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W.H.O. GUIDELINES TO COMBAT EBOLA VIRUS DISEASE AND CONTRIBUTION OF AYURVEDA

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ABSTRACT

Outbreak of Ebola virus is old to the medical community and was seen from time to time since 1976. But outbreak of 2014 proved deadly and grabbed attention from all over the world because of its high morbidity and mortality. To fight with the uncontrolled spread of this epidemic WHO has come to rescue and instructed the protocols to combat the EVD. Though the disease is not mentioned by same name in Ayurveda; Some disease with similar signs and symptoms are given in texts.

INTRODUCTION

Ebola virus disease (EVD), also known as Ebola hemorrhagic fever, Ebola virus infection or Viral Haemorrhagic fever is a severe often fatal (90%) illness in humans. Ebola hemorrhagic fever has made worldwide news because of its destructive potential. (1) It is a rare but deadly disease that causes bleeding inside and outside the body. (2)

EPIDEMOLOGY

EVD has occurred primarily in remote villages in Central and West Africa, near tropical rainforests. (3)

Table no.1 showing major outbreaks around the world.

YEAR	PLACE	SPECIES	INFECTED	DEATHS
1976	Nzara, Sudan	Sudan Virus	284	151
1976	Yambuku, Sudan. Democratic Republic of Congo	Ebola Virus	318	280
1995	Democratic Republic of Congo	Ebola Virus	315	254
2000	Uganda	Sudan Virus	425	224
2003	Republic of Congo	Ebola Virus	143	128
Aug'2007	Kampungu, Democratic Republic of Congo	Ebola Virus	264	187
Nov'2007	Uganda	Bundibugyo	149	37
Jun'2012	Uganda	Sudan Virus	31	21
Aug'2012	Democratic republican of Cargo	Bundibugyo	57	29
March 2014 (ongoing)	Guinea, Sierra Leone, Liberia and Nigeria	Ebola Virus	2127	1145

On 8 August 2014, the WHO declared the epidemic to be an international public health emergency, urging the world to offer aid to the affected regions. By 6 September 2014, 4,293 suspected cases including 2,296 deaths (underestimated) had been reported. On 8 September 2014, WHO warned the number of new cases in Liberia was increasing exponentially, and would increase by "many thousands" in the following 3 weeks.

In August 2014, attempts to contain the outbreak were enacted by placing troops on roads to cordon off the infected areas and stop those who may be infected from leaving and further spreading the disease. (4)

CAUSATIVE AGENT

Genus Ebola virus is 1 of 3 members of the *Filoviridae* family (filovirus), along with genus Marburg virus and genus Cueva virus. Genus Ebola virus comprises 5 distinct species: (5)

1. Bundibugyo Ebola virus (BDBV)
2. Zaire Ebola virus (EBOV)
3. Reston Ebola virus (RESTV)
4. Sudan Ebola virus (SUDV)
5. Taï Forest Ebola virus (TAFV)

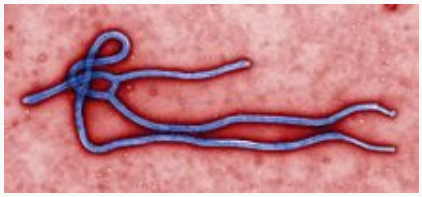
BDBV, EBOV, and SUDV have been associated with large EVD outbreaks in Africa, whereas RESTV and TAFV have not.

NATURAL HOST/RESERVOIR OF INFECTION

In Africa, fruit bats, particularly species of the genera *Hypsignathus monstrosus, Epomops franqueti* and *Myonycteris torquata*, are considered natural hosts for Ebola virus (6). The absence of clinical signs in these bats is characteristic of a reservoir species. Although non-human primates have been a source of infection for humans, they are not thought to be the reservoir but rather an accidental host like human beings.

