ROLE OF PHARMACISTS IN EBOLA VIRUS DISEASE MANAGEMENT: AN OVERVIEW

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ABSTRACT

Ebola virus disease or Ebola virus infections or Ebola hemorrhagic fever is a severe, often fatal illness, with a death rate of up to 90%. The illness affects humans and non-human primates (monkeys, gorillas, and chimpanzees). Ebola hemorrhagic fever is caused by infection with a virus of the family Filoviridae, genus Ebola virus. There are five identified subtypes of Ebola virus. The virus spreads person-to-person through contact with bodily fluids, such as blood or secretions, according to World Health Organization, Symptoms include fever, muscle pain and headache, followed by vomiting, diarrhea, rash and, in some cases, internal and external bleeding, severely ill patients require intensive supportive care. No licensed specific treatment or vaccine is available for use in people or animals. In this article, information about the Ebola virus, its transmission, signs, symptoms, diagnosis, some preventive and control measures are discussed.


INTRODUCTION

Ebola virus disease (EVD) or Ebola hemorrhagic fever (EHF) is the human disease caused by the Ebola virus. Ebola first appeared in 1976 in two simultaneous outbreaks, 1) in Nzara, and Sudan region, 2) in Yambuku and Democratic Republic of Congo region. The latter was in a
village situated near the Ebola River, from which the disease takes its name. The virus may be acquired upon contact with blood or bodily fluids of an infected animal (commonly monkeys or fruit bats). Transmission through the air has not been documented in the natural environment. Symptoms typically start within 2 days to 3 weeks after contracting the virus, with a fever, sore throat, muscle pains, and headaches. Typically nausea, vomiting, and diarrhea follow, along with diminished functioning of the liver and kidneys. At this point, some people begin to have bleeding problems. The Ebola virus attacks immune cells, and can cause the immune system to run out of control and release a “storm” of inflammatory molecules, which cause tiny blood vessels to burst. This blood-vessel damage can cause blood pressure to drop, and lead to multiple-organ failure. There is no specific treatment for the disease; efforts to help persons who are infected include, giving either oral rehydration therapy (slightly sweet and salty water to drink) or intravenous fluids. The disease has high mortality rate: often killing between 50% and 90% of those infected with the virus.\textsuperscript{[1, 2]}

**Table No. 1: Scientific Classification\textsuperscript{[7]}**

<table>
<thead>
<tr>
<th>Group</th>
<th>Group V (-) ssRNA</th>
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</thead>
<tbody>
<tr>
<td>Order</td>
<td>Mononegavirales</td>
</tr>
<tr>
<td>Family</td>
<td>Filoviridae</td>
</tr>
<tr>
<td>Species</td>
<td>Ebola</td>
</tr>
<tr>
<td>Genus</td>
<td>Ebola like viruses</td>
</tr>
<tr>
<td>Source</td>
<td>Ebola’s natural reservoir is unknown; Non human primates have been the source of human infections but are not thought to be the reservoirs</td>
</tr>
</tbody>
</table>

Ebola virus contain linear non-segmented, single-strand, non-infectious RNA genomes of negative polarity that possesses inverse-complementary 3’ and 5’ termini, do not possess a 5’ cap, are not polyadenylated, and are not covalently linked to a protein. The genomes of the five different Ebola viruses differ in sequence and the number and location of gene overlaps. RNA strand viruses (Coiled RNA in spike-covered envelope from host cell) are long rods. Its replication period is 8 hours, therefore, spreads rapidly.

Transmission Infections with Ebola virus are acute. There is no recorded carrier state. Since the natural reservoir of the virus is unknown, the manner in which the virus first appears in a human at the start of an outbreak has not been determined. However, researchers have hypothesized that the first patient becomes infected through contact with the body fluids of an
infected animal. Humans can spread the virus in several ways. People can be exposed to Ebola virus from direct contact with the blood and/or secretions of an infected person. Therefore the virus has often been spread through the families and friends of infected persons: in the course of feeding, holding or otherwise caring for them, family members and friends would come into close contact with such secretions. People also can be exposed to Ebola virus through contact with objects such as syringe needles that have been contaminated with infected secretions.

