Ebola Viral Disease

The opinions or assertions contained herein are the private views of the author, and are not to be construed as official, or as reflecting true views of the Department of the Army or the Department of Defense. Research was conducted in an AAALACi accredited facility in compliance with the Animal Welfare Act and other federal statutes and regulations relating to animals and experiments involving animals and adheres to principles stated in the Guide for the Care and Use of Laboratory Animals, NRC Publication, 2011 edition.
Outline

• Ebola
  - Epidemiology
  - Clinical aspects
  - Diagnosis
  - Treatment
  - Prevention
Case presentation

• Male investigator at Porton Down, UK

  ➢ 5 November
  • Pricks his thumb while transferring homogenized liver from a GP infected with a new virus

  ➢ 11 November
  • Temp rises to 37.4 C (99.32 F)
  • Central abdominal pain
  • Nausea
  • Subsequently develops exhaustion, anorexia
Convalescence:
- Weight loss slowly regained
- Scalp hair loss
- Hgb and WBC counts normalize after 3 months

Diagnosis:
Ebola Sudan
What is Ebola?
The Filovirus Family (Filoviridae)

• Two Genera Infect Humans:
  - Marburg virus
  - Ebola viruses – 5 species
    • Ebola virus (Zaire)
    • Sudan virus
    • Tai Forest virus (formerly Cote d’Ivoire)
    • Bundibugyo virus (Uganda)
    • Reston virus
Name derivation

- Filovirus from Latin filum = thread
- **Ebola River** in northern DRC. Headstream of the Mongala River, which leads to Congo River

Source - Wikipedia
VHFs exist worldwide
What is unique about Ebola?

• High mortality rate
• No treatment or vaccine (yet...)
• Comes from nowhere and causes explosive outbreaks
• Hospitals often the epicenter for spread
  ➢ Frequently unrecognized initially

• Public has been primed by the media to fear it
Where does Ebola “live?”
Figure 1: Locations of Ebolavirus infections and outbreaks

(A) Regions in Africa (approximate distribution 10° north and south of the equator) with reported outbreaks of Ebola haemorrhagic fever caused by the three central African species of Ebola virus, Zaire Ebola virus (ZEBOV), Sudan Ebola virus (SEBOV), and Bundibugyo Ebola virus (BEBOV). The Tai Forest region in Côte d’Ivoire reported the only case so far of Ebola virus in western Africa caused by the species Côte d’Ivoire Ebola virus (CIEBOV). (B) Reston ebolavirus REBOV has been introduced several times through imported macaques into USA from 1989 to 1996 (Philadelphia, PA; Reston, VA; San Antonio, TX) and into Italy (Siena) in 1992 (C). The source of the introduction in all cases of REBOV has been a primate export facility in the Philippines (Ferlite farm) (D). Animals of this farm have been diagnosed with REBOV infection several times in the 1990s. REBOV has been detected in pigs on two farms in the Philippines (Pangasinan, Bulacan). DRC=Democratic Republic of the Congo.
VHF Epidemiologic Triangle

HOST
(rodents, bats)

AGENT
(Ebola)

ENVIRONMENT
(poverty, crowding, burial practices, health infrastructure)
How does it spread?
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
- Taï 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.
How Ebola spreads

- Direct contact with infected blood or body fluids
  - Household family members
  - Care providers (splashes, needlesticks, mucus membrane contact)
  - Lab personnel
  - Patients receiving injections with contaminated needles
  - Eating infected bush meat
  - Direct contact with dead bodies during burial rituals

- Risk of spread increases as illness severity increases
- Doesn’t spread prior to illness
- Doesn’t spread through “the air”

CDC.gov
Contagious when symptomatic

How Ebola Symptoms Progress

Infection with the Ebola virus can lead to flu-like symptoms, bleeding (both visible and internal) and, in many cases, death. The current outbreak has a mortality rate of around 60 percent.

