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Outbreaks of Ebola Virus Disease in the West African Sub-Region

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Abstract

Background: Five West African countries, including Nigeria are currently experiencing the largest, most severe, most complex outbreak of Ebola virus disease in history. This paper provided a chronology of outbreaks of Ebola virus disease in the West African sub-region and provided an update on efforts at containing the present outbreak.

Methods: Literature from Pubmed (MEDLINE), AJOL, Google Scholar and Cochrane database were reviewed.

Results: Outbreaks of Ebola virus disease had frequently occurred mainly in Central and East African countries. Occasional outbreaks reported from outside of Africa were due to laboratory contamination and imported monkeys in quarantine facilities. The ongoing outbreak in West Africa is the largest and first in the sub-region; the number of suspected cases and deaths from this single current outbreak is already about three times the total of all cases and deaths from previous known outbreaks in 40 years. Prevention and control efforts are hindered not only by lack of a known vaccine and virus-specific treatment, but also by weak health systems, poor sanitation, poor personal hygiene and cultural beliefs and practices, including myths and misconceptions about Ebola virus disease – all of which are prevalent in affected countries. Constrained by this situation, the World Health Organisation departed from the global standard and recommended the use of not yet proven treatments to treat or prevent the disease in humans on ethical and evidential grounds.

Conclusion: The large number of people affected by the present outbreak in West Africa and the high case-fatality rate calls for accelerated evaluation and development of the investigational medical interventions for life saving and curbing the epidemic. Meanwhile, existing interventions such as early detection and isolation, contact tracing and monitoring, and adherence to rigorous procedures of infection prevention and control should be intensified.

Keywords: *Ebola Virus Disease, Outbreak, Treatments, Prevention, Control, West Africa*

Résumé

Contexte: cinq pays de l'Afrique de l'Ouest, y compris le Nigériaconnaissentactuellement le plus grand et le plus grave, la plus complexeépidémied'Ebola virus maladie de l'histoire. Ce document fourniunechronologie des épidémies de virus Ebola la maladiedans la sous-régionouest-africaineet a fourniunemise à jour sur les efforts visant à endiguer la flambéeactuelle.

Méthodes : La littérature de Pubmed (MEDLINE), AJOL, Google Scholar et Cochrane database ontétéexaminés.

Résultats : Des épidémies de virus Ebola la maladieavaitfréquemments'estproduiteprincipalement en pays d'Afriquecentrale et orientale. Occasionnellement des flambéesontétésignalées à l'extérieur de l'Afriqueétaientdus à la contamination laboratoireet singes importésdans les installations de quarantaine. La flambée en cours en Afrique de l'Ouestest la plus grande et la première dans la sous-région; le nombre de cas suspects et de décèsdus à cetteseuleépidémieactuelleest déjà environ troisfois le total de tous les cas et les décèsdus au précédentconnu des flambéesdans 40 ans. Les efforts de prévention et de luttesontentravées non seulement par le manque d'un vaccinconnu et virus de traitementspécifique, maisaussipar la faiblesse des systèmes de santé, le manqued'assainissement, la médiocrité de l'hygiènepersonnelle, les pratiques et les croyancesculturelles, y compris les mythes et idéesfausses au sujet de virus Ebola maladie - qui sonttous des répanduedans les pays touchés. Entravée par cette situation, l'Organisationmondiale de la Santé s'écartait de la normemondialeet a recommandél'utilisation de pas encore traitementséprouvés pour traiterouprévenir la maladie chez les humainssuréthique et motifs probante.

Conclusion : Le grand nombre de personnestouchéespar la flambéeactuelle en Afrique de l'Ouest et le haut taux de létalitéappelsd' uneévaluationaccélérée et le développement des médicamentsexpérimentaux interventions médicales pour sauver la vie et contrel'épidémie. Entre-temps, les interventions existantes tellesquedétectionprécoce et à l'isolement, recherche des contacts et la surveillance, et le respect de procéduresrigoureuses de prévention et de contrôle des infections doitêtreintensifiée.