Amongst the five virus types described, Ebola-Reston is not harmful to human species, but this virus can be spread through air. In a research centre of Virginia, Ebola-Reston was spread from monkey to monkey through the air. However no human transmissions were documented. The incubation period for EVD ranges from 2 to 21 days. The hope is that antibodies against Ebola that are present in survivors’ blood might have a protective effect in those infected with the virus. Although some patients have been given such 'convalescent' blood or plasma alongside other care, it is unclear whether it is safe and effective because no proper clinical trials have yet been done. The therapy would have the advantage that it could be scaled up quickly - there are now thousands of people who have survived Ebola in West Africa, many of whom are potential donors. By comparison, the Ebola vaccines that are currently under development might not be produced and deployed fast enough to help in the current epidemic, even if they prove to be effective. There is also no approved drug treatment for Ebola, which in this epidemic has a fatality rate of around 70%.

Convalescent blood therapy was discovered by the Prussian scientist Emil von Behring as an effective treatment for diphtheria and tetanus, work for which he won the first ever Nobel Prize in Physiology or Medicine in 1901. The therapy was widely used in the first half of the twentieth century to treat many infectious diseases, ranging from hepatitis A to poliomyelitis. It fell out of use with the development of antibiotic and antiviral drug treatments, although it is still used to treat some diseases, including Argentine haemorrhagic fever, a rodent-borne illness that is endemic in parts of Argentina. Antibodies extracted specifically from plasma - the fluid in which blood cells are suspended - are also used to treat several diseases, such as rabies and botulism. Liberia trial the first trial of the convalescent therapy began in Liberia late last week with the collection of plasma from survivors at the ELWA 2 hospital in Monrovia and the transfusion of the trial's first patient.
The trial is being funded by the Seattle-based Bill & Melinda Gates Foundation as part of its US$5.7-million support for developing and testing experimental Ebola treatments. It is being organized by Clinical RM, a contract research organization in Hinckley, Ohio, in coordination with national health authorities and the World Health Organization (WHO).

Diagnosis Samples from the patient are collected and tested to confirm infection tests used in diagnosis are listed in Table No. 2:

<table>
<thead>
<tr>
<th>Timeline of Infection</th>
<th>Diagnostic tests available</th>
</tr>
</thead>
<tbody>
<tr>
<td>Within a few days after symptoms begin</td>
<td>Immunosorbent assay (ELISA) testing, IgM ELISA, Polymerase chain reaction (PCR), Virus isolation</td>
</tr>
<tr>
<td>Later in disease course or after recovery</td>
<td>IgM and IgG antibodies</td>
</tr>
<tr>
<td>Retrospectively in deceased patients</td>
<td>Immunohistochemistry testing, PCR, Virus isolation</td>
</tr>
</tbody>
</table>

**Efforts to Control the Current Outbreak**

To implement prevention and control measures in both Guinea and Liberia, ministries of health with assistance from Medecins Sans Frontieres, the World Health Organization, and others, put in place Ebola treatment centers to provide better patient care and interrupt virus transmission. Teams from CDC traveled to Guinea and Liberia at the end of March as part of a response by the Global Outbreak Alert and Response Network to assist the respective ministries of health in characterizing and controlling the outbreak through collection of case reports, interviewing of patients and family members, coordination of contact tracing, and consolidation of data into centralized databases. Cases are categorized into one of three case definitions: suspected (alive or dead person with fever and at least three additional symptoms, or fever and a history of contact with a person with hemorrhagic fever or a dead or sick animal, or unexplained bleeding); probable (meets the suspected case definition and has an epidemiologic link to a confirmed or probable case); confirmed (suspected or probable case that also has laboratory confirmation).

In late April, it appeared that the outbreak was slowing when Liberia did not report new cases for several weeks after April 9, and the number of new reported cases in Guinea decreased to nine for the week of April 27. Since then, however, the EVD outbreak has resurged, with neighboring Sierra Leone reporting its first laboratory-confirmed case on May 24, Liberia reporting a new case on May 29 that originated in Sierra Leone, and Guinea reporting a new high of 38 cases for the week of May 25. As of June 18, the total EVD case count reported for all three countries combined was 528, including 364 laboratory-confirmed, 99 probable,
and 65 suspected cases, with 337 deaths (case-fatality rate = 64%). Guinea had reported 398 cases (254 laboratory-confirmed, 88 probable, and 56 suspected) with 264 deaths (case-fatality rate = 66%) across nine districts. Sierra Leone had reported 97 cases (92 laboratory-confirmed, three probable, and two suspected) with 49 deaths (case-fatality rate = 51%) across five districts and the capital, Freetown. Liberia had reported 33 cases (18 confirmed, eight probable, and seven suspected) with 24 deaths (case-fatality rate = 73%) across four districts.\[3,4,5,6\]