<table>
<thead>
<tr>
<th>EXPOSURE</th>
<th>INCUBATION</th>
<th>COURSE OF ILLNESS</th>
<th>DEATH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms typically begin 4–9 days after exposure, though incubation may last for up to 21 days.</td>
<td>DAYS 1–3: In the first few days of illness, patients have flu-like symptoms and profound weakness.</td>
<td>DAYS 4–7: Around days 4-7, patients may also have vomiting, diarrhea, nausea, low blood pressure, headaches and anemia.</td>
<td>DAYS 7–10: Toward the end of the illness, there is confusion and bleeding, both internal and visible. All of this progresses toward coma, shock and death.</td>
</tr>
</tbody>
</table>

More opportunities for spread:
- Diarrhea
- Vomiting
- Bleeding
- ?Coughing

Source: Dr. Nahid Bhadelia M.D., M.A., Associate Hospital Epidemiologist, Boston Medical Center Director of Infection Control, National Emerging Infectious Disease Laboratories, Boston University

THE HUFFINGTON POST

Courtesy of Clint Murray
Ebola spread in perspective

**How contagious is Ebola?**

How the Ebola virus compares with other contagious viruses. The reproduction rate or $R_0$, calculates the number of people likely to be infected by one person who has a disease.

**REPRODUCTION RATE ($R_0$)**

- **1 to 4 people**
- **2 to 4**
- **4 to 7**
- **5 to 7**
- **5 to 7**
- **6 to 7**
- **12 to 18**
- **12 to 17**

**DISEASE**

- Ebola
- SARS
- Mumps
- Polio
- Smallpox
- Rubella
- Measles
- Pertussis (Whooping cough)

**HOW IT SPREADS**

- Bodily fluids
- Airborne droplets
- Airborne droplets
- Fecal-oral route
- Airborne droplets
- Airborne droplets
- Airborne
- Airborne droplets

Sources: Michigan Center for Public Health; WHO; Transmission Dynamics and Control of Severe Acute Respiratory Syndrome, Nature; Understanding the Dynamics of Ebola Epidemics, National Institute of Health
Hospitals as epicenters for spread

- Reuse of contaminated needle/syringe
- Accidental needlesticks
- Exposures during surgery/deliveries
- Rubbing eyes with soiled gloves
- Blood/body fluid splashes


CDC. *Outbreak...Uganda.* MMWR 2001;50:5.

Other Aspects of Spread

- Fomites implicated but uncommon
- Airborne route postulated, not proven
- Mildly ill patients or early in illness may transmit – although rare
- Uncertain impact of asymptomatic infection
  - Unlikely to transmit

CDC. Review of human-to-human transmission of Ebola virus
What does it do to people?
Model of Filoviral Pathogenesis in Primates

1. Early infection of target cells
2. Release of Tissue Factor and microparticles
3. Release of Cytokines, Chemokines, and Nitric Oxide
4. Rapid apoptosis of bystander lymphocytes disables the host immune response
5. Infection of the liver and adrenal gland impairs the synthesis of clotting factors and steroid-synthesizing enzymes
6. Activation of the coagulation cascade and impairment of the endothelium leading to loss of homeostasis and shock
Early Clinical Features

- Potential Features
  - Maculopapular rash
    - Hard to see with darker skin
  - Sore throat
  - Conjunctival injection

Borrowed from James Lawler
Hemorrhagic signs near the end of the first week
- Bleeding doesn’t generally kill people, organ failure does

Gingival bleeding

Bleeding at IV Site

Borrowed from James Lawler
## Case Fatality Percentages
*(based on 19 Human Outbreaks 1976-2008)*

<table>
<thead>
<tr>
<th>Year(s)</th>
<th>Species</th>
<th>Cases</th>
<th>Deaths</th>
<th>CFR</th>
</tr>
</thead>
<tbody>
<tr>
<td>1976-2008</td>
<td>Zaire</td>
<td>1381</td>
<td>1084</td>
<td>78%</td>
</tr>
<tr>
<td>1976-2004</td>
<td>Sudan</td>
<td>760</td>
<td>404</td>
<td>53%</td>
</tr>
<tr>
<td>2007</td>
<td>Bundibugyo</td>
<td>149</td>
<td>37</td>
<td>25%</td>
</tr>
<tr>
<td>1994</td>
<td>Cote D’Ivoire</td>
<td>1</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>1989-2008</td>
<td>Reston</td>
<td>0</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td></td>
<td>2291</td>
<td>1525</td>
<td>66%</td>
</tr>
</tbody>
</table>