Mots-clés : *Virus Ebola Maladie, épidémie, les traitements, la prévention, le contrôle, l'Afrique de l'Ouest*

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Introduction

A large outbreak of haemorrhagic fever (subsequently named Ebola haemorrhagic fever) occurred in southern Sudan between June and November, 1976. The first victim to contract Ebola was a cotton factory worker from Nzara, Sudan. Soon after he came down with symptoms, so did his co-worker. Then, the co-worker's wife became sick with Ebola virus infection. The outbreak spread quickly to the Sudanese town of Maridi, where there was a hospital. Since no one in the medical field had ever seen this illness before, it took them sometime to realize that it was passed by close contact. By the time the outbreak was contained in Sudan, 284 people had become ill; out of these, 151 died. This new illness was labeled as *'a killer'*, giving a case fatality rate of 53%. This strain of the virus is now called Ebola-Sudan [1].

Between 1st September and 24th October, 1976, another outbreak of Ebola occurred in Zaire (now Democratic Republic of Congo) – this outbreak was probably more deadly than the outbreak in Sudan. The first victim of this outbreak was a 44-year-old teacher who had just returned from a tour of northern Zaire. He experienced symptoms suggestive of malaria and sought treatment from Yambuku Mission Hospital, where he received injections of an anti-malarial drug. Poor injection safety practices such as re-use of needles and non-sterilization of used needles helped in spreading Ebola virus to many of the hospital's staff and patients. This outbreak continued for four weeks but was contained by the closure of the hospital and isolation of Ebola infected patients. By this time however, the Ebola virus had been contracted by 318 people, 280 of whom died including 11 of the 17 hospital staff giving a case fatality rate of 88%. This strain of the Ebola virus now called Ebola-Zaire remains the most deadly of the Ebola viruses in Zaire. Yambuku is a village along the course of Ebola River which is a tributary of the Congo River. Thus, the virus was named after the river in the same way the Lassa virus was named after Lassa village in Borno State of Nigeria [2].

The Ebola virus came into a global focus on October 13, 1976, in Atlanta, United States of America after a radio report of its epidemic in African country. Dr. Frederick Murphy (now Professor of Pathology at the University of Texas Medical Branch at Galveston), who was then the chief of viral pathology branch at the Centre for Disease Control and Prevention was the first to detect this virus with the electron microscope. He described the shape of the virus as being dramatic and different from the other little round viruses just like Marburg virus. Patricia Webb worked with Murphy to culture the virus. There was no genetic technique for identification purposes but the virus was observed to grow very quickly.

Ever since these two outbreaks in 1976, Ebola virus disease has continued to occur mainly in Central and East African countries which have experienced about 70% of the outbreaks; these outbreaks resulted in a total of 2,345 EVD cases and 1,546 deaths. Occasional outbreaks reported from outside of Africa such as the Philippines, Russia and United States of America were due to laboratory contamination and imported monkeys in quarantine facilities [3].

The current epidemic of Ebola virus disease began in December 2013 in Guinée Forestière (Forested Guinea), the eastern sector of the Republic of Guinea. Guinea is located on the Atlantic coast of West Africa and has become the first country in this geographical region in which an outbreak of EVD has occurred; the outbreak has been described as the largest Ebola outbreaks in history and the first in West Africa. Five countries are presently affected, namely Guinea, Liberia, Nigeria, Sierra Leone and Senegal (Table 1) [4,5].