**Role of Ebola Virus Disease (EVD)**

Major challenges faced by all partners in the efforts to control the outbreak include its wide geographic spread, weak health-care infrastructures, and community mistrust and resistance.\[10\] Retrospective case investigation has indicated that the first case of EVD might have occurred as early as December 2013.\[2\] To control the outbreak, additional strategies such as involving community leaders in response efforts are needed to alleviate concerns of hesitant and fearful populations so that health-care workers can care for patients in treatment centers and thorough contact tracing can be performed. Enhancing communication across borders with respect to disease surveillance will assist in the control and prevention of more cases in this EVD outbreak. In June 2014, the World Health Organization, via the Global Outbreak Alert and Response Network, requested additional support from CDC and other partners, necessitating the deployment of additional staff members to Guinea and Sierra Leone to further coordinate efforts aimed at halting and preventing virus transmission. Persistence of the outbreak necessitates high-level, regional and international coordination to bolster response efforts among involved and neighboring nations and other response partners in order to expeditiously end this outbreak.\[7,8\]

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**Fig. 1:** Represents the considerations of Ebola virus disease.\[7,8\]
Transmission
Ebola is introduced into the human population through close contact with the blood, secretions, organs or other bodily fluids of infected animals. In Africa, infection has been documented through the handling of infected chimpanzees, gorillas, fruit bats, monkeys, forest antelope and porcupines found ill or dead or in the rainforest. Ebola then spreads in the community through human-to-human transmission, with infection resulting from direct contact (through broken skin or mucous membranes) with the blood, secretions, organs or other bodily fluids of infected people, and indirect contact with environments contaminated with such fluids. Men who have recovered from the disease can still transmit the virus through their semen for up to 7 weeks after recovery from illness. Health-care workers have frequently been infected while treating patients with suspected or confirmed EVD. This has occurred through close contact with patients when infection control precautions are not strictly practiced. However, Ebola is not a respiratory disease like the flu, so it is not transmitted through the air. Ebola is not a food-borne or water-borne illness. Individuals who are not symptomatic are not contagious. In order for the virus to be transmitted, an individual would have to direct contact with an individual who is experiencing symptoms.

Key facts
Ebola virus disease (EVD), formerly known as Ebola haemorrhagic fever, is a severe, often fatal illness in humans. The virus is transmitted to people from wild animals and spreads in the human population through human-to-human transmission. The average EVD case fatality rate is around 50%. Case fatality rates have varied from 25% to 90% in past outbreaks. Community engagement is key to successfully controlling outbreaks. Good outbreak control relies on applying a package of interventions, namely case management, surveillance and contact tracing, a good laboratory service, safe burials and social mobilization. Early supportive care with rehydration, symptomatic treatment improves survival. There is as yet no licensed treatment proven to neutralise the virus but a range of blood, immunological and drug therapies are under development.

Signs and symptoms
The incubation period, that is, the time interval from infection with the virus to onset of symptoms is 2 to 21 days. Humans are not infectious until they develop symptoms. First symptoms are the sudden onset of fever fatigue, muscle pain, headache and sore throat. This is followed by vomiting, diarrhea, rash, symptoms of impaired kidney and liver function, and
in some cases, both internal and external bleeding (e.g. oozing from the gums, blood in the stools). Laboratory findings include low white blood cell and platelet counts and elevated liver enzymes.\textsuperscript{[14]}

**Diagnosis**

Other diseases that should be ruled out before a diagnosis of EVD can be made include: malaria, typhoid fever, shigellosis, cholera, leptospirosis, plague, rickettsiosis, relapsing fever, meningitis, hepatitis and other viral hemorrhagic fever. Due to its characteristic course and epidemiology, a history of exposure in an endemic area (i.e. sub-Saharan Africa) may prompt clinical suspicion. Culture is positive during the acute stages, and laboratory confirmation via polymerase chain amplification and/or antigen detection may be used.\textsuperscript{[12, 13]}

**Treatment**

Supportive care—rehydration with oral or intravenous fluid and treatment of specific symptoms, improves survival. There is as yet no proven treatment available for EVD. However, a range of potential treatments including blood products, immune therapies and drug therapies are currently being evaluated. No licensed vaccines are available yet, but 2 potential vaccines are undergoing human safety testing.