Current outbreak is #25 and larger than all prior combined – 27,575 cases with 11,245 deaths (40.7%)
Survivors of infection by Ebola virus, already known to face vision, hearing and other problems during their recovery, may also be plagued with health issues such as depression, anxiety and nerve damage that surface after they leave the hospital, according to a small spot survey of 9 victims whose care was managed in the USA. Some of the signs and symptoms can persist for months, researchers from the Centers for Disease Control and Prevention in Atlanta have found.

16 Dec 2015 USA: New symptoms surface in Ebola patients months after initial recovery
<http://uk.reuters.com/article/us-health-ebola-survivor-symptoms-idUKKBN0TZ32B20151216>
Reported associations with fatality

- Higher viremia
- Elevated AST, BUN, creatinine
- Elevated cytokines:
  - IL6, IL8, IL10, Macrophage Inflam Protein 1β
- Elevated ferritin, D-dimer
- Decreased albumin, calcium
- Lack of antibody response


WHO Situation Summary Data Published on 30 DEC 2015
New WHO case counts released: 28601 cases; 11300 deaths.
Additional Associations with Elevated CFR in W. Africa Outbreak

- Higher viremia
- Older age
- At presentation:
  - Fever
  - Headache
  - Weakness
  - Dizziness
  - Diarrhea

Schieffelin JS, et al. NEJM 2014;371:2092-10
How do I diagnose it?
Differential Diagnosis

Distribution of RVF

Distribution of Malaria

Distribution of CCHF

Figure 1: Worldwide distribution of CCHF virus
Administration of preventive malaria treatment to contacts of patients with Ebola virus disease should be considered by public health officials when addressing Ebola virus disease outbreaks in countries and seasons where malaria reaches high levels of transmission.

Prophylaxis eliminates the problem of contacts who develop severe symptoms from malaria being mistaken for suspected EVD cases, and being admitted to an ETU.

Differential Diagnosis

Clinical presentation: Febrile, hemorrhage/purpura, thrombocytopenia, CNS signs, elevated LFTs, leukopenia, thrombocytopenia, DIC, multisystem / multi-organ failure

- **Protozoal**
  - Malaria

- **Bacterial**
  - Typhoid fever
  - Rocky Mountain Spotted Fever (*Rickettsia rickettsii*) & other rickettsioses
  - Leptospirosis
  - Meningococci
  - Q fever (*Coxiella burnetti*)
  - Plague

- **Viral**
  - Influenza
  - Viral meningitis / encephalitis (e.g. henipaviruses)
  - HIV / co-infection
  - Hemorrhagic smallpox

- **Other**
  - Vasculitis, thrombotic thrombocytopenic purpura (TTP), hemolytic-uremic syndrome (HUS), heat stroke
Ebola

Diagnosis

- Viral isolation
  - Vero, Vero E6, MA104

- Electron Microscopy
  - Cell culture supernatants

- ELISA
  - Ag detection
  - IgM / IgG

- IFA: strain differentiation
- IHC: Skin samples
- RT-PCR
EVD: Expected diagnostic test results over time

Critical information: Date of onset of fever/symptoms

- IgM: up to 3 – 6 months
- IgG: 3 – 5 years or more (life-long persistence?)

