Ebola:

What you need to know

Dr Ula Maniewski, internist
Instituut voor Tropische geneeskunde, Antwerpen
Reisgeneeskunde
Lid werkgroep werknemers in het buitenland VWVA

Nationale dagen voor arbeidsgeneeskunde
12-13 november 2015
What is ebola?

- Filovirus, which is found in subsaharian Africa

<table>
<thead>
<tr>
<th>Sterfte</th>
<th>60-90%</th>
<th>~25%</th>
<th>1 case</th>
<th>40-60%</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
|          |        |      |        |        | Non-pathogenic
**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.

**Ebola Viruses:**
- 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.

Following initial human infection through contact with an infected bat or other wild animal, human-to-human transmission often occurs.

Human-to-human transmission is a predominant feature of epidemics.
EVD: Event Timeline

Diagnose vereist RT-PCR op bloed

Inoculation ("challenge")

Onset clinical symptoms

Hosp. (Death)

Hosp. (Hosp.discharge)

Prepatent

Symptomatic

Recovery

9d (sd 7)

5d (sd 4)

7d (sd 5)

16d (sd 6)

<table>
<thead>
<tr>
<th>Early Symptoms</th>
<th>%</th>
<th>Late Symptoms</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>87</td>
<td>Cough</td>
<td>30</td>
</tr>
<tr>
<td>Headache</td>
<td>53</td>
<td>Dyspnea</td>
<td>23</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>66</td>
<td>Dysphagia</td>
<td>33</td>
</tr>
<tr>
<td>Vomiting</td>
<td>68</td>
<td>Sore throat</td>
<td>22</td>
</tr>
<tr>
<td>Muscle ache</td>
<td>39</td>
<td>Bleeding</td>
<td>18</td>
</tr>
<tr>
<td>Conjunct.</td>
<td>21</td>
<td>Confusion</td>
<td>13</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Jaundice</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rashes</td>
<td>6</td>
</tr>
</tbody>
</table>

Source:  Ebola Virus Disease in West Africa —The First 9 Months of the Epidemic and Forward Projections
WHO Ebola Response Team. NEJM, Sept 23rd, 2014
EVD evolves towards a systemic disease with multi-organ involvement and ultimately failure, from 3 days till 12 days after symptom onset.

- Fever
- Diarrhea and vomiting, fluid loss
- Hypotension
- Vascular permeability increased
- Renal failure, hepatitis
- Cerebral dysfunction
- Bleeding
- Circulatory collapse (shock)
Where has ebola occurred?
Ebola epidemic 2014-2015

Largest recorded EVD outbreak, crossing several borders

881 health care workers were infected

Ebola situation report, WHO, 9 nov 2015
How is the situation now? (9/11/2015)

- Liberia: free of ebola since 2/9/2015
- Sierra Leone: free of ebola since 9/11/2015
- Guinée: 1 new case: newborn

Ebola situation report, WHO, 9 nov 2015
Ebola is spread by contact with an infected person’s bodily fluids, but is less contagious than many common diseases, such as mumps and measles. In the current outbreak, each person with Ebola will infect 1-2 other people.

<table>
<thead>
<tr>
<th>Disease</th>
<th>Average Number of People Infected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ebola</td>
<td>1-2 people</td>
</tr>
<tr>
<td>SARS</td>
<td>2-5 people</td>
</tr>
<tr>
<td>HIV</td>
<td>2-5 people</td>
</tr>
<tr>
<td>Mumps</td>
<td>4-7 people</td>
</tr>
<tr>
<td>Smallpox</td>
<td>5-7 people</td>
</tr>
<tr>
<td>Pertussis (whooping cough)</td>
<td>12-17 people</td>
</tr>
<tr>
<td>Measles</td>
<td>12-18 people</td>
</tr>
</tbody>
</table>

Het virus

- Relatief besmettelijk...
- Maar makkelijk te doden!
  - Water en zeep
  - Klassieke ontsmettingsmiddelen (bv. chlooroplossing)
  - UV-licht
  - Uitdroging (van de omgeving)
  - Verhitting (60’ aan 60°C, of 5’ aan 100°C)
- Overleeft langer in donkere en vochtige plekken
- Afkoelen of invriezen dooit het virus niet
Detection of Ebola Virus in Different Human Body Fluids over Time

- **Viremia/Blood**: Acute phase
- **Saliva/Swab**: Saliva/Swab
- **Urine**: Urine
- **Tears/Conj.**: Tears/Conj.
- **Seminal**: Semen
- **Skin/Sweat**: Skin/Sweat
- **Vaginal**: Vaginal
- **Rectal/Fecal**: Rectal/Fecal
- **Milk**: Milk

Study details:
- Symptom Onset
- Mean Death Day
- Last Virus Isolation
- Last Detectable IgG

Date range:
- Days 1 to 120
- 1yr, 2yrs, 3yrs, 11yrs
“In March 2015, a woman in Liberia received a diagnosis of EVD and her only potential exposure that could be ascertained was sexual contact with a male survivor of EVD. Further investigation found Ebola virus RNA in the survivor’s semen 199 days after the onset of his symptoms, with a genetic sequence that matched the sequence from the case patient.”
But ... this epidemic runs in 3 countries with a total population of 20 million.

Africa has a population of about one billion (50x more)

The relative mortality of the Ebola epidemic at this stage for the 3 countries can be compared with road accidents or tuberculosis.

