Update on Ebola and Measles Outbreaks

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June 13, 2019
Ebola Update
Outbreaks of Ebola Virus Disease

- West Africa (Liberia, Sierra Leone, Guinea) – 2014-2016

- Democratic Republic of the Congo – 2018-2019
Outbreaks of Ebola Virus Disease

- West Africa (Liberia, Sierra Leone, Guinea) – 2014-2016

- Democratic Republic of the Congo – 2018-2019
Reported Ebola Virus Disease Cases in Guinea, Liberia, and Sierra Leone, 2014-2016

Guinea
3,814 cases / 2,544 deaths

Sierra Leone
14,124 cases / 3,956 deaths

Liberia
10,678 cases / 4,810 deaths

Total*:
28,616 cases
11,310 deaths

40% mortality

*Confirmed, probable and suspected cases

Source: WHO, 12/2016
Liberia MOH-NIAID Collaboration

- PREVAIL 1: Phase 2, two candidate vaccines vs placebos
- PREVAIL 2: ZMapp vs standard-of-care treatment
- PREVAIL 3: Study of Ebola survivors
- PREVAIL 4: GS-5734 vs placebo for persistent Ebola RNA in semen
- PREVAIL 5 (PREVAC): Phase 2, three vaccine strategies vs placebos
- PREVAIL 6: Genome-wide association study, genetic factors affecting Ebola
- PREVAIL 7: Cataract surgery in Ebola survivors and close contacts
Phase 2 Placebo-Controlled Trial of Two Vaccines to Prevent Ebola in Liberia
SB Kennedy, HC Lane et al. for the PREVAIL I Study Group

A Randomized, Controlled Trial of ZMapp for Ebola Virus Infection
The PREVAIL II Writing Group, for the Multi-National PREVAIL II Study Team. RT Davey, Jr., D Malvy et al.

A Longitudinal Study of Ebola Sequelae in Liberia
The PREVAIL III Study Group
Core principles of science and ethics in conducting clinical research should not change during an epidemic

- RCTs ethical and appropriate: most efficient, reliable way to determine safety and efficacy

- Clinical research studies must have
  - Scientific and social value
  - Respect for/engagement with affected communities
  - Post-trial access to candidate products proved safe/effective
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Outbreaks of Ebola Virus Disease

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Two Ebola Virus Disease Outbreaks – Democratic Republic of the Congo, 2018-Present

**April–July, 2018**
54 cases, 33 deaths in three towns in Équateur Province

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**August 1, 2018 through June 12, 2019**
2,084 confirmed and probable cases, including 1,405 deaths, in North Kivu and Ituri Provinces

Source: DR Congo MOH
Weekly Confirmed and Probable Ebola Cases, DRC, Aug. 1, 2018 – June 2, 2019

Number of cases

Aug 1: outbreak declared in DRC

Sources: WHO, DRC MOH
Randomized, Controlled Trial of Ebola Therapeutics (PALM)

- Opened November 2018 in the DRC
- Coordinated by WHO, led by DRC National Institute for Biomedical Research (INRB) & NIAID
- Four candidates: ZMapp, remdesivir, mAb114, REGN-3
- Target N = 500 (125 per arm)
- 323 patients enrolled as of 6/12/2019
The New York Times

March 1, 2019

‘Crippling’ Attacks Force Doctors Without Borders to Close Ebola Centers in Congo

The Telegraph

April 23, 2019

Ebola Doctor Killed As Violence Hampers Response to Outbreak in DRC

Ebola treatment center in Katwa, in northeastern DR Congo

Hospital General de Reference de Katwa

H.G.R. Katwa.

E-mail: hgrkatwa@yahoo.fr

Services Organisés:

- Urgences
- Ambulances
- Gynécologie
- Pédiatrie
- Pneumologie
- U.N.I.T.I.
- Laboratoire
- Pharmacie
- Cadre
- Dentiste
- Veterinaire

A.O.
Ring Vaccination with rVSV-ZEBOV in the Democratic Republic of the Congo

- Per WHO policy, vaccinating contacts, contacts of contacts, frontline workers

- As of June 12, 2019, 132,679 people have received investigational rVSV-ZEBOV vaccine

Image credit: Sam Mednick/AP

Source: DR Congo MOH
January 1, 2019: Vaccination Team Attacked Near Komanda, DRC
Uganda Confirms First Ebola Case Outside Outbreak in Congo
Two More Ebola Cases Diagnosed in Uganda as First Victim, 5, Dies
Ebola Outbreak May Last Up to 2 Years, WHO Says
Measles
Measles Virus