Fever

RT-PCR

ELISA IgM

ELISA IgG
Important

• Diagnostics early in illness may by negative
• Re-test in **72 hours**

*Case study example:*
Martin Salia
- Infected in Sierra Leone
- Became ill 4 Nov
- Tested Negative at that time

Tested Positive 10 Nov
Is there a treatment?
Treatment

- Mainstay of therapy has been supportive care
- No licensed therapies
- Several treatments have been tested
- Until recently, not much success
Lessons Learned from clinical care

- Significant loss of fluids through high volume diarrhea and vomiting
  - 4-6 liters/day

- Electrolyte abnormalities
  - Low levels of potassium, sodium, calcium, magnesium in the blood
  - Arrhythmias

- Low protein levels with significant edema
- Not adequately replenished with oral solutions

Ebola Prophylaxis/Therapy
Several have protected NHPs if begun shortly after exposure

- Immunomodulators:
  - Recombinant activated protein C (Xigris)
    - 2/11 NHP survivors (18%) at 30-60 mins
  - Recominant Nematode protein (rNAPc2)
    - 3/9 (33%) NHP survivors at 10 mins or 24 hours

- Vaccination: recombinant VSV Ebola vaccine

- Antivirals:
  - Antisense polymorpholino oligomers (PMOs)
    - 8/13 at 30-60 mins
  - Favipiravir (T705) – 5/5 in mouse model D6; NHPs pending
  - BCX4430- 5/6 (83%) at 1 hour; 6/6 at 24 hours; 6/6 at 48 hours (MARV)
Ebola Prophylaxis/Therapy

• Only two demonstrated benefit after illness or viremia in NHPs:
  – Monoclonal antibodies – 5 days post-infx
    • After illness, sometimes severe
  – Antiviral: Small interfering RNAs (SiRNAs)
    • After fever

• Human studies:
  – TKM Ebola-Guinea – ph 2 halted (Guinea/SL)
  – Brincidofovir – halted (Liberia)
  – Favipiravir – ph 2 (Guinea)
  – Convalescent Plasma ph 1/2 (Liberia, Guinea, SL)
What works in humans?

• We don’t know
  - Lower case fatality proportion seen in US and Europe
  - Uncertain role played by effective supportive care
  - Many patients treated with multiple experimental products
  - No way to discern effectiveness or safety

• Randomized, controlled trials needed
  - Significant scientific, practical, ethical challenges

Multicenter randomized safety and efficacy study of putative investigational therapeutics in the treatment of patients with known Ebola infection

- Collaboration among: NIH, CDC, FDA, DoD
- Optimized supportive care vs OSC + Rx (Zmapp)
- Participating sites:
  - 4 centers in the US
  - Liberia, SL, Guinea
- 47 enrollees as of 7 July
- DSMB reviewing data every 10 subjects
DoD Ebola Response Challenges

• INFECTIONOUS DISEASES WAR, NOT THE USUAL MISSION
  - Invisible “enemy,” varied individual responses
  - Knowledge gaps (science of Ebola incomplete)
  - Implications abroad and at home (risk of returning troops)
• ALIGNMENT BETWEEN DOD POLICY AND OTHER USG AGENCIES
  - Monitoring re-deployers
• BD-ID INTERFACE (COUNTERMEASURES)
• PUBLIC PERCEPTION
  - Africa: foreign military
  - U.S.: risk to community
• TIME SENSITIVITY OF MISSION

Liberian training site
Is there a vaccine?
Anatomy of a filovirus:
Genome encodes 7 structural proteins

- **Central helical nucleocapsid**
- **Polymerase**
- **Nucleoprotein VP30 & VP35** (Blocks INF induction)
- **Trimeric Glycoprotein:** (Binding/membrane fusion)
- **Lipid bilayer**

Most vaccines protecting NHPs have utilized the GP as the antigen.

