EDUCATIONAL COMMENTARY – EMERGING INFECTIOUS DISEASES WITH GLOBAL IMPACT

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Learning Objectives

On completion of this exercise, the participant should be able to

- define emerging infectious diseases;
- explain why early diagnosis of Ebola virus disease (EVD) and West Nile (WNV) virus is difficult;
- list laboratory tests that can help in the diagnosis of EVD and WNV; and
- discuss safety concerns relating to laboratory instruments used in the diagnosis of EVD and WNV.

Commentary

Every day, it seems we hear and read reports of outbreaks of difficult-to-treat, potentially deadly infections. Infections that were originally contained in hospitals or long-term care facilities are increasingly seen in schools, exercise facilities, and other public gathering places (e.g., methicillin-resistant Staphylococcus aureus [MRSA] and Escherichia coli O157:H7). High-morbidity, high-mortality infections that were once rare now have the potential to become pandemic.

These pathogens cause emerging infectious diseases (EIDs), infections that have increased in incidence in the past 20 years and/or that have the potential to increase in the near future. An EID may be a new strain of an organism, or a known pathogen that was dormant and is re-emerging based on incidents reported to public health agencies. Organisms previously limited to a specific geographic location are appearing in previously uninvolved locations. This commentary will concentrate on two infections, Ebola and West Nile virus, which have been, and continue to be, in the news. Ebola is considered an EID, whereas West Nile virus infections are becoming more commonplace.

Ebola Virus Disease

The Ebola virus was on everyone’s radar in 2014, when health care workers caring for people infected with Ebola in West Africa became infected themselves. The Centers for Disease Control and Prevention (CDC) considered this outbreak of Ebola to be localized in the countries of Guinea, Sierra Leone, and Liberia. Health care workers from Nigeria, Senegal, Spain, the United States, Mali, England, Scotland,
and Italy contracted the infection, and some did not manifest the disease until their return to their home country. These cases had the potential to lead to a pandemic if infection was not controlled swiftly. Fortunately, the precautions and preventive measures taken were sufficient to minimize the spread of Ebola.

Also known as Ebola hemorrhagic fever, EVD is caused by a virus of the family Filoviridae, genus *Ebolavirus*. It is a rare and deadly disease, with little treatment and no vaccine available at this time. Ebola virus disease initially presents with fever, chills, and malaise. Initial symptoms are similar to malaria and typhoid fever, as well as to more mundane illnesses such as influenza. However, as EVD progresses gastrointestinal symptoms develop, with severe watery diarrhea, vomiting, abdominal pain, and nausea. Other symptoms include chest pain, headache, cerebral edema, seizures, and bleeding. The bleeding events include petechiae, oozing from venipuncture sites, mucosal hemorrhage, and unexplained bleeding (the hemorrhagic fever). The mortality rate is high, but it varies depending on the care and support provided and the patient’s immune response. Mortality rates from 37% to 74% have been reported in regions of West Africa. Among the 27 patients infected in the 2014 outbreak who were cared for in Europe or the United States, the fatality rate was 18.5%.

Ebola takes its name from the Ebola River in the Democratic Republic of the Congo, near the place the virus was discovered in 1976. It is believed that the virus is animal-borne. Although the natural reservoir for the virus is unknown, it is suspected that bats are a carrier and likely reservoir. Within the genus *Ebolavirus* there are five species, named after the areas the virus was discovered. *Bundibugyo ebolavirus*, *Zaire ebolavirus*, *Sudan ebolavirus*, and *Tai Forest ebolavirus* infect humans. The fifth, *Reston ebolavirus*, has so far been found only in nonhuman primates. Although identified more than 40 years ago, infections have until recently been localized endemic outbreaks. Now the virus has traveled to different continents. EVD has the potential to cause serious public health consequences.

In humans, EVD is transmitted through contact with the blood or body fluids of an infected person who has symptoms, or of one who has died of EVD. Other routes of transmission are through objects (e.g., needles, materials in contact with the infected) that have been contaminated by the body fluid of infected living or deceased persons with EVD. It has been reported that the virus has been transmitted through contact with the semen of a man who had recovered from EVD.

**Laboratory Concerns**

The laboratory must be vigilant when there is a report of EVD. Testing specimens from an infected patient may contaminate mainframe laboratory instruments, which can become a potential source of infection. Once contaminated, the instruments must be removed from service. Laboratories must
consider the impact on current testing instruments; perhaps point-of-care testing (POCT) instruments should be considered. The cost associated with the POCT instruments can be justified should they need to be discarded. Laboratory tests are available for identifying the virus using enzyme-linked immunosorbent assay (ELISA), polymerase chain reaction (PCR), and immunoglobulin M (IgM) and G (IgG) antibody testing.