Antibodies against Ebola Zaire and Reston viruses have been found in fruit bats in Bangladesh, thus identifying potential virus hosts and signs of the filovirus in Asia. (7)

Virology



Electron micrograph of an Ebola virus virion

The Ebola virus life cycle begins with virion attachment to specific cell-surface receptors, followed by fusion of the virion envelope with cellular membranes and the concomitant release of the virus nucleocapsid into the cytosol. (8)

Pathophysiology

Endothelial cells, macrophages, monocytes, and liver cells are the main targets of infection. After infection, a secreted glycoprotein (sGP) known as the Ebola virus glycoprotein (GP) is synthesized. Ebola replication overwhelms protein synthesis of infected cells and host immune defences. The GP binds the virus to the endothelial cells lining the interior surface of blood vessels. The cytopathic effect, from infection in the endothelial cells, results in a loss of vascular integrity responsible for cell adhesion to the inter-cellular structure, and damage to the liver, which leads to improper clotting. The sGP interferes with the signalling of neutrophils, which allows the virus to

evade the immune system by inhibiting neutrophils activation. The presence of viral particles and cell damage results in release of chemical signals for fever and inflammation. (9)

MODE OF TRANSMISSION

Ebola is introduced into the human 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. (10) Bats drop partially eaten fruits and pulp, then land mammals such as gorillas etc. feed on them and get infected. Such infected animals used for consumption, bush meat, may result in a human outbreak. Since 2003, such outbreaks have been monitored through surveillance of animal populations with the aim of predicting and preventing Ebola outbreaks in humans. (11)

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 particularly needles and syringes. Ebola isn't as contagious as more common viruses like colds, influenza, or measles. (12) The potential for EVD infections is low as can only spread by direct contact with the secretions from infected person. You can't get Ebola from air, water, or food. The symptoms limit a person's ability to spread the disease as they are often too sick to travel.

Burial ceremonies in which mourners have direct contact with the body of the deceased person transmit 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. (13) A person who has Ebola but has no symptoms can't spread the disease, either. (14)

Nosocomial transmission to Health-care workers in African Countries has occurred when infection control precautions are not strictly practiced due to the reuse of needles and

RESTV appears not capable of causing disease in humans than other Ebola species. 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. (15)

INCUBATION PERIOD

2-21 days. (16)

CLINICAL FEATURES

EVD is characterized by the sudden onset of influenza like symptoms. Early symptoms of EVD may be similar to those of malaria, dengue fever or other tropical fevers, before the disease progresses to the bleeding phase.

Early symptoms include:

- Fever (greater than 38.6°C or 101.5°F) (17)
- Fatigue
- Muscle pain
- Headache
- Sore Throat
- Nausea
- Vomiting
- Diarrhoea
- Abdominal (stomach) pain
- Loss of appetite
- Arthritis
- Weakness

Late symptoms include (Bleeding phase; 5 to 7 days after first symptoms)

- Bleeding from eyes, ears, and nose
- Bleeding from the mouth and rectum (gastrointestinal bleeding)
- Eye swelling (conjunctivitis)
- Genital swelling (labia and scrotum)
- Impaired kidney and liver function (to multiple organ dysfunction syndrome)
- Feeling of pain in the skin (Maculopapular rash-Bleeding into the skin create petechiae, purpura, ecchymosis and hematomas; especially around injection sites).
- Roof of mouth looks red
- Internal and external bleeding (e.g. oozing from the gums, blood in the stools)

There may be signs and symptoms of:

- Coma
- Disseminated intravascular coagulation
- Shock (18)

COMPLICATIONS

Prolonged cases are often complicated by inflammation of the testicles, joint pains, muscle pains, skin peeling, or hair loss. Eye symptoms, such as light sensitivity, excess tearing, iritis, iridocyclitis, choroiditis, blindness hav e also been described. (19) Some who become sick with Ebola are able to recover. We do not yet fully understand why. (20)

PROGNOSIS

As of April 2014, information from WHO puts the overall fatality rate at 60%-65%. Patients usually die from low blood pressure (shock) rather than from blood loss. (21) Early and effective treatment of symptoms may reduce the fatality. If an infected person survives, recovery may be quick and complete.