- Highly contagious airborne virus that survives up to 2 hours in the air after a cough or sneeze

- Paramyxovirus, Genus *Morbillivirus*

- Genome sequencing helps identify origin of imported cases

- Potential for virus eradication:
  - Global eradication of closely related animal virus in 2011
Disease Progression of Measles

- Initial symptoms include fever and cough

- Rash occurs 2-4 days later, lasts 5-6 days

- Contagious from 4 days before → 4 days after rash appears

Source: CDC
<table>
<thead>
<tr>
<th>Complication</th>
<th>Percentage/Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhea</td>
<td>8%</td>
</tr>
<tr>
<td>Otitis media</td>
<td>7 – 9%</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>1 – 6%</td>
</tr>
<tr>
<td>Hospitalized</td>
<td>1 in 4 cases</td>
</tr>
<tr>
<td>Encephalitis</td>
<td>1 per 1,000 cases</td>
</tr>
<tr>
<td>Death</td>
<td>1 – 3 per 1,000 cases</td>
</tr>
<tr>
<td>Subacute Sclerosing Panencephalitis</td>
<td>1 per 100,000 cases</td>
</tr>
</tbody>
</table>

Source: CDC, 5/2019
Groups at High Risk for Complications

- Infants and children < 5 years old
- Pregnant women
- Immunocompromised people
- Adults > 20 years old
Global Burden of Measles Before and After Vaccination

- Pre-vaccine era: ~2.6 million deaths each year
- Dramatic decrease after vaccine introduced in 1963
- 21.1 million deaths prevented from 2000 – 2017
- 110,000 deaths in 2017, mostly in children < 5 years
Pre-Vaccine Measles Burden in the U.S.

- 3,000,000 to 4,000,000 measles cases each year
- \(~48,000\) hospitalizations each year
- \(~500\) deaths each year
Measles Vaccine

- Licensed in 1963 in the U.S.
- Combination measles-mumps-rubella (MMR) vaccine licensed in 1971
- Vaccine effectiveness:
  - 1-dose: ~93%
  - 2-doses: ~97%
- Excellent safety profile over last 50 years
  - Low risk of febrile seizures in children aged 12 – 23 months (1 in 3,000 doses)
  - Temporary pain/stiffness in joints (teenage or adult women)
  - Temporary low platelet count (1 in 30,000 doses)

Source: CDC, 5/2019
Success of U.S. Measles Vaccination

2000: Elimination of measles in U.S.
- Absence of sustained transmission of virus for > 12 months

Source: CDC
Perspective

Measles in 2019 — Going Backward

CI Paules, HD Marston and AS Fauci
International Importations of Measles Virus into the United States During the Postelimination Era, 2001–2016

AD Lee, PA Gastanaduy et al.

553 imported cases-majority were U.S. residents who had traveled
– 87% unvaccinated or unknown vaccination status
Number of U.S. Measles Cases Reported By Year, 2010-2019

Source: CDC

*Preliminary case count, as of December 29, 2018.
**Preliminary case count, as of June 6, 2019.
U.S. States with Reported Measles Cases, 2019 (total n=1,022)

Source: CDC, 6/10/2019
U.S. Areas with >10 Measles Cases, 2019

Sources: CDC; state and county health departments, 6/10/2019
Reasons for Increase in Measles Cases

- An increase in the number of travelers who contract measles abroad and bring it into the U.S.

- Further spread of measles in U.S. communities with pockets of unvaccinated people
Optimal Measles Vaccine Coverage for Herd Immunity

93% - 95%
Reasons for Increase in Measles Cases (cont.)

- **Vaccine hesitancy**—the delay or refusal of vaccines despite their availability
  - Misconceptions/misinformation/lack of information about vaccines and their safety
  - Concerns the large number of injections; moral or religious objections; cost or other access problem; and concerns about side effects, particularly autism.

- **Nonmedical exemptions (NMEs) from vaccine mandates**
  - Tend to occur in geographic clusters and are associated with higher rates of measles
  - 47 states allow NMEs for religious beliefs; 16 states allow so-called philosophical or “personal belief” exemptions
WHO: Anti-Vaccine Movement a Top Threat in 2019

A refusal to vaccinate alongside air pollution and climate change as a top global threat

By Megan Trimble, Digital News Editor