Methodology

The authors reviewed literature using key words of the thrust of the paper; hence, search terms such as Ebola virus disease, outbreak, clinical features,

Table 1: 2014 Ebola Outbreak in West Africa - Affected Areas

Countries	Affected areas
Guinea	Conakry, Coyah, Forecariah, Gueckedou, Kouroussa, Macenta, Siguiri, Pita, Nzerekore, Dubreka, Yomou, Kerouane**No longer active**: Boffa, Dabola, Dinguiraya, Kissidougou, Telimele
Liberia	Lofa, Montserrado, Margibi, Bomi, Bong, Grand Cape Mount, Nimba, Grand Bassa, Grand Gedeh, RiverCess, River Gee, Sinoe, Gbarpolu
Nigeria	Port Harcourt, Lagos
Sierra	Kailahun, Kenema, Kono, Kambia, Bombali, Tonkolili, Port Loko, Pujehun, Bo, Moyamba, Bonthe, LeoneWestern area
Senegal	Dakar

treatments, prevention and control in West Africa were used. Literature on cross-sectional, observational and randomized control studies published on the subject between 2000 and 2014 served as the main sources of information; these were obtained from the commonly used medical databases such as PubMed (Medline), AJOL and Google Scholar. Cochrane Library was searched for systematic reviews while websites of international organizations served as sources for experts' reports and updates on the subject matter.

Results

Virology and pathogenesis of Ebola virus

Ebola Virus Disease (EVD) is a viral haemorrhagic fever (VHF) caused by the Ebola virus; other VHF include Marburg, Lassa, Dengue, etc. The causative agent is Ebola virus. Together with Marburg virus, it forms the family Filoviridae. Filoviridae have a non-segmented single-strand genome with minus polarity and therefore belong to the order Mononegavirales. They are closely related to the genus pneumovirus. Marburg virus and Ebola virus each constitute a separate genus, based on differences in their genome organisation. Maridi virus which was isolated in 1976 during an epidemic in Sudan is distinct from Ebola virus-Zaire. Ebola virus-Ivory Coast (1994) appears to represent an even more distantly related subtype [6]. There are currently five known strains of the Ebola virus: Zaire, Sudan, Côte d'Ivoire, Bundibugyo and Reston. So far, the Zaire strain remains the most deadly (80% death rate) and the Reston the least (0% death rate). However, the Ebola-Zaire and Ebola-Sudan strains have caused all the major known outbreaks.

Ebola virus enters the body through mucous membranes, breaks in the skin, or parenterally. It enters the cells by endocytosis. The pathogen infects many cell types, including monocytes, macrophages, dendritic cells, endothelial cells, fibroblasts, hepatocytes, adrenal cortical cells, and epithelial cells [7]. Whatever the point of entry into the body, macrophages and dendritic cells are probably the first cells to be infected. Filoviruses replicate readily within these ubiquitous "sentinel" cells, causing their necrosis and releasing large numbers of new viral particles into extracellular fluid [8, 9]. Spread to regional lymph nodes results in further rounds of replication, followed by dissemination of virus to dendritic cells and fixed and mobile macrophages in the liver, spleen, thymus, and other lymphoid tissues. Rapid systemic spread is aided by virus-induced suppression of type I interferon responses [10]. In addition to causing extensive tissue damage, filoviruses also induce a systemic inflammatory syndrome by inducing the release of cytokines, chemokines, and other proinflammatory mediators from infected macrophages and other cells [8, 9]. Macrophages infected with Ebola-Zaire virus produce tumor necrosis factor (TNF)-alpha, interleukin (IL)-1beta, IL-6, macrophage chemotactic protein (MCP)-1, and nitric oxide (NO) [11]. These and other substances have also been identified in blood samples from Ebola-infected macaques and from acutely ill patients in Africa [12, 13]. Breakdown products of necrotic cells also stimulate the release of the same mediators [14]. It is thus the host response to infection, rather than any toxic effect of the virus, that is responsible for the fever, malaise, vasodilatation, increased vascular permeability, hypotension, and shock of filoviral disease [15].