Because the virulence of EVD is so high and it can take up to 21 days before symptoms are manifested, the CDC recommends placing these patients in the category of persons under investigation (PUI) for EVD. Testing for Ebola should be limited to the PUI until their infection status is determined. PUI are provided appropriate care until a definitive diagnosis is made. At a minimum, limited laboratory testing must be provided to help treat these patients. A combination of laboratory tests and clinical signs and symptoms are the route to diagnosing EVD.

Recommended tests for the care and diagnosis of a patient with suspected EVD include the following:

- “Chem 7,” which includes sodium, potassium, bicarbonate, chloride, urea nitrogen, creatinine, and glucose
- Liver function tests
- Complete blood cell count (CBC)
- Prothrombin time/ international normalized ratio (PT/INR)
- Dipstick urinalysis
- Blood culture
- Malaria and influenza virus testing

Current treatment is to provide supportive measures. Recommended care includes maintaining blood pressure, managing dehydration caused by severe diarrhea and vomiting, replacing fluid volume, and treating secondary infections. In the case of hemorrhage, appropriate therapy must be provided. Vaccines against Ebola are being developed and are in clinical trials. However, no vaccine has been successful in preventing disease. Experimental treatment with plasma collected from persons recovering from EVD has been used. However, due to limited controlled studies, there is insufficient data to determine whether this treatment is effective.

**West Nile Virus**

The West Nile virus (WNV) also presents with symptoms similar to those of other, more common, infections that produce febrile reactions. First identified in Uganda in 1937, WNV came to public attention in the U.S. after an outbreak in New York in 1999 that involved humans, horses, dogs, and other animals.
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(cont.)

By 2002, infections had reached the west coast of the United States, and a 2012 outbreak in Texas caused 1,868 documented cases, with 844 having serious complications.

WNV is an arbovirus, a virus transmitted by arthropods, most commonly mosquitoes and ticks. The most common vector for WNV is the mosquito. The natural hosts of WNV are nonhuman mammals and birds. Humans are most commonly infected by the bite of an infected mosquito. Person-to-person transmissions (e.g., from a blood transfusion) are rare.

Presentation includes headache and gastrointestinal involvement. Because it mimics other infections, WNV is often initially misdiagnosed, thereby delaying appropriate treatment and care. The CDC reports that an estimated 70% to 80% of WNV cases are subclinical or asymptomatic. In less than 1% of cases, the infection develops into neuroinvasive disease such as encephalitis, meningitis, or acute flaccid paralysis. Most patients with WNV infections without neurologic involvement recover completely.

Prompt diagnosis helps with early management, and a timely public health response helps contain the further spread of infection. Laboratory tests for WNV are most commonly immunoassays for IgG and IgM. Other tests include viral cultures, PCR, and immunohistochemical assays on collected tissue. WNV can quickly spread, and the most useful tests are for WNV-specific IgM antibodies. IgM antibodies are detectable within 3 to 8 days of infection and indicate a recent infection. Because WNV is a reportable disease, prompt identification of localized infections will trigger containment efforts by public health agencies to prevent further infections and spread.

IgG antibodies are also detectable. They appear shortly after IgM antibodies are detected. IgG antibodies indicate an infection sometime in the past and are useful for identifying the virus. However, because IgG persists for many years, it is less useful than IgM from an epidemiologic viewpoint.

There are no approved vaccines to prevent WNV. There is no specific treatment other than to manage pain associated with headaches, and provide antiemetic therapy and appropriate rehydration to offset dehydration caused by nausea and vomiting. Patients whose WNV develops into encephalitis require monitoring for, and treatment of, increased intracranial pressure and seizures.

The best course of action against WNV is prevention. The goal is to remove the vector responsible for its spread, the mosquito. Prevention of mosquito bites that may transmit WNV includes using screens on doors and windows, removing the standing water that is the mosquitoes’ habitat, and wearing long sleeves and pants. Monitoring and screening for WNV in blood and organ donations is also an important measure.
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Summary

There is no effective vaccine for either Ebola virus or West Nile virus. Treatment is management of symptoms with supportive care. From an epidemiologic perspective, EVD and WNV are best managed by containment of the infection and prevention of transmission and spread.

Suggested Reading

There are many resources about EVD and WNV from the CDC and the WHO. Here is a sample:


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