Ebola — Hospital Response, Precautions and Communications

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Kaiser Permanente at a Glance

- Nation’s largest not-for-profit Integrated Healthcare System
- $53.1 billion revenue
- 8 states and District of Columbia
- 9.5 million members
- 38 medical centers
- 618 medical office buildings
- 17,425 physicians
- 174,415 employees

Protecting Health Care Delivery
Expanding the “Continuity” Function
Healthcare Continuity Management Oversight Group

Executive Oversight Group

Clinical Workgroup
Community Linkages Workgroup
Legal Workgroup
Public Policy Workgroup
Communication & Education Workgroup
Facilities Workgroup
People Workgroup
Supply Chain Workgroup
Finance Workgroup
Pharmacy Workgroup
IT Workgroup
MSSA Workgroup

Ongoing Risk Mitigation

Healthcare Risks → Work Group Activity → Risk Mitigation Tools

California Hospital Association

September 23, 2014
Planning is Paramount to Response

Web Resources

http://insidekp.kp.org/insidekp/communicate/readiness/index.html
Actual Responses

Federal Acknowledgement

• “With the exception of Kaiser Permanente, we have been unable to locate other healthcare specific entities that have addressed operational sustainability in a standardized or systematic format.”

• “With the help of private companies, such as Kaiser Permanente, over 3,400 volunteers were processed and over 1,000 volunteers were deployed.”
Case Summary

Ebola Virus Disease

David Witt, MD
Chief of Infectious Diseases
Kaiser Permanente San Rafael
History

- Named after the Ebola River in the DRC (formerly Zaire), near the first epidemics
- Two species were identified in 1976:
  - Zaire ebolavirus (ZEBOV) and
  - Sudan ebolavirus (SEBOV)
- Case fatality rates of 83% and 54% respectively
- Additional species continue to be identified
Animal Pathogen Evolution

<table>
<thead>
<tr>
<th>Stage</th>
<th>Transmission to humans</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 1: agent only in animals</td>
<td>None</td>
</tr>
<tr>
<td>Stage 2: primary infection</td>
<td>Only from animals</td>
</tr>
<tr>
<td>Stage 3: limited outbreak</td>
<td>From animals or (few cycles) humans</td>
</tr>
<tr>
<td>Stage 4: long outbreak</td>
<td>From animals or (many cycles) humans</td>
</tr>
<tr>
<td>Stage 5: exclusive human agent</td>
<td>Only from humans</td>
</tr>
</tbody>
</table>

Distribution in Africa

Photos courtesy of Travel Approved (for Lassa and Ebola), Mehedj et al. 2011 (for Marburg)
**Prior Ebola Outbreaks**

<table>
<thead>
<tr>
<th>Year</th>
<th>Ebola Sub-type</th>
<th>Country</th>
<th># of Cases</th>
<th>% of deaths</th>
<th>Situation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1976</td>
<td>Ebola-Zaire</td>
<td>Zaire (DRC)</td>
<td>318</td>
<td>88%</td>
<td>Spread by close personal contact and by use of contaminated needles and syringes in hospitals/clinics. First recognition of the disease.</td>
</tr>
<tr>
<td>1976</td>
<td>Ebola-Sudan</td>
<td>Sudan</td>
<td>284</td>
<td>53%</td>
<td>Disease spread through close personal contact within hospitals. Many medical care personnel were infected.</td>
</tr>
<tr>
<td>1976</td>
<td>Ebola-Sudan</td>
<td>England</td>
<td>1</td>
<td>0%</td>
<td>Laboratory infection by accidental stick of contaminated needle.</td>
</tr>
<tr>
<td>1977</td>
<td>Ebola-Zaire</td>
<td>Zaire</td>
<td>1</td>
<td>100%</td>
<td>Noted retrospectively in the village of Tandala.</td>
</tr>
<tr>
<td>1979</td>
<td>Ebola-Sudan</td>
<td>Sudan</td>
<td>34</td>
<td>65%</td>
<td>Occurred in Nzara. Recurrent outbreak at the same site as the 1976 Sudan epidemic.</td>
</tr>
<tr>
<td>1989</td>
<td>Ebola-Reston</td>
<td>USA</td>
<td>0</td>
<td>0%</td>
<td>Ebola-Reston virus was introduced into quarantine facilities in Virginia, Texas, and Pennsylvania by monkeys imported from the Philippines. Four humans developed antibodies to Ebola-Reston virus but did not become ill.</td>
</tr>
<tr>
<td>1990</td>
<td>Ebola-Reston</td>
<td>USA</td>
<td>0</td>
<td>0%</td>
<td>Ebola-Reston virus was introduced once again into quarantine facilities by monkeys from the Philippines. Four humans developed antibodies but did not get sick.</td>
</tr>
<tr>
<td>1992</td>
<td>Ebola-Reston</td>
<td>Italy</td>
<td>0</td>
<td>0%</td>
<td>Ebola-Reston virus was introduced into quarantine facilities in Sienna by monkeys imported from the same export facility in the Philippines. No humans were infected.</td>
</tr>
<tr>
<td>1994</td>
<td>Ebola-Zaire</td>
<td>Gabon</td>
<td>49</td>
<td>59%</td>
<td>Occurred in Mokouka and other gold-mining camps deep in the rain forest.</td>
</tr>
</tbody>
</table>