The coagulation defects seen in Marburg and Ebola virus disease are also induced indirectly. Virus-infected macrophages synthesize cell-surface tissue factor (TF), triggering the extrinsic coagulation pathway. Pro-inflammatory cytokines also induce macrophages to produce TF [16]. The simultaneous occurrence of these two stimuli helps to explain the early appearance, rapid development, and ultimate severity of the coagulopathy in filovirus infection. As the disease progresses, hepatic injury may also cause a decline in plasma levels of certain coagulation factors.

Failure of adaptive immunity, through impaired dendritic cell function and lymphocyte apoptosis, helps to explain how these viruses are able to cause severe and frequently fatal illness [17]. Filoviruses act both directly and indirectly to disable antigen-specific immune responses. Dendritic cells, which have primary responsibility for the initiation of adaptive immune responses, are a major site of filoviral replication. In vitro studies have shown that infected cells fail to undergo maturation and are unable to present antigens to naive lymphocytes, potentially explaining why patients dying from Ebola hemorrhagic fever do not develop antibodies to the virus [18-20]. Adaptive immunity is also impaired by the massive loss of lymphocytes that accompanies lethal Ebola virus infection [20]. Lymphocytes remain uninfected, but undergo "bystander" apoptosis, presumably induced by inflammatory mediators and/or the loss of support signals from dendritic cells. A similar phenomenon is observed in septic shock [21-24]. However, one study has shown that, at least in mice, virus-specific lymphocyte proliferation still occurs, in spite of the surrounding massive apoptosis, but it arrives too late to prevent a fatal outcome [25].

Discovering ways to accelerate and strengthen such responses may prove to be a fruitful area of research.

Epidemiology, diagnosis, treatment and prevention of Ebola virus disease

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. Burial ceremonies in which mourners have direct contact with the body of the deceased person can also play a role in the transmission of Ebola. 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.

Among workers in contact with monkeys or pigs infected with Reston ebola virus, several infections have been documented in people who were clinically asymptomatic. Thus, RESTV appears less capable of causing disease in humans than other Ebola species.

However, the only available evidence available comes from healthy adult males. It would be premature to extrapolate the health effects of the virus to all population groups, such as immuno-compromised persons, persons with underlying medical conditions, pregnant women and children. More studies of RESTV are needed before definitive conclusions can be drawn about the pathogenicity and virulence of this virus in humans.
(Source: WHO 2014 - Ebola virus disease Fact sheet N°103, Updated April 2014) [26]

Signs and symptoms

The incubation period i.e. the time interval from infection with the virus to onset of symptoms, on average is 6 to 9 days, with a range of 2 to 21 days.

EVD is a severe acute viral illness often characterized by the sudden onset of fever, intense weakness, muscle pain, headache and sore throat. This is followed by vomiting, diarrhoea, rash, impaired kidney and liver function, and in some cases, both internal and external bleeding. Laboratory findings include low white blood cell and platelet counts and elevated liver enzymes.

People are infectious as long as their blood and secretions contain the virus. Ebola virus was isolated from semen 61 days after onset of illness in a man who was infected in a laboratory.
(Source: WHO 2014 - Ebola virus disease Fact sheet N°103, Updated April 2014) [26]

All ages are susceptible, but 20 - 40 years old persons are mostly affected. A hemorrhagic diathesis was found in 75% of the cases, and a maculopapular exanthema was found in 50% of the cases [5]

Diagnosis of Ebola virus disease

Case-classification criteria for Ebola virus disease

Ebola cases are classified as suspected, probable, or confirmed depending on whether they meet certain criteria as follows:

A suspected case

Any person, alive or dead, who has (or had) sudden onset of high fever and had contact with a suspected, probable or confirmed Ebola case, or a dead or sick animal OR any person with sudden onset of high fever and at least three of the following symptoms: headache, vomiting, anorexia/ loss of appetite, diarrhoea, lethargy, stomach pain, aching muscles or joints, difficulty swallowing, breathing difficulties, or hiccup; or any person with unexplained bleeding OR any sudden, unexplained death.