**Preventive Steps**

- Reducing the risk of wildlife-to-human transmission from contact with infected fruit bats or monkeys/apes and the consumption of their raw meat.
- Animals should be handled with gloves and other appropriate protective clothing. Animal products (blood and meat) should be thoroughly cooked before consumption. Reducing the risk of human-to-human transmission in the community arising from direct or close contact with infected patients, particularly with their bodily fluids.
- Close physical contact with Ebola patients should be avoided.
- Barrier nursing techniques include:
  - i) Wearing of protective clothing (such as masks, gloves, gowns, and goggles).
  - ii) Using infection-control measures (such as complete equipment sterilization and routine use of disinfectant).
  - iii) Isolating patients with Ebola from contact with unprotected persons.
  - iv) Regular hand washing is required after visiting patients in hospital, as well as after taking care of patients at home.
Case Report

Fig. 2: Case Report Based On Ebola Disease.

In 2004, a virologist at USAMRIID was working in a BSL-4 laboratory with mice that had been infected 2 days before with a mouse-adapted variant of the Zaire species of Ebola virus (ZEBOV).\(^2\) The virulence and infectious dose of this variant of ZEBOV are unknown in humans; wild-type virus has a case-fatality rate of up to 90%.\(^3\)

The person had been following standard procedure, holding the mice while injecting them intraperitoneally with an immune globulin preparation. While the person was injecting the fifth mouse with a hypodermic syringe that had been used on previous mice, the animal kicked the syringe, causing the needle to pierce the person’s left-hand gloves, resulting in a small laceration. The virologist immediately squeezed the site to force the extravasation of blood. After decontamination of the blue suit in the chemical shower, the injured site was irrigated with 1 liter of sterile water and then scrubbed with povidone-iodine for 10 minutes. In terms of exposure risk, the needle was presumed to be contaminated with virus-laden blood, although it was suspected that low levels of virus were present on the needle. The animals had not yet manifested signs of infection, and much contamination may have been removed mechanically when the needle pierced the gloves. The local decontamination of the site also reduced potential for infection.
USAMRIID medical, scientific, and executive staff concluded that the person with potential exposure warranted quarantine in the MCS. Contact plus airborne precautions (gown, gloves, N95 mask, and eye protection) were used, with a plan to upgrade to BSL-4 precautions for signs or symptoms of illness. These extra precautions were instituted while the patient was asymptomatic for several reasons:

1) The timing of initial clinical manifestations with regard to potential for shedding virus were not known for this specific isolate in human infection.

2) There was interest in ensuring all infection control procedures were being followed appropriately in advance of clinical illness.

3) There was interest in reducing any potential cofounders, such as a caregiver transmitting a febrile respiratory infection to the patient, which might lead to unnecessary procedures or additional isolation. The person was monitored for routine vital signs; daily laboratory studies (coagulation studies, blood counts, chemistries, viral isolation, D-dimer) and regular physician assessments were performed.

Over the next several days, discussions were held with several internationally recognized filovirus experts regarding potential treatments or post exposure prophylaxis options. Local and state public health officials were also notified. The consensus opinion was that there was no safe, readily available source of immune plasma and little evidence existed to support its use. Emergency investigational new drug (IND) protocols were established for treatment with recombinant nematode protein (rNAPc2) and antisense oligomers, with the intention to consider implementation only if the patient demonstrated evidence of infection. Ultimately, none of the 5 mice had confirmed viremia at the time of the incident. The patient did not become ill or seroconvert and was discharged after 21 days. The story received national and local media attention.

The study will involve around 70 subjects, says David Hoover, a senior scientific adviser at Clinical RM. That will include a comparison group of Ebola patients who will not receive plasma but will otherwise be given the same standard of care as the treatment group, Hoover says. The comparison group will contain patients who would not be eligible for treatment because their blood type is incompatible with that of any of the available plasma.

