Global threat of Ebola and MERS-CoV infection: Are we adequately prepared?

Prof. (DR.) MD. ISMAIL PATWARY
MBBS: FCPS: MD (MEDICINE), FACP
Professor and Head Dept. of Medicine,
MAG Osmani Medical College, Sylhet
The world is facing an unprecedented outbreak of one of the deadliest virus called **Ebola virus disease (EVD)**

On 2014 WHO Announces Ebola epidemic as Public Health Emergency which first spread in Guinea, Sierra Leone, Liberia and Nigeria with a case fatality rate up to 65%

There have been 16129 reported Ebola cases in eight countries since the outbreak began, with 6928 reported deaths (up to 03rd December 2014; source-WHO)
Ebola endemic zone

[Map showing the regions affected by the Ebola outbreak in West Africa, with varying numbers of cases indicated by color coding.]
## countries with Cases of Ebola

<table>
<thead>
<tr>
<th>Countries with widespread transmission</th>
<th>Affected areas</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guinea</td>
<td>Entire country</td>
</tr>
<tr>
<td>Liberia</td>
<td>Entire country</td>
</tr>
<tr>
<td>Sierra Leone</td>
<td>Entire country</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>countries with an initial case or cases and/or localized transmission</th>
<th>Affected areas</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mali</td>
<td>Kayes, Kourémalé, and Bamako</td>
</tr>
<tr>
<td>United States</td>
<td>Dallas, TX, New York</td>
</tr>
</tbody>
</table>
Ebola cases, per outbreak

Source: CDC, WHO
<table>
<thead>
<tr>
<th>Species name</th>
<th>Virus name (Abbreviation)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zaire ebolavirus</td>
<td>Ebolavirus (EBOV)</td>
</tr>
<tr>
<td>Sudan ebolavirus</td>
<td>Sudan virus (SUDV)</td>
</tr>
<tr>
<td>Bundibugyo ebolavirus</td>
<td>Bundibugyo virus (BDBV)</td>
</tr>
<tr>
<td>Tai  Forest ebolavirus</td>
<td>Tai forest virus (TFV)</td>
</tr>
<tr>
<td>Reston ebolavirus</td>
<td>Reston virus (RESTV)</td>
</tr>
</tbody>
</table>
Genome
Single-stranded RNA virus of Filoviridae family

Structure
Like all filoviruses ebolavirions are filamentous particles in the shape of a "U" or a "6", may be coiled, toroid, or branched.
In general, Ebolavirions are 80 nm in width but vary somewhat in length.
Transmission:

✓ Introduced into human through close contact with blood, secretion, organs or body fluids of infected animals.

✓ In Africa, infection has been documented through the handling of infected chimpanzees, gorillas, fruit bats, monkeys, antelope. Fruits bats of *Pteropodidae* family are considered to be the natural host of the ebola virus.
Human to human transmission

Direct: Handling of blood, organ and body fluids of infected people.

Indirect: By contact with contaminated medical equipments i.e. infected needles, nosocomial transmission in hospital.

Man who has recovered from the disease can still transmits the virus through his semen for up to 7 weeks

Health-care workers have frequently been infected while treating patients with suspected or confirmed EVD.
Ebola virus Ecology

**Enzootic Cycle**
New evidence strongly implicates bats as the reservoir hosts for ebolaviruses, though the means of local enzootic maintenance and transmission of the virus within bat populations remain unknown.

**Ebolaviruses:**
- Ebola virus (formerly Zaire virus)
- Sudan virus
- Tai Forest virus
- Bundibugyo virus
- Reston virus (non-human)

**Epizootic Cycle**
Epizootics caused by ebolaviruses appear sporadically, producing high mortality among non-human primates and duikers and may precede human outbreaks. Epidemics caused by ebolaviruses produce acute disease among humans, with the exception of Reston virus which does not produce detectable disease in humans. Little is known about how the virus first passes to humans, triggering waves of human-to-human transmission, and an epidemic.

Human-to-human transmission is a predominant feature of epidemics.

Following initial human infection through contact with an infected bat or other wild animal, human-to-human transmission often occurs.
Niemann-pick C1 (NPC1), a cholesterol transporter protein appears to be essential for ebolavirus infection.

When the cells from Niemann-pick disease, type C1 patient (who have mutated form of NPC1) are exposed to ebolavirus in the laboratory, the cell survived and appears immune to the virus.
Cycle of Infection and Replication

3. Uncoating
   Envelope removed

2. Penetration
   Virus entry

4. Transcription
   Synthesis of mRNAs

5. Translation
   Synthesis of 5 structural proteins

6. Processing
   G-protein glycosylation

7. Replication
   Production of genomic RNA from intermediate strand

8. Assembly

9. Budding
   Complete virions

1. Adsorption
   Receptors and virion interaction

Host cell receptors
Pathophysiology

Ebola virus

\[ \downarrow \text{Primary target} \]

Endothelial cell, hepatocyte, mononuclear phagocyte

\[ \downarrow \]

Ebola virus GP forms after infection

\[ \downarrow \]

GP binds virus with endothelial cell lining of blood vessels

\[ \downarrow \]

Evades the immune system by inhibition of neutrophilic activation

\[ \downarrow \]

Viral particles damage cells with release of cytokines like TNFα, IL6, IL8

Effect: Fever and inflammation
Pathophysiology (contd.)