A probable case

Any suspected case evaluated by a clinician OR any person who died from 'suspected' Ebola and had an epidemiological link to a confirmed case but was not tested and did not have laboratory confirmation of the disease.

A confirmed case

A probable or suspected case is classified as confirmed when a sample from that person tests positive for Ebola virus in the laboratory.

Laboratory diagnosis

Plama, EDTA-treated blood, urine, or liver and spleen from deceased persons are suitable for the detection of the virus by electron microscopy, isolation in cell culture (vero cell clone E6), RTPCR and antigen detection with an antigen capture ELISA. These tests should only be performed by experienced personnel

in special laboratories with Biosafety Level (BSL)-4 precautions [5].

Amplification products should always be sequenced and if possible, the diagnosis should be confirmed by the amplification of an additional sequence product from another viral gene. During a recent outbreak in 2000, an antigen ELISA, an antibody ELISA and RT-PCR were used for the diagnosis. A serological diagnosis based on IgM capture ELISA is superior to immunofluorescence towards the end of the first week of the disease. ELISA tests are used in epidemiological surveys [5]

During an outbreak, virus isolation is often not feasible. The most common diagnostic methods are therefore real time PCR and ELISA detection of proteins, which can be performed on the field or in mobile hospitals [27]. Filovirions can be seen and identified in cell culture by electron microscopy due to their unique filamentous shapes, but electron microscopy cannot tell the difference between the various filoviruses despite there being some length differences [28]. Table 2 shows the types of diagnostic tests which can be used during the course of infection.

Table 2: Timelines of infection and diagnostic tests

Timeline of Infection	Diagnostic tests available
Within a few days after symptoms begin	· Antigen-capture enzyme-linked immunosorbent assay (ELISA) testing - IgM ELISA
Polymerase chain reaction (PCR)	- Virus isolation
Later in disease course or after recovery	· IgM and IgG antibodies
Retrospectively in deceased patients	· Immunohistochemistry testing PCR Virus isolation

Differential Diagnosis

It is important to keep in mind that haemorrhages are only seen in some of the patients, especially in those with a fatal course. Some bacterial agents may cause hemorrhagic fever more frequently than Ebola virus, e.g. meningococci, leptosipres, rickettsiae, salmonellae and shigellae. Hemorrhagic fever caused by viruses like yellow fever and other flavivirus infections as well as Lassa fever, Crimean-Congo hemorrhagic fever, hantavirus, and Marburg virus infections have to be excluded in the differential diagnosis [5].

Vaccine and treatment

No licensed vaccine for EVD is available. Though several vaccines are being tested, but none are available for clinical use [26]. No Ebola virus-specific treatment exists [29]. However, new drug therapies are being evaluated. Severely ill patients require intensive supportive care. These measures may include: pain management, medications for nausea, fever and anxiety, as well as oral rehydration with solutions containing electrolytes or intravenous fluids [27] as patients are frequently dehydrated.

Blood products such as packed red blood cells, platelets or fresh frozen plasma may also be used [27]. Other regulators of coagulation have also been tried including heparin in an effort to prevent disseminated intravascular coagulation and clotting factors to decrease bleeding. Medication for malaria and bacterial infections have often been used as initially the diagnosis is usually not clear. Early treatment may increase the chance of survival. A number of experimental treatments are being studied. The United States Food and Drug Administration has allowed two drugs, Z-Mapp and an RNA interference drug called TKM-Ebola, to be used in people infected with Ebola under these drug trials during the 2014 outbreak [30].

Local herbs

There is no evidence that bitter cola, ginger, aloe vera, garlic or any other local preparation has any effect on any virus.