**Prior Ebola Outbreaks (cont.)**

<table>
<thead>
<tr>
<th>Year</th>
<th>Ebola Sub-type</th>
<th>Country</th>
<th># of Cases</th>
<th>% of deaths</th>
<th>Situation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1994</td>
<td>Ebola-Ivory Coast</td>
<td>Ivory Coast</td>
<td>1</td>
<td>0%</td>
<td>Contracted after conducting an autopsy on a wild chimpanzee in the Tai Forest.</td>
</tr>
<tr>
<td>1995</td>
<td>Ebola-Zaire</td>
<td>DRC</td>
<td>315</td>
<td>81%</td>
<td>Index case worked in forest. Epidemic spread through families and hospitals.</td>
</tr>
<tr>
<td>1996</td>
<td>Ebola-Zaire</td>
<td>Gabon</td>
<td>31</td>
<td>68%</td>
<td>Chimpanzee found dead in the forest was eaten. Nineteen people who were involved in the butchery of the animal became ill; other cases occurred in family members.</td>
</tr>
<tr>
<td>1996</td>
<td>Ebola-Zaire</td>
<td>Gabon</td>
<td>60</td>
<td>75%</td>
<td>Index case was a hunter who lived in a forest camp. Disease was spread by close contact with infected persons. A dead chimpanzee found in the forest at the time was infected.</td>
</tr>
<tr>
<td>1996</td>
<td>Ebola-Zaire</td>
<td>South Africa</td>
<td>2</td>
<td>50%</td>
<td>HCW traveled from Gabon to South Africa, after having treated Ebola virus-infected patients. Hospitalized, and a nurse who took care of him became infected and died.</td>
</tr>
<tr>
<td>1996</td>
<td>Ebola-Reston</td>
<td>USA</td>
<td>0</td>
<td>0%</td>
<td>Ebola-Reston virus was introduced into a quarantine facility in Texas by monkeys imported from the Philippines. No human infections were identified.</td>
</tr>
<tr>
<td>1996</td>
<td>Ebola-Reston</td>
<td>Philippines</td>
<td>0</td>
<td>0%</td>
<td>Ebola-Reston virus was identified in a monkey export facility in the Philippines. No human infections were identified.</td>
</tr>
<tr>
<td>2000-2001</td>
<td>Ebola-Sudan</td>
<td>Uganda</td>
<td>425</td>
<td>53%</td>
<td>Major risks associated with infection were attending funerals of Ebola patients; contact with patients in family, and providing medical care to patients without adequate protection.</td>
</tr>
<tr>
<td>2001-2002</td>
<td>Ebola-Zaire</td>
<td>Gabon and DRC</td>
<td>122</td>
<td>79%</td>
<td>Outbreak occurred over the border of Gabon and DRC.</td>
</tr>
</tbody>
</table>
Where Does Ebola Hide?

- 2002: Fruit Bats — do not show any symptoms
- Best candidate to be the reservoir
- Antibodies against Ebola
- Primate outbreaks often precede human outbreaks
- Ebola gene sequences in liver and spleen and many other mammals

Ebola Virus — Risk Factors

- Hunting and butchering wild animals, especially non-human primates
- Healthcare workers and family

Photo courtesy of Nathan Wolfe

Photo courtesy of the CDC PHIL
Transmission

- Direct contact with the blood, secretions, organs or semen of infected persons:
  - Risk factors among 27 surviving members in Kikwit
    - Direct contact during late hospital phase were at very high risk
    - Those with no physical contact with infected remained uninfected
  - Transmission through semen occurs up to 80 d.
  - Recent report 14 cases - funeral preparations
- Handling dead infected people or chimps
- Neonatal
- Droplets or small filovirus particle aerosols confirmed in alveoli of monkeys during Reston outbreak and BT evaluations

Clinical Presentation

- High Fever
- Severe prostration
- Diffuse maculopapular rash (day 5)
- Bleeding
- Myalgia — severe
- Bradychardia
- Desquamation — late
- Loss of appetite
Ebola — Symptoms and Signs

- Sudden onset of malaise, sore throat, cough, fever, chills, chest pain, myalgia, nausea, vomiting and diarrhea
- Severe headaches, fatigue, confusion, coma
- Edema and conjunctivitis

Ebola — Symptoms and Signs (cont.)

