium, Hct, Hgb, Glucose, Lactate

**Other testing available:**

Radiology – a portable chest x-ray will be available on the isolation unit. Nursing will be trained on use of the portable x-ray machine to limit exposure to radiology staff. A portable ultrasound unit will be available to the PICC team for PICC placement. The ultrasound machine will likely not be kept on
isolation unit but could be available at request later in the patient’s care. CT and MRI will not be available for EVD patients.

Telemetry/Vitals – telemetry will be available. The frequency of vital sign measurement including heart rate, blood pressure, and oxygen saturation will be determined based on severity of illness and discussed during daily team rounds.

**Care Team:** The “Special Pathogens Team” will include care providers, patient family members, and ancillary staff. There will be a planned team meeting each morning to discuss the day’s care plan, with specific discussions about team organization (providers planning to enter patient room), treatment plan, laboratory testing plan, safety review, and reconciliation of questions/concerns. The proposed time for this meeting is 9am and the suggested location for this meeting is the EVD-dedicated F6/5 unit staff lounge that is located outside of the isolation unit.

**Physician roles:**

Adult Core Team – The Core Physician team will be a Hospital Medicine-Critical Care dyad. The Physician team will be responsible for coordinating care across the spectrum of disciplines, with specific attention to patient-centeredness and staff safety. A physician is expected to physically examine the patient at least once daily and be available at all times. A patient will be deemed "ICU status" if in refractory shock requiring vasoactive medications, if mechanically ventilated, and as deemed appropriate on a case-by-case basis.

Pediatric Core Team - The admitting physician will be either a Hospitalist or Intensivist, depending on the acuity of the patient at presentation. A physician is expected to physically examine the patient at least once daily and be available at all times. The Intensivist will be available to assist with sedation for any necessary procedures for general care patients. Destabilization will result in care transition to the Intensivist, and a second Intensivist may be assigned to the care team if needed. Remote monitoring from the PICU will also be available for critically ill children. Elective endotracheal intubation will be performed by the Intensivists, with pediatric otolaryngology support if a difficult intubation is anticipated. When entering the convalescent phase, care may be transitioned back to the Hospitalist physician.

Consultants - Consultative services will be provided outside the unit as much as possible. There will be video conference capabilities to interview the patient. It is not under consideration to offer invasive cares including surgery, endoscopy, or laryngoscopy to patients with active EVD; patients in the convalescent phase will be addressed on a case-by-case basis. Intubation may be provided electively but not emergently or in acute respiratory arrest, by Anesthesia staff. Renal replacement therapy and dialysis access may be provided if necessary by Nephrology staff. The following consultative services have endorsed a remote consult model: Infectious Disease, Hematology, Surgical Nutrition, and Pharmacy.

Pediatric Consultants - All patients will have an Infectious Disease consultation on admission. All necessary consultants will be engaged via video technology. Any decision surrounding initiation of
dialysis will require multi-disciplinary input including nephrology, dialysis personnel, pediatric nursing, pediatric Intensivist and the patient's family.

**Anesthesia roles:** The Department of Anesthesiology has identified a number of physicians who have volunteered to perform intubations and vascular access procedures in adult EVD patients should it become necessary.

**Nursing roles:** A separate document/guideline outlines nursing roles and flow in detail – protocols are available at [http://blogs.uwhealth.org/ebola/](http://blogs.uwhealth.org/ebola/). Nurse staffing allows for 24 hour coverage with 3 RNs, with staggered 12 hour shifts. The 3 RNs will rotate through 4 hour assignments that include 1) Bedside care 2) Documentation and Communication and 3) Quality Assurance/PPE. The model has been arranged so that if needed, 2 RNs could provide direct bedside care at once. Less severely ill patients may need less frequent bedside care. Pediatric patients will be cared for by a mixed team of adult and pediatric nurses, with at minimum one pediatric nurse on the team each shift.

**Respiratory Therapy roles:** Respiratory therapy will be available via streaming video to the patient room, but will not enter the patient room. Nursing will be trained on expected respiratory therapy techniques and ventilator management. Respiratory therapy will set up ventilator outside of the room and provide step-by-step advice to nursing for in-room set up.

**Trainees:** Trainees (learners including medical students, residents, and fellows) will not have direct contact with the patient except in epidemic circumstances where multiple EVD patients need concurrent care. Trainees may participate in discussions about EVD patients as part of a consultative team, but should not enter the F6/5 isolation unit.

**Critical Care/Procedures:**

Vasopressors – early PICC placement is planned for aggressive IV fluid and electrolyte repletion and blood draw safety, but could be used to deliver vasopressors in the event of volume-refractory shock. Vasopressor use should follow common practices as directed by the Critical Care physicians.

Invasive arterial blood pressure monitoring – Insertion of an arterial line is a relatively high risk procedure given the need for sharps and the potential for blood spray; therefore this procedure is not recommended.

Airway management – Pulmonary involvement with EVD is rare, but respiratory failure can occur in severe cases (secondary to shock, acidosis, hemorrhage, comorbid conditions/infections). No NIPPV will be used, including BiPAP or CPAP. Early intubation should be considered in those patients with signs of respiratory failure. Suggested PPE for invasive procedures such as endotracheal intubation includes PAPR with hood (either with multicomponent or full body suit) as this procedure could generate aerosolized body secretions.

Organ support (HD, CRRT, ECMO) – Intermittent HD and ECMO will not be available. CRRT may be considered, but decisions about instituting this therapy should be made on a case-by-case basis.
Nephrology consultation is paramount, and that team will likely be available for placement of a HD-catheter if needed.