Drug treatment trials

As at 14th August, 2014, the FDA has not approved any medications or vaccines to treat or prevent Ebola and advised people to watch out for fraudulent products [31]. The unavailability of experimental treatments in the most affected regions during the 2014 outbreak spurred controversy; one school of thought called for experimental drugs to be made more widely available in Africa on a humanitarian basis while another warned that making unproven experimental drugs widely available would be unethical, especially in the light of past

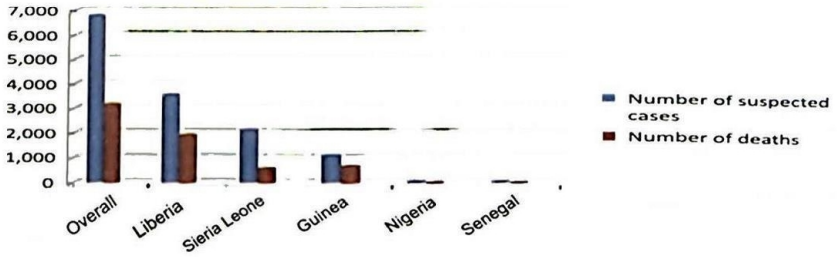
experimentation conducted in developing countries by Western drug companies [32].

The number of suspected cases and deaths from this single current outbreak is already about three times the total of all cases and deaths from previous known outbreaks in 40 years [3, 33]; yet, the epidemic is far from being contained. As of September 2014, the World Health Organisation, the United States Centres for Disease Control and Prevention (CDC) and the affected countries had reported a total of 6,808 suspected cases and 3,159 deaths (Figure 1); out of these, 3,751 cases and 2,850 deaths were laboratory confirmed [33]. In view of this, the current epidemic has been described as the largest, most severe and most complex outbreak of Ebola virus disease in history. This is because apart from lack of a known vaccine and virus-specific treatment, prevention and control efforts are hindered by certain factors or conditions such as weak health systems for epidemic preparedness and response particularly for viral haemorrhagic fevers, poor sanitation, poor personal hygiene, cultural practices as well as myths and misconceptions about EVD – all of which are prevalent in the affected countries.

Secondly, many of the areas that have been affected are areas of extreme poverty with limited access to soap or running water to help control the spread of disease [34]. Thirdly, high risk practices such as hiding of EVD patients, home-based management of EVD patients, traditional folk remedies, customary treatment of dead bodies such as washing the body of the deceased and extensive movement of people within and across borders for socio-cultural activities e.g. visiting sick relatives or attending to burial ceremonies of relatives have complicated tracking and follow up of contacts [35]. Fourthly, in some areas, people have become suspicious of both the government and hospitals; some hospitals have been attacked by angry protesters who believed that the disease is a hoax or that the hospitals are responsible for the disease.

The complex situation described above calls for extra-ordinary measures aimed at halting and reversing the epidemic as a matter of urgency. In responding to this situation, the World Health Organisation was constrained to depart from the well-established, historically evolved system of regulation and

Figure 1: Number of suspected cases and deaths by countries



Firstly, many hospitals lack basic infrastructure, supplies and equipment such as isolated wards, dedicated bed spaces, appropriate personal protective wears and laboratory required to investigate, diagnose and manage patients infected with a biosafety level 4 pathogen like an Ebola virus; in addition, the health facilities are understaffed and the existing staff were poorly trained. This situation has increased the chance of health care workers contracting the virus and they have accounted for about 10% of the dead in the current epidemic [33].

governance of therapies and interventions globally and alluded to the recommendation of consultative experts on Ebola that it would be acceptable on both ethical and evidential grounds to use as potential treatments or for prevention unregistered 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, provided that certain ethical and scientific criteria are met. These criteria include transparency about all

aspects of care, information sharing, fair distribution in the face of scarcity, promotion of cosmopolitan solidarity, informed consent, freedom of choice, confidentiality, respect for the person, preservation of dignity, involvement of the community and best possible assessment of risk and benefit from the available information [36].

