Family Medicine Grand Rounds
University of Washington

Ebola: Global Update, and CDC Activities

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CME

This live series activity, UW Family Medicine Grand Rounds, is under review for 1 Prescribed Credit by the American Academy of Family Physicians. Attendees should claim only the credit commensurate with the extent of their participation in the activity.

Learning Objectives

At the end of this activity, the participant will be able to:

1. Identify the origins of the current epidemic of Ebola in West Africa and elsewhere.
2. Describe the usual presentation of Ebola Virus Disease.
3. Describe the activities of the CDC in the US regarding advising medical providers and public health departments regarding patients who potentially have Ebola.

Disclosure: Conflicts of Interest

Dr. Sanford states:

Neither I, nor any immediate family member has any financial relationship with, or interest in, any commercial interest connected with this presentation.

Disclosure of Off-Label Drug Use

The of material in this CME activity will not include discussion of unapproved or investigational uses of products or devices.

Odd names in tropical medicine

- orf: a.k.a. contagious pustular dermatitis, caused by a parapoxvirus, associated with exposure to goats and sheep, a zoonosis.

- craw-craw: itchy skin caused by microfilarial worm, onchocerciasis (river blindness), transmitted by black flies

- bung eye: caused by filarial nematode *Mansonella perstans*, transmitted by midges

Ebola

- Virus discovered in 1976 in Zaire (what is now the DRC [Democratic Republic of Congo])
- Disease originally called a hemorrhagic fever

Ebola River,
Democratic Republic of Congo

Family of viruses: Filoviridae

- Each member virus is a filovirus.

- **Genera:**
- Cuevavirus
- Ebolavirus
- Marburgvirus

- All genera within Filoviridae cause severe illness in humans and non-human primates.

Ebolavirus and Marburgvirus are

- WHO Risk Group 4 Pathogens (requiring Biosafety Level 4-equivalent containment)
- NIH/Nat'l Institute of Allergy and Infectious Diseases Category A Priority Pathogens
- CDC Category A Bioterrorism Agents

There are five identified subtypes of Ebolavirus.

- Four of the five have caused disease in humans:
  - Ebola-Zaire
  - Ebola-Sudan
  - Ebola-Ivory Coast
  - Ebola-Bundibugyo.

- The fifth, Ebola-Reston, has caused disease in nonhuman primates, but not in humans.

Transmission

- Ebola is most commonly transmitted by exposure to blood or secretions from an infected person. Close contact with an infected person is necessary for transmission.

Ebola is transmitted through direct contact of broken skin and mucous membranes with:

- blood or bodily fluids of an infected person or animal
  - e.g. urine, saliva, sweat, tears, feces, vomit, breast milk, semen
  - objects (e.g. needles, medical equipment, utensils, clothes, linen, gloves, gowns, masks) that have been contaminated with infected blood or bodily fluids, or infected animals

Ebola is not transmitted through

- air (exception: aerosolizing procedures)
- food (exception: handling bushmeat)
- water
- mosquitos or other insects

Transmission (cont.)

- Consuming “bushmeat” (e.g. monkey meat) and handling fruit bats also transmits Ebola.

Baboon.
Uganda.
Don’t eat him.

Corpses can transmit Ebola

- A study on deceased Ebola-infected macaques found that viable virus could be recovered for at least seven days after death.

- Prescott J, et al. Post-mortem stability of Ebola virus. *Emerging Infectious Diseases* DOI: 10.3201/eid2105.150041 (2015). http://wwwnc.cdc.gov/eid/article/21/5/15-0041_article

At highest risk

- Healthcare workers (HCWs). HCWs and family and friends are at the highest risk of becoming infected because they may come in contact with blood or body fluids of ill patients.

- As of late October, 2014: over 500 healthcare workers infected with Ebola in current epidemic, almost 300 deaths.

Transmission (cont.)

- Once someone recovers from Ebola, they can no longer spread the virus.
- Exception: EV has been found in semen for up to 3 months i.e. need to abstain from sex or use condoms for 3 months

Key time periods

- Mean incubation period: 11.4 days. Symptom onset after exposure is under 21 days in 95% of patients (which is the recommended follow-up period for contacts).
- Mean time from admission to hospital to death (in Africa): 4.2 days.