- **VP40** (matrix protein) and **VP24:** (Assembly/release of viral particles) link to surface lipid bilayer.
Vaccines at the head of the pack

- Recombinant Chimpanzee Adenovirus
  - NIH/GSK
  - Phase 2/3

  *Chimpanzee Adenovirus Vector Ebola Vaccine — Preliminary Report*
  
  Julie E. Ledgerwood, D.O., Adam D. DeZure, M.D., Daphne A. Stanley, M.S.,
  The New England Journal of Medicine

- Recombinant Vesicular Stomatitis Virus
  - Walter Reed Army Institute of Research/NIH/Merck-Newlink/Canada
  - Phase 2/3

  *A Recombinant Vesicular Stomatitis Virus Ebola Vaccine — Preliminary Report*

  J.A. Regules, J.H. Beigel, K.M. Paolino, J. Voell, A.R. Castellano, P. Muñoz,
  The New England Journal of Medicine

- Ad26/MVA-BN-filo
  - J&J/Bavarian Nordic; Phase 2


Research & Development: Therapeutics

**JPEO-CBD**
- TKM-Ebola, Tekmira
- Favipiravir, Fuji Film – Toyama / MediVector

**CONUS**
- NIH manages a master treatment protocol, ZMapp and others?
- Emory, Nebraska, NIH, DoD MTFs?

**WEST AFRICA**
- Favipiravir
  - French National Institute of Health
  - Guinea, phase 2b, sequential
- NIH trial in Liberia, ZMapp
- New lots of Tekmira-Guinea?

Avigan, a drug approved as an anti-influenza drug in Japan, is showing promise in treating ebola. Credit Issei Kato/Reuters
RESULTS OF EBOLA VIRUS DISEASE VACCINE TRIALS TO DATE:

- BRINCIDOFOVIR (LIBERIA): STOPPED BY CHIMERIX AFTER 4 PATIENTS, REASONS UNCLEAR.

- FAVIPIRAVIR (GUINEA): COMPLETED, MORE THAN 200 PATIENTS INCLUDED, PUTATIVE SIGNAL OF EFFICACY.

- PLASMA (LIBERIA): STOPPED AFTER 6 PATIENTS. (SIERRA LEONE): STOPPED AFTER 3 PATIENTS. (GUINEA): COMPLETED, 102 PATIENTS INCLUDED.

- WHOLE BLOOD (LIBERIA): STOPPED, STATUS UNCLEAR.

- ZMAPP (LIBERIA, SIERRA LEONE, GUINEA, USA): ABOUT 70 PATIENTS ENROLLED IN ONGOING RCT (RANDOMIZED CONTROL TRIAL).

- TKM-EBOLA (SIERRA LEONE): STOPPED AFTER 14 PATIENTS, DRUG DEEMED UNLIKELY TO WORK.

- INTERFERON-BETA (GUINEA): STOPPED AFTER 9 PATIENTS.

- GSK AND MERCK VACCINES (LIBERIA): SUSPENDED AFTER 500 VOLUNTEERS RECEIVED EACH VACCINE.

- MERCK VACCINE (GUINEA): RING STUDY: MORE THAN 4000 VACCINATED, EFFICACY DEMONSTRATED. FRONTLINE WORKER STUDY: 2000 VACCINATED.

- MERCK VACCINE (SIERRA LEONE): FRONTLINE WORKER STUDY, 8000+ VACCINATED.

[IT WOULD BE INTERESTING TO KNOW THE REASONS WHY SOME OF THE TRIALS WERE STOPPED AFTER AS FEW AS 4 WERE TREATED OR AS MANY AS 500 WERE VACCINATED. - MOD.JW]
How to protect Health Care Workers?
Definition

• “Biocontainment Patient Care unit”
  - Clinical facility
  - Designed to minimize nosocomial transmission of highly contagious and hazardous diseases
  - Incorporate engineering and safety measures used in containment laboratories

Designing a Biocontainment Unit to Care for Patients with Serious Communicable Diseases: A Consensus Statement

PHILIP W. SMITH, ARTHUR O. ANDERSON, GEORGE W. CHRISTOPHER, THEODORE J. CIESLAK, G. I. DEVREDEE, GLEN A. FOSDICK, CARL B. GREINER, JOHN M. HAUSER, STEVEN H. HINRICHs, KERMIT D. HUEBNER, PETER C. IWEN, DAWN R. JOURDAN, MARK G. KORTEPETER, V. PAUL LANDON,

BIOSECURITY AND BIOTERRORISM: BIODEFENSE STRATEGY, PRACTICE, AND SCIENCE

Volume 4, Number 4, 2006
The “Slammer”

Referred to also in the VHF class
“Hard-wired” Features of the Slammer

- External direct pass-thru entry
- Positive pressure “space” suits
- Intake/exhaust HEPA filtration
- Lab sewer system with steam sterilization
- UV light boxes
- Dunk tanks
- Autoclave
- Decon shower
- Telemetry, video monitoring
- On-site lab
Basic Infection Control Precautions: What is really needed?