Consequently, the World Health Organisation released a statement on 12th August, 2014 that the use of not yet proven treatments is ethical in certain situations in an effort to treat or prevent the disease [36]. This pronouncement seemed to provide ethical and scientific backing to the experimental drug, *Z-Mapp,* which consists of three monoclonal antibodies produced in a plant and previously first tested on humans in July 2014. It was administered to two Americans who had been infected with Ebola virus, and both appeared to have had positive results [37, 38, 39]. Z-Mapp was also administered to a 75 year-old Spanish priest with Ebola virus disease but died [40, 41]. A British nurse was also *'successfully treated'* with Z-Mapp before the manufacturer announced that its supplies had now been exhausted [42].

Favipiravir, an anti-viral drug approved in Japan for stockpiling against influenza pandemics, appeared to be useful in a mouse model of Ebola [43]. The Estrogen receptor drugs used to treat infertility and breast cancer, *clomiphene* and *toremifene*, have been shown to inhibit the progress of Ebola virus in infected mice [44]. A 2014 study found that *Amiodarone*, an *ion channel blocker* used in the treatment of heart arrhythmias, blocks the entry of Ebola virus into cells *in vitro* [45].

Given their oral availability and history of human use, these drugs would be agents for treating Ebola virus infection in remote geographical locations, either on their own or together with other antiviral drugs. Other promising treatments rely on antisense technology. Both small interfering RNAs (siRNAs) and phosphorodiamidate morpholino oligomers (PMOs) targeting the Zaire Ebola virus (ZEBOV) RNA polymerase L protein could prevent disease in non-human primates [46, 47].

Prevention and control

(Source: WHO 2014 - Ebola virus disease Fact sheet N°103, Updated April 2014)

Controlling Reston Ebola virus in domestic animals
No animal vaccine against RESTV is available. Routine cleaning and disinfection of pig or monkey farms (with sodium hypochlorite or other detergents) should be effective in inactivating the virus.

If an outbreak is suspected, the premises should be quarantined immediately. Culling of infected animals, with close supervision of burial or incineration of carcasses, may be necessary to reduce the risk of animal-to-human transmission. Restricting or banning the movement of animals from infected farms to other areas can reduce the spread of the disease.

As RESTV outbreaks in pigs and monkeys have preceded human infections, the establishment of an active animal health surveillance system to detect new cases is essential in providing early warning for veterinary and human public health authorities.

Reducing the risk of Ebola infection in people
In the absence of effective treatment and a human vaccine, raising awareness of the risk factors for Ebola infection and the protective measures individuals can take is the only way to reduce human infection and death.

In Africa, during EVD outbreaks, educational public health messages for risk reduction should focus on several factors:

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. Gloves and appropriate personal protective equipment should be worn when taking care of ill patients at home. Regular hand washing is required after visiting patients in hospital, as well as after taking care of patients at home.

Communities affected by Ebola should inform the population about the nature of the disease and about outbreak containment measures, including burial of the dead. People who have died from Ebola should be promptly and safely buried.

Pig farms in Africa can play a role in the amplification of infection because of the presence of fruit bats on these farms. Appropriate biosecurity measures should be in place to limit transmission. For RESTV, educational public health messages should focus on reducing the risk of pig-to-human transmission as a result of unsafe animal husbandry and slaughtering practices, and unsafe consumption of fresh blood, raw milk or animal tissue. Gloves and other appropriate protective clothing should be worn when handling sick animals or their tissues and when

slaughtering animals. In regions where RESTV has been reported in pigs, all animal products (blood, meat and milk) should be thoroughly cooked before eating.

Controlling infection in health-care settings

Human-to-human transmission of the Ebola virus is primarily associated with direct or indirect contact with blood and body fluids. Transmission to health-care workers has been reported when appropriate infection control measures have not been observed.

It is not always possible to identify patients with EBV early because initial symptoms may be non-specific. For this reason, it is important that health-care workers apply standard precautions consistently with all patients – regardless of their diagnosis – in all work practices at all times. These include basic hand hygiene, respiratory hygiene, the use of personal protective equipment (according to the risk of splashes or other contact with infected materials), safe injection practices and safe burial practices.