Cytopathic effect of infection in endothelial cell -
Loss of vascular integrity

Further synthesis of GP results in reduction of integrins responsible for cell adhesion

Liver damage

Coagulopathy

GP: Glycoprotein
Symptoms and signs

- Fever,
- Intense weakness,
- Muscle pain,
- Headache
- Sore throat,
- Vomiting,
- Diarrhea,
- Rashes,
- Impaired liver and kidney functions,
- and in severe cases a combination of internal and external bleeding
EBOLA VICTIM
EVD’s most important clinical indicator is the person’s medical history specially travel and occupation history and patient’s exposure to wild life

Other diseases that should be ruled out before a diagnosis of EVD: malaria, typhoid fever, shigellosis, cholera, leptospirosis, plague, rickettsiosis, relapsing fever, meningitis, hepatitis and other viral haemorrhagic fevers.
Diagnosis (condt.)

Laboratory investigation:
• Reverse transcriptase polymerase chain reaction (RT-PCR) assay
• Antibody-capture enzyme-linked immunosorbent assay (ELISA)
• Antigen detection tests
• serum neutralization test
• Electron microscopy
• Virus isolation by cell culture.
Treatment

No specific treatment is available

Early supportive care with particular attention to
- Maintenance of hydration,
- Circulatory volume,
- Electrolyte balance,
- Blood pressure
- Avoidance of invasive procedures,
- Administration of anticoagulant to prevent DIC in early stage of disease,
- Antibiotics or antimycotics to treat secondary infection
• There is as yet no licensed treatment but potential treatments including blood products, immunological therapy (humanized mouse antibodies—"ZMapp").

Two vaccines

- Inserted Ebola genes encoding glycoprotein’s
- and recombinant vesicular stomatitis Indiana virus pseudotypes are currently being evaluated

Already under way are safety trials in humans of two experimental vaccines, produced by GlaxoSmithKline (GSK) and the Public Health Agency of Canada.
• Convalescent blood and plasma therapy - using blood from Ebola patients who have survived, which contains antibodies that successfully fought off the virus, to boost sick patients' immune systems.
Ebola virus- chance of entry in Bangladesh

- Around 800 army members of Bangladesh are working in UN peace keeping mission in Liberia and Sierraleone.
- Other professionals like telecommunication engineers, doctors, labours of Bangladesh are working in different areas of Western Africa.
- As there is no vaccine and no specific treatment is yet available against the disease, the virus can enter in Bangladesh when these persons come to our country.
1) Training of the health care provider, medical staffs, laboratory technicians regarding the effects of ebola and its mode of transmission.

2) Early diagnosis of ebola infection

3) Isolation of the patient

4) Quarantine

5) Strict hygienic practices: immediate cessation of all needle sharing, barrier nursing- use of face mask, gloves, goggles, gowns for medical personnel and visitors

6) Incineration of carcasses of infected animals and humans. Traditional burial and rituals should be discouraged.

7) Avoid endemic zones during outbreaks.
Hospital staffs are wearing protective clothings before entering to the ebola infected patient’s ward in Nigeria.

Workers of the UNICEF are spraying disinfectant over a dead body of a ebola suspected patient to prevent the spread of infection in Sierra Leone.
Protective clothing are washed and dried in sun after using in ebola infected patient ward in Nzara, Sudan.
Disinfectants are sprayed in hospital corridor to prevent transmission of ebola among the visitors of the patient.

Disinfectants are sprayed over the body of health staff after coming from ebola infected patient ward.
Steps taken by our government to prevent entry & spread of Ebola virus

Ministry of Health declared precautionary initiative to prevent Ebola infection on 10\textsuperscript{th} August '14.

Under this initiative special teams are employed in all entry points of Bangladesh to detect travellers suffering from Ebola.

A 20 bed specially equipped ward has been established in Kurmitola hospital in Dhaka.

Sources from Ministry of Health also stated that specimen from suspicious patient will be sent to CDC, Atlanta USA for further investigation.
In general, outcomes are poor with 65% of all cases resulting in death. If an infected person survives, recovery may be quick and complete, or prolonged with long term problems, such as inflammation of the testicles, joint pains, muscle pains, skin peeling, or hair loss.

Eye symptoms, such as light sensitivity, excess tearing, iritis, iridocyclitis, choroiditis and blindness have also been described.