DIFFERENTIAL DIAGNOSIS

Other diseases that should be ruled out before a diagnosis of EVD include: Malaria, Typhoid fever, Shigellosis, Cholera, Leptospirosis, Plague, Rickettsiosis, Relapsing fever, Meningitis, Hepatitis, Viral haemorrhagic fevers, Gram negative septicaemia, Scrubtyphus, Q fever, Cadidiasis, Histoplasmosis, Trypanosomiasis, Visceral Leishmaniasis, Haemorrhagic small pox and measles. Non-infectious diseases like acute promyelocytic leukaemia, Haemolytic uremic syndrome, Snake envenomation, Clotting factor deficiencies/ Platelet disorders, thrombotic thrombocytopenic purpura, Hereditary hemorrhagic telangiectasias, Kawasaki disease and Warfarin poisoning. (22)

DIAGNOSIS

Ebola viruses are World Health Organization Risk Group 4 pathogens, requiring bio safety level 4-equivalent containment. Laboratory researchers must be properly trained in BSL-4 practices and wear proper personal protective equipment. The virus becomes ineffective quickly in open air. (23)

Ebola virus infections can be diagnosed through several types of tests:

Non Specific Tests

- CBC (low white blood cell and platelet counts, Patient show impaired blood clotting and death due occurs within 7 to 16 days).
- Electrolytes
- Tests of how well the blood clots (coagulation studies)
- Liver function tests (elevated liver enzymes) Tests to show whether someone has been exposed to the Ebola virus (virus-specific antibodies)

Specific Tests

- Virus isolation by cell culture.

- Antibody-capture enzyme-linked immunosorbent assay (ELISA) (early detection)
- Reverse transcriptase polymerase chain reaction (RT-PCR) assay
- Antigen detection tests
- Serum neutralization test
- Electron microscopy

Samples from patients are an extreme biohazard risk; testing should be conducted under maximum biological containment conditions. (24)

MANAGEMENT (PREVENTION AND CONTROL)

WHO guidelines for Prevention and control

If an outbreak is suspected, the premises should be quarantined immediately. Culling of infected animals, with close supervision of burial or incineration of carcasses, is necessary to reduce the animal-to-human transmission. Restricting the movement of infected can reduce the spread of the disease. (25)

WHO guidelines for reducing the risk of Ebola infection in people

- Raising awareness of the risk factors and the protective measures for Ebola infection can reduce human infection and death.
- Reducing the risk of wildlife-to-human transmission. 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 from direct or close contact with infected patients and their body fluids. Gloves and appropriate personal protective equipment should be worn while caring patients. Regular hand washing is required after visiting patients or after taking care of patients.
- Infected communities 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 safely buried (avoiding burial washing or embalming of bodies).
- For RESTV, educational public health messages should focus on reducing the risk of pig-to-human transmission by unsafe animal husbandry and slaughtering and unsafe consumption.
- Gloves and other appropriate protective clothing should be worn when handling infected animals.. In regions where RESTV has been reported in pigs, all animal products (blood, meat and milk) should be thoroughly cooked before eating. (26)

Controlling infection in health-care settings

- Human-to-human transmission is associated with contact with blood and body fluids, when appropriate control measures have not been observed.
- Health-care workers should apply **standard precautions** with all patients – regardless of their diagnosis – in all work practices at all times. Viz. Hand hygiene, respiratory hygiene, use of personal protective equipment, prevention of needle stick and injuries from other sharp instruments, and safe burial practices.

- Health-care workers caring for patients with Ebola virus should apply, in addition to standard precautions, other infection control measures to avoid exposure to body fluids and direct unprotected contact with the 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).
- Samples taken from suspected human and animal Ebola cases for diagnosis should be handled by trained staff and processed in suitably equipped laboratories. (27)
- The Ebola virus can be eliminated with heat (heating for 30 to 60 minutes at 60 °C or boiling for 5 minutes). On surfaces, some lipid solvents such as some alcohol-based products, detergents, sodium hypochlorite (bleach) or calcium hypochlorite (bleaching powder).

Contact tracing

It involves finding everyone who had close contact with infected individuals and watching for signs of illness for 21 days. If any of these contacts comes down with the disease, they should be isolated, tested, and treated. (28)

TREATMENT

Medicines

Severely ill patients require intensive supportive care. (29) These measures may include

- Pain management.
- Medications for nausea, fever and anxiety.
- Patients are frequently dehydrated and require oral rehydration with solutions containing electrolytes or intravenous fluids.
- Blood products such as packed red blood cells, platelets or fresh frozen plasma may also be used.
- 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 has often been used as initially the diagnosis is not clear.
- Early treatment may increase the chance of survival.