- Hemorrhagic symptoms infrequent (<10% of cases) hematemesis, hemoptysis, melena, bleeding of mucosal membranes (gut, nose, vagina)
- Skin: rash, petechiae, hematomas, purpura
- Death from multiple organ dysfunction syndrome due to disseminated intravascular coagulation, hypotension, and focal tissue necroses
Other Diagnostic Criteria

- Leukopenia (Low White Blood Cell Count)
- Thrombocytopenia (Low Platelet Count)
- Coagulation Studies
- Abnormal Electrolytes
- Lymphopenia followed by neutrophilia

Diagnostic Tests for Ebola

- ELISA (Enzyme-Linked Immunosorbent Assay)
- Rapid Tests
- Can’t differentiate Ebola strains with electron microscope
- Indirect fluorescent antibody test (IFAT)
- Western blot analysis
- Radioimmunoprecipitation assay
- Skin biopsies
Ebola Diagnosis

- Specimen collection and handling
- Public health vs. hospital responsibilities
- Notification of test results

Clinical Course

- 2-21 day incubation time (mean 12)
- 50-90% mortality
- Variability of clinical presentations complicate early detection and management
- Non-specific prodrome typically lasts < 1 week
- 10-12 days after the onset of disease, the sustained fever may break, with improvement and eventual recovery of the patient
- 1-2 weeks after onset of symptoms: death often preceded by hemorrhagic diathesis, shock, multi-organ system failure
Differential Diagnosis

- Malaria (most likely)
- Dengue
- Leptospirosis
- Plague
- Rickettsiosis
- Relapsing fever
- Hepatitis
- Typhoid
- URI
- Other hemorrhagic fevers (Yellow, Marburg, Lassa)

What is ZMapp?

- **ZMapp**: three humanized monoclonal antibodies
- Manufactured in the tobacco plant nicotiana, known as “pharming” by Kentucky BioProcessing, a subsidiary of Reynolds American
- Monoclonal antibodies created in mice with antigens from Ebola, harvesting their spleens, and fusing mature B-cells producing monoclonal antibodies with cancer cell lines to create hybridomas
What is ZMapp? (cont.)

- The gene encoding the antibody was extracted, and portions replaced with portions encoding human proteins (humanization)
- To produce the humanized mAbs at commercial scale, Mapp used “Rapid Antibody Manufacturing Platform” (RAMP) — “magnification,” tobacco plants are infected with the viruses
- Subsequently, antibodies are extracted and purified from the plants

Vaccines

- In June, Jones and his colleagues, Dr. Heinz Feldmann of Winnipeg and Dr. Thomas Geisbert at Fort Detrick, Maryland announced that they had successfully vaccinated monkeys against the deadly Ebola virus
- The Ebola vaccine is based on the 1976 strain of the Zaire species and protects from the 1995, but not the other 2 species that affect humans
### Ebola Summary — August 20

<table>
<thead>
<tr>
<th></th>
<th>New (1)</th>
<th>Confirmed</th>
<th>Probable</th>
<th>Suspect</th>
<th>Totals</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Guinea</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cases</td>
<td>28</td>
<td>443</td>
<td>139</td>
<td>25</td>
<td>607</td>
</tr>
<tr>
<td>Deaths</td>
<td>10</td>
<td>264</td>
<td>139</td>
<td>3</td>
<td>406</td>
</tr>
<tr>
<td><strong>Liberia</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cases</td>
<td>110</td>
<td>269</td>
<td>554</td>
<td>259</td>
<td>1082</td>
</tr>
<tr>
<td>Deaths</td>
<td>48</td>
<td>222</td>
<td>267</td>
<td>135</td>
<td>624</td>
</tr>
<tr>
<td><strong>Nigeria</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cases</td>
<td>1</td>
<td>12</td>
<td>0</td>
<td>4</td>
<td>16</td>
</tr>
<tr>
<td>Deaths</td>
<td>1</td>
<td>5</td>
<td>0</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td><strong>Sierra Leone</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cases</td>
<td>3</td>
<td>804</td>
<td>40</td>
<td>66</td>
<td>910</td>
</tr>
<tr>
<td>Deaths</td>
<td>18</td>
<td>353</td>
<td>34</td>
<td>5</td>
<td>392</td>
</tr>
<tr>
<td><strong>Totals</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cases</td>
<td>142</td>
<td>1528</td>
<td>733</td>
<td>354</td>
<td>2615</td>
</tr>
<tr>
<td>Deaths</td>
<td>77</td>
<td>844</td>
<td>440</td>
<td>143</td>
<td>1427</td>
</tr>
</tbody>
</table>
Ebola — Outbreak Containment and Control

1. Logistics and coordination: barrier nursing supplies
2. Social mobilization: outreach to the public
3. Laboratory diagnosis
4. Epidemiology and surveillance: database of cases and case contacts

Key Strategies for Crisis Settings

- **Isolation**: find a separate room or building for infected patients, but a corner of a large room can still help reduce nosocomial spread
- Use tarps or sheets to separate beds to avoid cross contamination with spills or splashes
- Minimize flow of people through the area, and put most severe cases toward the back
Ebola — Reducing Transmission

Supplies for Low-Resource Settings

Photos courtesy of the CDC PHIL

Pictures courtesy of the CDC
Lessons Learned

Questions?
Thank you!

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