EBOV and SUDV may be able to persist in the sperm of some survivors, which could give rise to secondary infections and disease via sexual intercourse.
Middle East respiratory syndrome (MERS)

- **Middle East respiratory syndrome (MERS)** is a novel corona virus (MERS CoV) that has been circulating in the Arabian Peninsula since 2012 and causing severe respiratory infections in humans.
- The illness has a high mortality rate (approx. 30%). As of 11 June, 699 laboratory-confirmed cases of human infection with Middle East respiratory syndrome coronavirus (MERS-CoV) have been reported to WHO, including at least 209 deaths.
• An additional 113 cases occurring between 2012 and 2014 were reported by the Saudi Arabian Ministry of Health on 3 June 2014. These cases are not reflected in the current case count as investigation into these cases is currently ongoing with Saudi officials.
Showing Area affected
• MERS-CoV has limited human to human transmission and spread from ill people to others through close contact, such as caring for or living with an infected person (large droplet transmission).

• Infected people have spread MERS-CoV to others in healthcare settings, such as hospitals and in immunocompromised patients.
Electron microscopy shows a MERS-CoV particle with club-shaped surface projections surrounding the periphery of the particle, a characteristic feature of coronaviruses.

Image source: Cynthia Goldsmith/Azaibi Tamin
MERS-CoV particles as seen by negative stain electron microscopy. Virions contain characteristic club-like projections emanating from the viral membrane.

Image source: Cynthia Goldsmith/Maureen Metcalfe/Azaibi Tamin
An electron micrograph of a thin section of MERS-CoV, showing the spherical particles and cross-sections through the viral nucleocapsid.

Image source: Maureen Metcalfe/Azaibi Tamin
• Researchers studying MERS have not seen any ongoing spreading of MERS-CoV in the community but human and camel genetic sequence data demonstrate a close link between the virus found in camels and that found in people.
Sign and symptoms

• **A typical case** of MERS consists of fever, cough, and shortness of breath.

• For many people with MERS severe complications followed, such as diarrhea, vomiting, pneumonia, renal failure, septicemia and DIC.

• Most of the people who died had an underlying medical condition such as diabetes, cancer, chronic lung and heart or kidney disease.
Persons who meet the following criteria should be reported and evaluated for MERS-CoV infection:

- A person with an acute respiratory infection, which may include fever (≥38°C, 100.4°F) and cough
- Suspicion of pulmonary parenchymal disease (e.g., pneumonia or acute respiratory distress syndrome based on clinical or radiological evidence of consolidation)
• History of travel from the Arabian Peninsula or neighbouring countries within 14 days

• Symptoms not already explained by any other infection or aetiology, including clinically indicated tests for community-acquired pneumonia
Probable Case of MERS-CoV

Any person who meets:

- The criteria for Patient Under Investigation and has clinical, radiological, or histopathological evidence of pulmonary parenchyma disease (e.g. pneumonia or ARDS), but no possibility of laboratory confirmation exists, either because the patient or samples are not available or there is no testing available for other respiratory infections.
Confirmed Case of MERS-CoV

- A person with laboratory confirmation of infection with MERS-CoV.
**Diagnosis** is confirmed by

- RT-PCR,
- IFA (Immunofluorescent assay),
- and more definitive confirmatory test called the neutralizing antibody test.
Management

Currently, there is no vaccine to prevent MERS-CoV infection or no specific antiviral treatment.
• For severe cases, current treatment includes care to support vital organ functions.
• Preventive measures like maintenance of general hygiene, hand washing, avoid personal contact with sick people or animal, and not to drink raw camel milk or undercooked meat (camel meat).
Environmental Infection Control

- Follow standard procedures, per hospital policy and manufacturers' instructions, for cleaning and/or disinfection of:
  - Environmental surfaces and equipment
  - Textiles and laundry
  - Food utensils and dishware
Travellers guidelines

• CDC recommends that travellers to countries in or near the Arabian Peninsula pay attention to their health during and after their trip.
CDC does not recommend that most travellers change their plans because of MERS. However, the Saudi Arabia Ministry of Health has made special recommendations for travellers to Hajj and Umrah. (For immunocompromised patient, old person and children)
• Pilgrims and travellers should pay attention to their health when travelling in the Arabian Peninsula and seek medical care if they develop a fever with cough or shortness of breath within 14 days after returning from their trip.
Bangladesh is at low risk of being hit by the deadly Ebola and MERS CoV outbreak, but any infected traveler enters the country undetected, the consequence might be devastating as a weak infection control system and lack of critical care facilities will pose major challenges for public hospitals.
• So community engagement and active participation of government and NGO’S is key to successfully controlling outbreaks of Ebola and MERS CoV infection.
A package of interventions namely surveillance, contact tracing, quarantine of suspected cases, a good laboratory service, case management, safe burials, social mobilization and the measures to reduce human to human transmission and wildlife to human transmission is the key elements in containment of these deadly viral infection
THANK YOU