The trial's main goal is to test whether antibodies lower viral load. The small size of the study and the difficulty of working in the midst of an epidemic mean that it may not be possible to conclusively establish whether the therapy can save lives. It will take about ten weeks to
enroll all the patients in the study, and results will be shared as soon as possible. Hoover says
Guinea trial at the end of the year, a large consortium of European and African research and
blood-transfusion organizations will start a separate trial in Guinea. The study, which has €2.9
million (US$3.6 million) in funding from the European Union and further support from the
London-based biomedical charity the Welcome Trust, will be done in cooperation with the
humanitarian organization Medecins Sans Frontieres (also known as Doctors Without
Borders) at its Donka Ebola treatment centre in Conakry. The Guinea trial will involve 200 to
300 patients, with a comparison group as in the Liberia trial. With its larger size, it will aim to
assess the effect of the therapy on survival rates 14 days after treatment. Johan van
Griensven, a clinical researcher at the Institute of Tropical Medicine in Antwerp, Belgium,
who is coordinating the Guinea trial, says that the plan is to begin evaluating convalescent
plasma in late December or early January.

Blood versus Plasma

Using whole blood is less complicated than using plasma, which must first be separated from
blood by centrifugation. For responses to an epidemic, however, plasma is preferable,
because the remaining red blood cells can then be pumped back into the donors’ bodies. This
means that survivors can donate up to a litre of plasma, depending on their body weight,
every two weeks, whereas whole blood can be donated only once every three to four months.
Plasma can also be preserved for a year, whereas whole blood lasts for only a month or
so. The results of the Guinea trial could be available within two months or less, says van
Griensven, adding that he is "moderately optimistic" that the therapy will be effective.

In preparation for the trials, the organizers, together with national authorities, the WHO and
other international agencies, have been working to reinforce the region’s blood-transfusion
infrastructure — which in many places was almost non-existent. They have been training
health-care workers and providing tools to screen donated blood for pathogens such as HIV.

Convalescent blood and plasma would seem to be plausible treatments for Ebola, given that
tests of an experimental cocktail of monoclonal antibodies known as Z Mapp gave 100%
protection against the virus in rhesus macaques, says Calum Semple, a paediatrician and
clinical virologist at the University of Liverpool, UK, who is involved in the trial in Guinea.
But, he adds; only clinical trials can establish whether the therapy works. If it does,
production of convalescent serum will be scaled up immediately in West Africa. In Sierra
Leone, the third of the three countries most affected by the epidemic, the group Sierra Leone
Action plans to launch its own trials of convalescent plasma. Created by researchers and clinicians in the country and by Sierra Leoneans who have emigrated, the group hopes to begin collecting plasma later this month. [16, 17, 18]

Management Considerations [20, 22]

Given increasing interest in construction of additional laboratories for study of BSL-4 agents, potential exists for clinicians to manage an occupational exposure to these viruses. Our experience led us to formulate a stepwise approach that might help others plan for and manage similar incidents.

Step 1: Prepare

Occupational health clinics associated with containment laboratories should develop methods of assessing need for isolation and laboratory decontamination, exit, and notification procedures. Maintaining a close relationship with the bio safety office, thereby knowing the agents in use, will make planning appropriate treatments in advance easier.

It should be determined in advance where an asymptomatic patient might be observed and where to isolate and treat an infected patient. Separate locations may be required, but moving an ill patient may be challenging.

Step 2: Assess the Patient
A primary physician should be designated to develop the treatment/isolation plan in consultation with other experts. New diseases or medications need to be queried at the time of exposure evaluation if employees did not previously notify occupational health officials. This information must be gathered in a non-punitive environment so that reporting of potential exposures is not discouraged.

Risks for exposure and disease should be estimated with available information as reported. Care for family members, including children, the elderly, or pets, may need to be addressed, in addition to issues such as powers of attorney, advanced directives, last wills and testaments, and similar legal matters.[13]

**Step 3: Gather Appropriate Consultants and Team**
Designating another person to coordinate other activities surrounding a high-profile exposure (arranging conferences with external experts, handling media inquiries, issuing press releases, and interacting with external agencies) frees the primary physician to care for the patient. For any clinically important exposures, especially in the absence of licensed therapeutics, it is appropriate to seek advice of consultants. These persons may vary, depending on the organization, the pathogen in question, and individual expertise.