Symptoms

- Early: fever, sore throat, “pinkeye,” headache, muscle aches, rash, and weakness.
- Later findings may include bleeding from mucous membranes and IV puncture sites, pulmonary edema, and myocarditis.
- In terminally ill patients, rapid heart rate, low blood pressure, inability to produce urine, and coma are seen.

Diagnosis

- Early
  - PCR
  - ELISA
  - virus isolation
- Later
  - IgG, IgM antibodies. IgG antibody has been detected in a survivor as long as 11 years after initial infection.

New rapid antigen test

- The ReEBOV Antigen Rapid Test Kit (Corgenix, U.S.), the first rapid test for Ebola virus, is eligible for procurement after evaluation under WHO's Emergency Use Assessment and Listing procedure and has been authorized by U.S. FDA, under Emergency Use Authorization, for use in circumstances where a rapid test is determined to be more appropriate than the use of an authorized Ebola virus nucleic acid test. Results with a sensitivity of 92% and a specificity of 85% are available within 15 minutes compared to 12-24 hours for PCR. Rapid test results should be confirmed with PCR. Commercial availability is expected in March 2015.

Ebola 1976-2008: 22 outbreaks

- Relatively small: 1-425 cases/outbreak.
- DRC, Sudan, Gabon, Uganda, Ivory Coast.
- Average # of cases per outbreak: 104 cases.
- Fatality rate: 25-90%.
- Infections are acute. There is no carrier state.
- Usually rural.
  - 1995 Kitwit, Zaire, pop. 400,000, about 250 deaths
  - 2001: Gulu, Uganda, pop. 100,000, about 250 deaths

Reservoir

- Fruit bats, family Pteropodidae.

Zoonoses

- If a disease has no non-human reservoir, it can be eradicated.
  - E.g., smallpox—already eradicated.
  - Polio—theoretically eradicable.
- If a disease has a non-human reservoir, it cannot be eradicated.

December 2013

- Index case (patient zero): 2-year old in Guinea, with fever, vomiting, black stool.
- Route of transmission to index case: possibly that he played in a tree with bats.
- Initially thought to be Lassa fever.
- Not identified as Ebola until February 2014.

Timeline

- 23 March 2014: WHO's African Regional Office reports outbreak of Ebola virus disease in Guinea. 49 patients, 29 deaths.
- 29 March 2014: 1st case in Liberia reported.
- 25 May 2014: 1st case in Sierra Leone reported.
- June 2014: cases appear in cities.