- Standard Precautions
- Transmission-based Precautions
  - Contact
  - Droplet
  - Airborne

- Sperm can carry the Ebola virus for at least 82 days, (WHO) so condoms must be used for sexual intercourse
Outbreak Management:
- Isolation
- Barrier precautions
- **SEPARATE HIGH/LOW RISK ENTRANCES**
- **FLOW FROM LOW TO HIGH RISK**
- **TRIAGE PATIENTS TO SUSPECTED +EVD**
- **PERIMETER SECURITY**

Diagrams of ELWA 3 Ebola Management Center, Monrovia, Liberia.
Panel A shows the high-risk zone, and Panel B shows the complete center. Adapted from Médecins sans Frontières.

Chertow SW. NEJM Nov 2014 epub
Number of infected health care workers declined after barrier nursing practices were begun during the Ebola HF outbreak in Kikwit, DRC, 1995.

CDC guidelines

- Standard, contact, and droplet precautions
  - Gloves, impermeable gown, eyewear, facemask
- Single patient room
- Dedicated medical equipment
- Minimize needles, sharps, phlebotomy, procedures
- Avoid aerosol generating procedures
  - Conduct in neg pressure room; N95 or higher mask

www.cdc.gov accessed 13 Sept 2014
Glass Half Empty: spread still occurs


Borchert M. BMC-ID 2011;11:357.
During the outbreak: a Disconnect?

Policy

Practice
A single case in Dallas changed our thinking!


Courtesy of Clint Murray
March “Madness” – nosocomial risk continues

CDC investigating potential exposures of American citizens to Ebola in West Africa

On March 13, an American volunteer healthcare worker in Sierra Leone who tested positive for Ebola virus returned to the U.S. by medevac and was admitted to the NIH Clinical Center for care and treatment. As a result of this case, CDC is conducting an investigation of individuals.

http://www.cdc.gov/media/releases/2015/s0313-potential-ebola-exposure.html
Accessed 3/21/15

17 others

Nebraska 5  Georgia 3  Maryland 3
The Problem

• At peak infection, virus in the blood or secretions
  ➢ Up to 100,000,000+ virions per ml

• Number needed to infect:
  ➢ 1-10 virions

• There is no room for error
• Like the BSL-4 lab, redundancy is key
4 High Level Containment Care Facilities in the US

- NIH – Bethesda, MD
- Emory Univ – Atlanta, GA
- St. Patrick’s Hospital, Missoula, MT
- Univ of Nebraska Medical Center, Omaha, NB

Why do specialized units make sense?
• Rare Infection – clinicians and staff unfamiliar
• High mortality rate
• No proven effective vaccine or therapies
• Propensity to infect health care providers
• Many infection control challenges – mitigated by special units:
  ➢ Highly trained staff/continually reinforced
  ➢ Training, policies, procedures, logistics ready in advance
  ➢ Disposal of significant volumes of waste and human waste

• Added reassurance to the public
• Still can’t engineer out human error or sharps injuries
PPE Evolution – Back to the Future?