Health-care workers caring for patients with suspected or confirmed Ebola virus should apply, in addition to standard precautions, other infection control measures to avoid any exposure to the patient's blood and body fluids and direct unprotected contact with the possibly contaminated environment. When in close contact (within 1 metre) of patients with EBV, health-care workers should wear face protection (a face shield or a medical mask and goggles), a clean, non-sterile long-sleeved gown, and gloves (sterile gloves for some procedures).

Laboratory workers are also at risk. Samples taken from suspected human and animal Ebola cases for diagnosis should be handled by trained staff and processed in suitably equipped laboratories.

International responses to the outbreaks of Ebola Virus Disease in the West African Sub-Region

United Nations Mission for Ebola Emergency Response (UNMEER)

The United Nations Mission for Ebola Emergency Response (UNMEER) has recently been commissioned and has its headquarters in Accra, Ghana. Its aim is to lead the world body's efforts in containing the spread of the disease. The strategy of UNMEER is built around five pillars: stopping the outbreak, treating the infected, ensuring essential services, preserving stability and preventing any further outbreaks [48].

World Health Organization (WHO)

The World Health Organization is providing leadership for the containment of the Ebola virus disease outbreak in West Africa. In collaboration with the governments of 11 African countries, response partners, Ebola survivors, representatives of airlines and mining companies, and the donor communities, WHO has instituted a Strategy for Accelerated Response to Ebola Outbreak in West Africa [49]. The goals of this strategy are:

1. Stop transmission of EVD in the affected countries through scaling up effective, evidenced-based outbreak control measures.
2. Prevent the spread of EVD to the neighbouring at-risk countries through strengthening epidemic preparedness and response measures.

United States Centres for Disease Control and Prevention (CDC)

The United States Centres for Disease Control and Prevention (CDC) is working with other U.S. government agencies, the World Health Organisation (WHO), and other domestic and international partners and has activated its Emergency Operations Centre to help coordinate technical assistance and control activities with partners. CDC has deployed more than 100 personnel including teams of public health experts to West Africa and hundreds of personnel at their Emergency Operations Centre in Atlanta have provided around the clock logistics, staffing, communication, analytics, management, and other support functions. To date, CDC has spent more than $100 million to address urgent interventions such as purchase of personal protective equipment, mobile laboratories, logistics and relief commodities, and support for community health workers [50].

Médecins Sans Frontières (MSF)

Médecins Sans Frontières (MSF) is the largest non-governmental organisation working in the affected regions of Guinea, Sierra Leone and Liberia. The NGO is providing treatment services to EVD patients in an effort to contain the Ebola outbreak. MSF offers medical and psychosocial care in specialised Ebola treatment centres, ambulance services, disinfection of bodies and safe burials. MSF is also carrying out activities to clean areas contaminated by the virus such as treatment centres, homes, and public places, and is offering support in contact tracing and epidemiological analysis [51].

United Nations Children's Fund (UNICEF)

The United Nations Children's Fund (UNICEF) recently alerted the whole world that at least 3,700 children had become orphans following outbreak of Ebola Virus Disease in Sierra Leone, Liberia and Guinea. These children are living through the deaths

of their mother, father or family members from Ebola and urgently need special attention and support; yet many of them feel unwanted and even abandoned. Orphans are usually taken in by a member of the extended family, but in some communities, the fear surrounding Ebola is becoming stronger than family ties [52].

In response, UNICEF is accelerating its strategy on both traditional and new ways of helping these orphaned children with the provision of necessary physical and emotional healing. These measures include training of 400 mental health and social workers in Liberia and training of 2,500 Ebola survivors, who are now immune to the disease and are expected to provide care to quarantined children in Sierra Leone. Another service is to provide an estimated 60,000 children in Guinea living among Ebola-affected communities with psychosocial support [52].

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