<table>
<thead>
<tr>
<th>Disease mortality rate compared</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Most flu</td>
<td>0.1</td>
</tr>
<tr>
<td>Spanish flu</td>
<td>2.5</td>
</tr>
<tr>
<td>Plague</td>
<td>10 (with antibiotics)</td>
</tr>
<tr>
<td>Polio</td>
<td>5 in children, up to 30 in adults</td>
</tr>
<tr>
<td>Smallpox</td>
<td>30</td>
</tr>
<tr>
<td>Bird flu</td>
<td>60</td>
</tr>
<tr>
<td>Current Ebola outbreak</td>
<td>60-70</td>
</tr>
<tr>
<td>The Marburg virus</td>
<td>90</td>
</tr>
<tr>
<td>Rabies</td>
<td>100</td>
</tr>
</tbody>
</table>

Source: CDC, WHO
Treatment options
EVD prophylaxis and treatment

- Mechanical barriers
- Vaccines
- Immunotherapy
- Antivirals
  - Nucleoside analogues
  - RNA silencing molecules
  - Antisense oligomers

Supportive treatment !!!
Efficacy and effectiveness of an rVSV-vectored vaccine expressing Ebola surface glycoprotein: interim results from the Guinea ring vaccination cluster-randomised trial

Ana María Henao-Restrepo, Ira M Longini, Matthias Egger, Natalie E Dean, W John Edmunds, Anton Camacho, Miles W Carroll, Moussa Doumbia, Bertrand Draguez, Sophie Duraffour, Godwin Enwere, Rebecca Grais, Stephan Gunther, Stefanie Hossmann, Mandy Kader Kondé, Souleymane Kone, Eeva Kuismia, Myron M Levine, Sema Mandal, Gunnstein Norheim, Ximena Riveros, Aboubacar Soumah, Sven Trelle, Andrea S Vicari, Conall H Watson, Sakoba Kéïta, Marie Paule Kiény*, John-Arne Røttingen*

Summary

Background A recombinant, replication-competent vesicular stomatitis virus-based vaccine expressing a surface glycoprotein of Zaire Ebolavirus (rVSV-ZEBOV) is a promising Ebola vaccine candidate. We report the results of an interim analysis of a trial of rVSV-ZEBOV in Guinea, west Africa.
EVD experimental treatments

### Immunotherapy
- Convalescent plasma
- Monoclonal antibodies
  - Zmapp (Leafbio Inc.)
- Horse hyperimmune globulins

### Antivirals
- Nucleos(t)ide analogues
  - T-705, favipiravir (Toyama)
  - CMX001, brincidofovir (Chimerix)
  - BCX4430 (BioCryst)
- Small interfering RNA molecules
  - TKM-100802, TKM-Ebola (Tekmira)
- Antisense phosphorodiamidate morpholino oligomers (PMOs)
  - AVI-7537 (Sarepta)

### Vaccines
- Recombinant vesicular stomatitis virus vectored EBOV-GP vaccine (rVSV-EBOV)
- Chimpanzee adenovirus 3 vectored EBOV-GP vaccine (cAd3 EBOV)
- Heterologous prime-boost Ad26-modified vaccinia Ankara vectored EBOV-GP

WHO Sep and Nov 2014; EMA Nov 2014
Er is meer dan ebola!!!

Case 28-2015 — A 32-Year-Old Man with Fever, Headache, and Myalgias after Traveling from Liberia
Paul D. Biddinger, M.D., David C. Hooper, M.D., Erica S. Shenoy, M.D., Ph.D., Ednan K. Bajwa, M.D., M.P.H., Gregory K. Robbins, M.D., M.P.H., and John A. Branda, M.D.

Malaria

Original Research | 2 June 2015

Differential Diagnosis of Illness in Travelers Arriving From Sierra Leone, Liberia, or Guinea: A Cross-sectional Study From the GeoSentinel Surveillance Network
Leptospirosis? DOXY

H7N9? H5N1? HxNz?? ISOLATE

melioidosis? CEFTAZIDIME

Peni R S. Pneumoniae? CA-Klebsiella pn.? ?CARBAPENEM

Rickettsiosis/scrub typhus? DOXY

MERS-CoV? ISOLATE

Institute of Tropical Medicine
Fever and rash after travel

- Dengue
- Rickettsiae
- Leptospirosis
- Acute HIV

- (sec. syphilis)
- (CMV)
- ...
Welke raad kan ik geven aan de werknemers?

- Voorkom dat uw werknemer koorts ontwikkelt en hierdoor verwarring ontstaat met EVD

- **DUS:**
  - Malariapreventie!!!!!
    - medicamenteus en
    - niet medicamenteus
  - Basis handhygiëne
Prevention

Do NOT touch blood and body fluids of others (pee, poop, spit, vomit, sweat, semen).

Do NOT touch items that could have a sick person's blood or body fluids on them (bedding, needles, medical tools).

Do NOT touch the body of someone who has died of Ebola.

Prevent Healthcare infection control, safe burial practices, avoiding bushmeat

INFECTION CONTROL

SAFE BURIAL PRACTICES

BUSHMEAT
Wat als de werknemer ziek wordt?

Stel de 3 vragen:

1. In epidemisch gebied verbleven in de afgelopen 21 dagen?

2. Koorts +/- andere klachten (braken, diarrhee, bloedingsneiging,...)?

3. Blootstelling in risicogebied aan zieken, lichaamsvochten?

Zorgvuldige en gedetailleerde anamnese
Stel patiënt gerust dat goede zorgen altijd gegeven worden
Overleg met arts infectieziektenbestrijding
A SERIOUS OUTBREAK OF STUPID...

QUARANTINE HER!!

"I JUST CAME FROM THE LIBRARY, NOT LIBERIA!"

"KID, YOU CAN NEVER BE TOO CAREFUL."

Institute of Tropical Medicine
Want to know more?
www.ebola.be
Dank voor uw aandacht!