Per Mike Kurilla
EVD Risk Assessment

**HIGH-RISK EXPOSURE**
- Percutaneous (e.g., needle stick) or mucous membrane contact with blood or body fluids from an Ebola patient
- Direct skin contact with, or exposure to blood or body fluids of, an Ebola patient
- Processing blood or body fluids from an Ebola patient without appropriate personal protective equipment (PPE) or biosafety precautions
- Direct contact with a dead body (including during funeral rites) in a country with wide-spread Ebola transmission** without appropriate PPE

**LOW-RISK EXPOSURE**
- Household members of an Ebola patient and others who had brief direct contact (e.g., shaking hands) with an Ebola patient without appropriate PPE
- Healthcare personnel in facilities with confirmed or probable Ebola patients who have been in the care area for a prolonged period of time while not wearing recommended PPE

**NO KNOWN EXPOSURE**
- Residence in or travel to a country with wide-spread Ebola transmission** without HIGH- or LOW-risk exposure
Regardless of whether one believes in containment care wherever patient care occurs:

• CARE MUST BE DELIBERATE
• EVERY PROCEDURE MUST BE PRACTICED AND FOLLOW RISK/BENEFIT
• ANYONE CAN AND SHOULD CALL A SAFETY STOP

Supervision and buddy assistance

Training is as (or more) important as PPE
  *Repeatedly reinforced*

Healthy respect (not fear) for what the virus can do

As of 2 July: ~2 dozen new/wk
27,575 cases/11,245 deaths (40%)
HCWs 893 cases/516 deaths (57%)

~5,700 lives lost since the beginning of 2015,- almost all of them in Guinea, Liberia and Sierra Leone. (WHO, NOV 2015)
New confirmed Ebola virus disease cases by district in West Africa, during the most recently reported three-week period.

**New Confirmed Cases**
- 0 cases
- 1 - 10 cases
- 11 - 20 cases

As of dates:
- Guinea, 10 JUN - 1 JUL
- Sierra Leone, 10 JUN - 1 JUL
- Liberia, 10 JUN - 1 JUL

All information has been verified unless noted otherwise. Sources include WHO, and the Guinea, Liberia, and Sierra Leone Ministries of Health.
What has fueled the West Africa outbreak?

• **Information:**
  - Distrust in health care system, government, foreign HCWs
    - “Spreading Ebola,” “Selling blood”
    - Go into hospital to die
    - Hiding patients at home
    - Burial practices

• **Infrastructure/poverty:**
  - Collapse of already limited infrastructure
    - Remaining medical staff flee
  - Crowded conditions
  - Difficult to track cases, deaths in a chaotic and dangerous environment

• Response has been slow and incremental
How do we get out of this?

Improve care infrastructure

Local providers return

Restores confidence in medical care

$$$$s

People

Logistics

Patients out of hiding, thus easier to trace

Families cooperate; educate public

TRUST
Still learning about sequelae of Infection

- Uveitis with recoverable virus 14 weeks after onset of illness
- Extent of other sequelae TBD
  - Skin sloughing
  - Hair loss
  - Myalgias
  - Parotitis
  - Orchitis
  - Hearing loss
  - Neurologic signs

Varkey JB, et al. NEJM 2015
Have we learned anything?

- Infectious diseases have no boundaries
  - Global health matters
  - Need awareness of public health and security implications

- Diseases move faster than our responses
  - There is always a risk of a relapse
  - We can’t afford to be complacent
  - Leaders need to remember lessons of the past
  - Investigational products can accelerate with multi-agency cooperation

- We need a robust and responsive public health infrastructure
  - Training is as important as having the right equipment
  - Information flow is suboptimal

- Response must be in a context acceptable to local population
  - Ebola can disrupt an entire social structure
  - We must be equipped to address flare-ups of EVD

1. Ebola virus may persist in various body fluids, resulting in reactivation illness.

2. Reinfection with Ebola virus may be possible due to waning or lowered immunity or high viral challenge.

3. With over 17 000 survivors in West Africa, precautions should be taken to minimize the risk of new cases and outbreaks.

4. Surveillance systems in high-risk countries should be capable of rapid detection and control of new outbreaks.

Conclusions

- Ebola in West Africa presented a unique problem set
- DOD’s enduring investment in global health
  - Provided a foundation to begin responding
  - SME, Research platforms in Africa
- Coordinating R&D response across the DOD was challenging
- Creating an inclusive communication venue helped
  - Leveled understanding, Synchronized communications
  - Advanced R&D activities and opportunities
- DOD’s biomedical future in West Africa unclear
Questions?