**Codes:** No overhead “code blue,” "Anesthesia STAT," or rapid response will be called. A separate policy regarding code status has been completed and can be found via the UW Ebola Preparedness site: [http://blogs.uwhealth.org/ebola/](http://blogs.uwhealth.org/ebola/); in short, patients with suspected or confirmed EVD infection will be LIMITED CPR until EVD is ruled out or has resolved. No chest compressions or emergent intubation will be provided. A defibrillator with adhesive pads will be available for use in certain circumstances (acute electrolytes disturbances); manual defibrillation with paddles should be avoided. *Under no circumstances should a healthcare provider rush through proper PPE donning procedure to assist an arresting EVD patient.*

**EVD patient - family interaction:** No family member should enter the room of a patient isolation for EVD (suspected or confirmed). A live video chat system will be available to family members and will be housed outside the isolation unit. Counseling and spiritual support will be available to patient family members as well. Exceptions may be made on a case by case basis especially for pediatric cases.

**Investigational Therapies/Pharmaceutical Research Center (PRC):** Several investigational therapies that have been utilized for patients with EVD. The UW Health PRC and Infectious Disease physician will assist in submitting the paperwork to obtain these medications/treatments if indicated and available. PRC Pharmacist pager #2717 should be contacted to facilitate pursuing such options. Information available specific to these treatment options are included in a summary document with individual monographs as appendixes. In the event one of these is obtained, additional information will be supplied from the manufacturer upon receipt of the medication that may supersede current information as included here.

- Potential treatments directed against EVD SUMMARY (APPENDIX 2)
- Brincidofovir monograph (APPENDIX 3)
- ZMapp monograph (APPENDIX 4)
- TKM-Ebola monograph (APPENDIX 5)
- BCX4430 monograph (APPENDIX 6)

Plasma/whole blood from EVD survivor – this therapy has been used for EVD patients in the current outbreak as well as in past outbreaks with encouraging anecdotal results. Specific processes of obtaining convalescent plasma or whole blood from an EVD survivor are actively being investigated at UW. General guidelines from the World Health Organization with regards to use of convalescent plasma or whole blood can be found at [http://apps.who.int/iris/bitstream/10665/135591/1/WHO_HIS_SDS_2014.8_eng.pdf](http://apps.who.int/iris/bitstream/10665/135591/1/WHO_HIS_SDS_2014.8_eng.pdf)

**Healthlink considerations for documentation:** Patient suspected or confirmed to have EVD will be admitted to the “Special Pathogens” team in Healthlink, with the Hospitalist or Critical Care physician on call as the admitting attending. As outlined previously, a dedicated order set can be utilized as a framework. Daily labs and POC labs will not be ordered through Healthlink, but results will be posted to a special section labeled “EPP” within the normal results section in Healthlink. As with all protected health information, it is of the utmost importance that only those providing direct care for the patient
access the chart. Privacy and security of the medical record is of utmost importance. Documentation in the chart will be done as usual.

**Infection Control:** For detailed Infection Control plans, please refer to the UWHC Infection Control website and the UW Health Ebola Preparedness website under Preparedness Plans, Identification and Control Plan: [http://blogs.uwhealth.org/ebola/](http://blogs.uwhealth.org/ebola/)

Specific instructions on Personal Protective Equipment (PPE) use, including donning and doffing directions can be found at that website. In addition, the EVD Identification and Control Plan document is accessible from the website and is updated as needed. An Infection Control Practitioner and an Emerging Pathogen MD (pager #4400) will be available on the F6/5 isolation unit for real-time discussions about Infection Control as it relates to a specific patient.

Every provider with potential to directly care for an EVD patient should undergo PPE training in the Simulation Center. Once trained, care providers are strongly encouraged to continue practicing PPE donning and doffing – materials and location for practice is arranged.

**Management of exposure of healthcare worker to EVD:** Questions about specific processes will be addressed by Infection Control on the unit if an exposure were to occur. If there is a question about a potential exposure, call/page for advice at the time of the exposure. If needed, post-exposure monitoring and follow-up care would be arranged through UWHC Employee Health – detailed plan is being crafted and will be available.

**Psychological Support for Providers/Post-care Issues:** Caring for a patient with EVD carries with it significant stress and legitimate concerns. Careful use of personal protective equipment and adherence to Infection Control practices makes the possibility of EVD transmission very low. Individuals involved in direct patient care will be required to self-monitor for fever or symptoms once patient care period is over. In the case of a clear exposure, Infection Control will assist in estimating degree of exposure and determine follow-up plan.

Care providers wishing to avoid returning home during or after patient care periods will have housing provided to them. If a provider is unable to return to normal duties or reach usual work hours because of the structure of EVD patient care or after-care monitoring, usual compensation will be provided. In addition, there will likely be additional pay for EVD direct care providers.

Counseling and spiritual services will be made available to any care provider who is interested.

**Patient Death:** For full details on general considerations, please refer to the CDC website [http://www.cdc.gov/vhf/ebola/hcp/guidance-safe-handling-human-remains-ebola-patients-us-hospitals-mortuaries.html](http://www.cdc.gov/vhf/ebola/hcp/guidance-safe-handling-human-remains-ebola-patients-us-hospitals-mortuaries.html)

In the event that a suspected/confirmed EVD patient dies, no autopsy will be performed unless required by state law. Handling of the corpse will be kept at a minimum; medical devices, clothing, and soilage will not be removed. The remains will be disposed of in accordance with CDC guidelines as listed above.
References:


APPENDIX 1: Anti-diarrheal medication for the treatment of diarrhea induced by the Ebola virus (11/6/14)

APPENDIX 2: Potential treatments against EVD Summary (10/29/14)

APPENDIX 3: Brincidofovir monograph (10/30/14)

APPENDIX 4: ZMapp monograph (10/30/14)

APPENDIX 5: TKM-Ebola monograph (10/30/14)

APPENDIX 6: BCX4430 monograph (10/30/14)