**Consultants to consider for establishing a team to manage a potential laboratory exposure**
Local and state public health agencies will need to be part of discussions if there is potential public health impact; these organizations will likely be fielding queries from the public and the press simultaneously. Local hospitals should be informed if there is potential for transferring the patient to those facilities. The Food and Drug Administration should be informed if establishment of an emergency use IND is contemplated. Any laboratory that might test clinical samples should also be informed in advance of specimens arriving.

**Step 4: Determine the Appropriate Level of Infection Control Measures**
Although specialized containment care procedures and facilities may play a limited role in certain extraordinary cases, such as those discussed here, CDC has published guidance for management of viral hemorrhagic fevers in more conventional settings.[19, 21] Standard, contact, and droplet precautions and a private room are recommended in initial outpatient or inpatient assessments in early stages of illness, and a face mask should be placed on patients with respiratory symptoms. A room capable of airborne isolation should be considered early
to prevent later need for transfer. Precautions should be upgraded to airborne isolation if a prominent cough, vomiting, diarrhea, or hemorrhage develops in a patient, or if the patient undergoes procedures that may stimulate coughing or generation of aerosols.

**Step 5: Provide Additional Communications**

Because filovirus exposure has a particular cachet and media interest may be intense, it is preferable to inform the media proactively. Public affairs personnel will need to develop press releases and arrange interviews in conjunction with a medical or scientific expert. Lessons can be learned from the negative publicity received after the tularemia exposures at Boston University [33, 34] and the death of the Russian researcher from infection with Ebola virus after a delay in disseminating that information. [12]

**Step 6: Conduct Appropriate Isolation Logistics**

A patient in quarantine results in logistical challenges (providing food and equipment and decontaminating personal, medical, and food waste) even before illness develops. CDC provides recommendations for specimen handling of viral hemorrhagic fever patients that include. [19, 21]

1) Minimizing laboratory procedures,
2) Alerting the laboratory of the nature of the specimens,
3) Transporting specimens in decontaminated leak-proof plastic containers,
4) Processing laboratory specimens in a class II biologic safety cabinet with BSL-3 practices, and
5) Performing virus isolation or culture in a BSL-4 laboratory.

If possible, CDC recommends pretreatment of serum specimens with heat (56°C) combined with polyethylene glycol p-tert-octylphenyl ether (Triton X-100) at a concentration of 10 μL/mL of serum to reduce viral titer; however, 100% inactivation may not occur. [21] Automated analyzers should be cleaned and disinfected according to manufacture recommendations or with sodium hypochlorite at a concentration of 500 ppm (1:100 dilutions). [20, 21]

One should also limit the number of staff performing 24 hour monitoring and establish restricted room access and an entry-tracking log. If the patient becomes ill, some staff that entered the room may require illness surveillance, especially if there were any breaches in infection control practices. A visitation policy may need to be addressed. Because spending
weeks in quarantine can be particularly stressful for the patient, it is useful to consider ways to keep the patient occupied, such as Internet connectivity, a television/video player, and a telephone.

**Step 7: Decide on Treatment**

Decisions on treatment/prophylaxis are difficult for viruses requiring BSL-4 precautions that lack any licensed therapy or prophylaxis. Therefore, having access to subject matter experts (as discussed in step 3) is essential. Collectively, difficult treatment decisions may be required that balance risk from investigational therapies against presumed risk for disease.

**Step 8: Keep a Journal**

Designation of a scribe early on should be considered to track major events, decision points, and options that were considered. Records of dates and times of important contacts should be included. Meeting minutes should be generated. Maintaining accurate logs may be useful to defend difficult decisions later and may help drive an after-action review.

**Step 9: Learn from the Experience**

It is useful to conduct a formal incident review that assesses how the event was managed. Results from any safety or epidemiologic investigations should be included. With appropriate review of procedures and training, additional potential exposures may be prevented.