Vaccines

No licensed vaccine for EVD is available. (30) It is hoped that one will be available by November of 2014.

ONGOING RESEARCH

Blood transfusion: The blood serum from those survived an infection is currently being studied to see if it is an effective treatment.

Vaccines: Intravenous antibodies appear to be protective in non-human primates who have been exposed to large doses of Ebola. (31)

EBOLA IN AYURVEDA AND ITS TREATMENT

Ayurveda is ancient science of health. The word Ebola is obviously not mentioned in *Ayurveda*. As *Acharya Charak* has mentioned that all *nija-vyadhis* is caused by *vata, pitta* and *kapha*, wise physician can name any disease on the basis of violation of the *doshas*, its symptoms and cause which may not be mentioned in the classics of *Ayurveda*. (32) The sign and symptoms that we see today in Ebola hemorrhagic fever can be related differentially to one of the thirteen *Sannipatik Jwar* (*Rak-*

tasthiwi Sannipatik Jwar) (33), *Raktapitta Upadrava* and *Rakta-atisar*. Though few sign of EVD may be present in *Raktapitta Upadrava* and *Rakta-atisar* but, most of the signs are similar to *Raktasthiwi Sannipatik Jwar*.

Rakta is Blood, *Sthiwan* is to spit out and *sannipat* is like involvement of different *doshas*. *Yogaratnakar* classifies it as *asadhya*.

Where one splits out blood from the mouth, with fever, vomiting, thirstiness, delirium, body ache, diarrhoea, hiccups, abdominal distension, burning sensation in eyes, shortness of breath, loss of consciousness, colour of tongue is too black or red; these symptoms are associated with the disease *Raktasthiwi Sannipat Jwar*. This is famous for taking away the life. Although its fatal, time limit of *Raktasthiwi Sannipat Jwar* is 10 days which may vary from person to person (34).

Raktapitta Upadrava presents weakness, dyspnoea, cough, fever, vomiting, drowsiness, anaemia, burning sensation, heart ache, thirstiness, diarrhoea, foul smelling spit, indigestion and burping (35).

Prevention *Acharya Sushruta* has enlisted the mode of transmission of *Upsargaja roga* as sexually transmitted diseases (*Prasanga*), direct contact to infected person (*Gatrasansparsha*), air droplet infection (*Nihshwasa*), eating in same vessel (*Sahbhojnat*), sleeping together (*Sahsayyasana*), sharing clothes and accessories (*Vastramalyanulepnat*) etc. Thus avoiding such contact may prevent the transmission of disease. (36)

Treatment

Parpatadi kwatha preparation for *Raktasthiwi Sannipat Jwara* consists of *Pittapapada* (*Fumaria indica*), *Yawasa* (*Alhagi camelorum*), *Adusa (Adhatoda Vasica*), *Bhustrin)*, *Kutaki (Picrorhiza kurroa*) and *Phula priyangu* (*Callicarpa macrophylla*) – all taken in equal amount. The decoction of these ingredients are taken with sugar (*sarkara*); this helps to prevent blood from mouth (37)

Nagarmotha (*Cyprus rotundus*) along with *Padma kastha*(*Prunus cerasoides*), *Pittapapada*(*Fumaria indica*), *Shweta chandan*(*Santalum album*), *jasmin*, *Shatavari* (*Asparagus racemosus*), *Mulethi* (*Glyrhiza glabra*), *Mitha neem* (*Melia azadiratch*), *Sugandhabala, Chitrak* (*Plumbago zeylanica*), and *Rakta Chandan* ; all are taken in equal amount and made decoction. This also stops vomiting of blood (38).

Treatment of *Raktapitta Upadrava*: Decoction of *Ushir* (*Viteveria zizanoidis*), *Chandan* (*Santalum album*), *Patha* (*Cissampelos pareira*), *Draksha* (*Vitis vinifera*) , *Madhuka* (*Glycirrhyza glabra*) and *Pippali* (*Piper longum*) taken with Honey (39).

Treatment of *Rakta-atisar*: Extract of fresh leaves of *Jambu* (*Syzygium cumini*), *Aamra* (*Mangifera indica*), *Amla* (*Emblica officinalis*) with Honey, Clarified butter and Milk (40).

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