Ebola Facts
October 20, 2014
Clinical Progression of Ebola

**Disease Progression**

**Exposure**
- Incubation period is 2-21 days following exposure. Symptoms appear on average 3-10 days following exposure. (CDC)

**Symptom Onset**
- Weakness
- Fever - greater than 101.5°F
- Headache
- Muscle Pain
- Joint Pain
- Conjunctivitis
- Nausea
- Throat Pain
- Abdominal Pain
- Diarrhea
- Hiccups

**Early Stages**
- Confusion
- Irritability
- Chest Pain
- Diarrhea
- Vomiting
- Skin Rash
- Internal/External Bleeding
- DIC
- Miscarriage
- Respiratory Distress
- Shock
- Convulsions

**Late Stages**
- Visual Complications
- Joint Pain
- Anemia
- Risk for transmission up to 3 months in tears and semen

*Early and late stage symptoms may overlap; all symptoms may not manifest in all infected patients*

Source: Jonathan B. Perlin, MD, PhD and HCA Clinical Excellence Knowledge Center, 2014
# Clinical Evidence

## Disease Pathophysiology

Research suggests the virus first infects **dendritic cells**, disabling immune system, and then attacks the **vascular system**, causing hemorrhage, hypotension and shock. The virus also affects the **liver** (impacting coagulation proteins), the **adrenal gland** (affecting steroid synthesis for blood pressure stabilization) and the **gastrointestinal tract** (diarrhea).

## Hemodynamic Support

**Hypotension/Shock**: Aggressive IV fluid resuscitation resembling the approach to the septic shock patient is identified by the CDC as one of three interventions that impact mortality through observation and case series. **Base fluid selection (Lactated Ringers or Normal Saline) on patient electrolyte status.** One animal study examined supplemental fluid resuscitation of infected, hypotensive rhesus macaques, which resulted in improved renal parameters. **Hydrocortisone** may be considered to support viral disruption in steroid synthesis.

**Hemorrhage/DIC**: Management of hemorrhage is **inconsistent in literature**. Literature around previous outbreak transfusion strategies includes various blood products, antifibrinolytics, and clotting factors. One recent report suggests the use of melatonin to combat endothelial disruption, disseminated intravascular coagulation (DIC) and multiple organ hemorrhage due to potential benefit, high safety profile, and limited alternative therapies.

## Respiratory Support

**Maintain adequate oxygenation** (titrate to SpO₂ >90%). To protect the airway and/or treat multisystem organ failure, standard mechanical ventilation practices should be followed with the addition of **HEPA filtration of airflow gases**. Methods of **non-invasive ventilation are not ideal** due to increased potential for aspiration and infection transmission. Additional measures including placement of ventilated patients in a negative pressure room, use of video/optical laryngoscopy for intubation, use of rapid sequence intubation with neuromuscular blockade, and use of a ventilator-patient monitoring system interface to minimize entry into the patient room should be considered.

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Source: Jonathan B. Perlin, MD, PhD and HCA Management Services, L.P. 2014
## Clinical Evidence

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<tr>
<th>CARE COMPONENT</th>
<th>CLINICAL MANAGEMENT</th>
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<tbody>
<tr>
<td><strong>Infection Support</strong></td>
<td>Treat fever with acetaminophen (avoid aspirin and NSAIDs due to antiplatelet activity). Identify any additional sources of infection and treat with appropriate empiric antimicrobials. If sepsis develops, administer broad-spectrum IV antibiotics within 1 hour and <strong>follow Surviving Sepsis Early Goal Directed Therapy (EGDT)</strong>. <strong>Antiviral and antimalarial agents are not efficacious</strong> for Zaire Ebola virus. <strong>Consider passive immunotherapy</strong> early in disease course by transfusing whole blood or plasma donated from a convalescent patient.</td>
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<td><strong>Fever, secondary infection, malaise, plasma transfusion, antivirals</strong></td>
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| **Renal/Hepatic Support** | **Renal:** Advanced stage may lead to **impaired kidney function, increased creatinine and BUN, and decreased urine output.** Renal failure has been reported in fatal cases. Patients may experience persistent oliguria, hematuria and proteinuria despite IV fluid resuscitation. Reports of peritoneal and hemodialysis show no consistent correlation on survivability, and **transmission risk to healthcare workers** should be considered.  
  **Hepatic:** Patients demonstrate **impaired liver function, hepatomegaly and elevated liver enzymes (ALT/AST)**, but severity is lower than that seen in hepatitis A/B or yellow fever. One study showed AST was several times higher than ALT in fatal cases. |
| **Pain Management**       | Treat **mild pain with acetaminophen and moderate to severe pain with opioids. Avoid diclofenac, ibuprofen and other NSAIDS** due to antiplatelet activity; avoid tramadol due to seizure activity. The management of pain **resembling the approach to a critically ill patient** with potential multi-organ failure should be followed due to high risk of renal and hepatic failure. |
| **Neurologic Support**    | Monitor the patient for **confusion, anxiety and seizures.** Treat anxiety and seizures with benzodiazepines. **Avoid the use of other medications that may reduce seizure threshold.** Late in the disease progression, monitor neurologic status for increased **intracranial pressure and intracranial hemorrhage.** |

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| Gastrointestinal Support<sup>1,10</sup>  
*Nutrition, Nausea/Vomiting, Diarrhea* | Provide **rehydration therapy** to prevent volume depletion.  **Correct abnormal electrolytes.** Proton pump **inhibitors** should be administered for dyspepsia and gastrointestinal bleed prophylaxis. Administer **antiemetics** for nausea/vomiting. Monitor for dehydration.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| Survivability<sup>2,3</sup> | Dependent upon access to basic care and patient immune status. Current West Africa Ebola strain has reported 70% mortality rate (October 14, 2014).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| Recovery<sup>2,13</sup> | Recovery (weeks to months) is highly dependent on supportive care and immunologic response of patient. Men can still transmit Ebola virus through **semen for up to 3 months** so abstinence is encouraged during this time. Once fully recovered, patients are no longer able to transmit the virus. **Development of antibodies** last at least 10 years but it is unknown if this confers lifelong immunity or if infection with other strains is possible. **Acute complications** include: generalized weakness, weight loss, headache, sensory distortion, migratory arthralgias, skin sloughing, alopecia, and persistent anemia. Uveitis and orchitis can occur weeks after illness, and virus can persist in aqueous humor and semen.  
Experimental Therapies<sup>2,4</sup> | No experimental vaccines or antiviral medications have been fully tested for safety or efficacy. ZMapp (Mapp Biopharmaceutical, Inc.), is an experimental treatment of three monoclonal antibodies that bind to viral protein. All available doses have been distributed at this time. Several experimental vaccines and treatments in animal models show promise. |
REFERENCES AND EVIDENCE CLASSIFICATION


See handout for evidence classification.

Source: Jonathan B. Perlin, MD, PhD and HCA Management Services, L.P. 2014