Each occurrence was reported to the highest degree of spatial resolution available based upon the information provided, as long as they could be categorised into one of: index, secondary or imported cases. This ranged from point locations (indicative of a precise location, such as a village), to areas, termed polygon locations, which correspond approximately to administrative regions or custom digitised areas based on site descriptors within the primary articles. Administrative regions were defined as classified by the Food and Agriculture Organization’s Global Administrative Unit Layers (GAUL) coding.\[26]\]

These classify national boundaries as admin units, states or provinces as admin1 units and districts as admin2 units. By classifying Ebola occurrences as polygons we were able to represent the geographic uncertainty around the exact location of Ebola transmission which could have occurred anywhere within the defined region. For towns, the coordinates of the centre were recorded, unless a specific part of the town (or an explicit latitude and longitude) was described. Coordinates for point locations were extracted using Google Earth. If the area
concerned could not be assigned to a finer resolution than 50 km × 50 km, it was entered as polygon rather than point data. If specified regions could not be linked to an admin1 or admin2 unit, custom polygons were digitised using site descriptions in the text articles. For imprecise descriptors e.g., ‘150 km from the town’ with no direction specified or ‘cases occurred on a north-south road between village X and Y’, circular polygons were digitised based on radius distances given or extreme points that defined the geographic limits of transmission.

These circular polygons could be trimmed if their area included admin1 or admin2 administrative regions which reported no EVD patients. Some articles referred to ‘healthcare districts’ that did not correspond to admin1 or admin2 units, but were definable based on maps presented in the primary literature that were digitised or were available on the map sharing website IKI (www.ikimap.com).[27] For index cases that referred to suspected zoonotic transfer in specific forests or game reserves, polygons were drawn based on the specified park or forest geographic boundary as shown in Google Earth. Two exceptional cases were present.[13] The index case transmission site description merely mentioned a case being reported as ‘near the town of Mbandza’. In this instance a circular polygon was defined with radius of half the distance to the next specified location of transmission (7.50 km).[15]

In the second, for outbreak, two locations described in the primary literature could not be located, but were described as ‘near to the town of Booue’.[18] As a result the same procedure was undertaken and a radius of 30 km was defined around the village of Booue. The total number of cases for each outbreak was obtained from the most recent primary source. Cases included both clinically suspected and laboratory confirmed cases at the point of care, or diagnosed retrospectively. The number of people who died with a suspected or confirmed diagnosis of EVD was also recorded. These data were spatially disaggregated as much as possible from the information given in the text to give measures of spatial variation in case fatality rate within an outbreak.[9]

**Signs & Symptoms**

The signs and symptoms of EVD are not the same for all patients. The table below outlines symptoms of the disease according to the frequency with which they have been reported in known cases. Researchers do not understand why some people are able to recover from EVD and others are not. However, it is known that patients who die usually have not developed a significant immune response to the virus at the time of death.
Treatment
There is no standard or specific treatment is available. No vaccine for EVD is available. Several vaccines are being tested, but none are available for clinical use. Severely ill patients require intensive supportive care. Patients are frequently dehydrated and require oral rehydration with solutions containing electrolytes or intravenous fluid. No new drug therapies are being evaluated.

Prevention
The risk of becoming infected with the Ebola virus can be lowered by avoiding locations where it is found, especially during times when there is an outbreak of Ebola fever. Whenever traveling to Africa, avoid handling live or dead wild animals. Also, it is always better to wear special protective clothing (gown, gloves, full face mask and eye goggles) around a person with Ebola fever. Some species of animals besides primates may carry the Ebola virus. The African subtypes of the virus have also been found in forest antelopes and fruit bats.\textsuperscript{[25, 26]}

Preventive measures [WHO, 2014]\textsuperscript{[28, 31]}
1. Stop the consumption of animal meat.
2. Isolate the sick.
3. Prompt disposal of victim’s bodies.
4. Trace those who had contact with infected.
5. Disinfect homes of the dead and sick.
6. Protective clothing for health care workers, anyone handling infected animal.

Controlling the spread of Ebola
a. Hospitals must follow precautionary methods, such as:
   1. Wearing gloves
   2. Isolating infected individuals
   3. Practicing nurse barrier techniques
   4. Proper sterilization and disposal of all equipment

b. Burials must be done correctly
   1. No washing or touching carcass
2. Put into body bags and bury outside city
c. Report any questionable illness to officials.

CONCLUSIONS[35, 36]
The Ebola is a deadly virus but need not worry about this, as spreading of the virus can be stopped by preventive measures. So far so good the history showed that, many of the so called deadly diseases and outbreaks have been either eradicated or sure cure is available, through scientific research. The day is not far when a vaccine or cure is available for EVD.

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