23 June 2014:

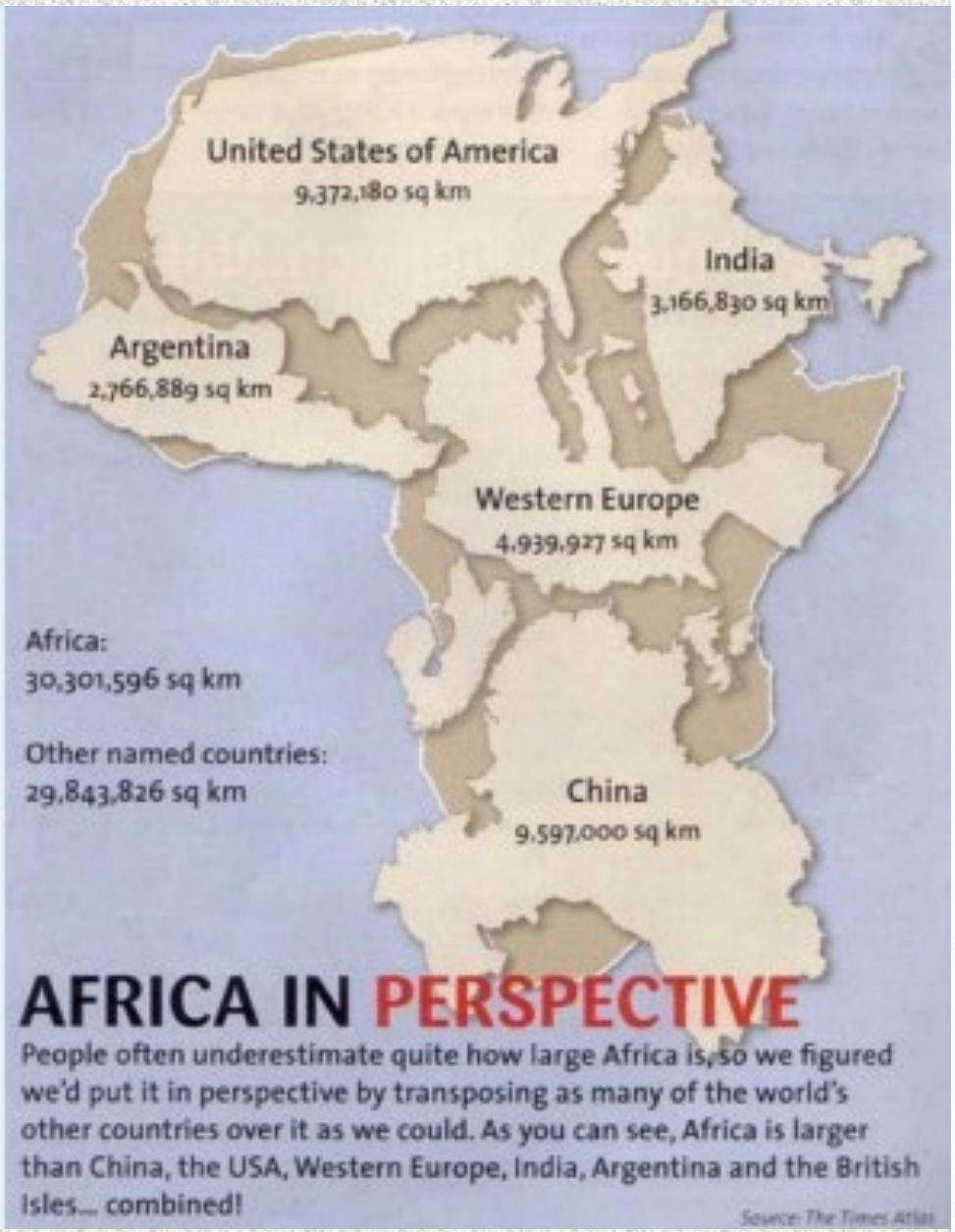
- Doctors Without Borders states epidemic is “out of control.”
- 528 cases, 337 deaths.

CDC Alert

- The Centers for Disease Control and Prevention (CDC) issued an Alert Level 3 for Sierra Leone, Guinea, and Liberia, encouraging travelers to defer nonessential travel to these nations.


MOROCCO
CANARY ISLANDS (SP.)
Laayoune (El Áaiún)
Western Sahara
ALGERIA
LIBYA
Banghāzī
MAURITANIA
Nouakchott
MALI
Tombouctou
NIGER
CHAD
CAPE VERDE
Praia
Dakar
SENEGAL
Banjul
THE GAMBIA
Bissau
GUINEA-BISSAU
Bamako
BURKINA FASO
Ouagadougou
Niamey
Kano
N'Djamena
GUINEA
Conakry
Freetown
SIERRA LEONE
BENIN
NIGERIA
Abuja
CÔTE D'IVOIRE
Yamoussoukro
GHANA
TOGO
Lomé
Ogbomoso
Ibadan
Lagos
CENTRAL


NO EBOLA
GUINEA
SIERRA LEONE
LIBERIA
NO EBOLA


United States of America
9,372,180 sq km
India
3,166,830 sq km
Argentina
2,766,889 sq km
Western Europe
4,939,927 sq km
Africa:
30,301,596 sq km
Other named countries:
29,843,826 sq km
China
9,597,000 sq km
AFRICA IN PERSPECTIVE
People often underestimate quite how large Africa is, so we figured we'd put it in perspective by transposing as many of the world's other countries over it as we could. As you can see, Africa is larger than China, the USA, Western Europe, India, Argentina and the British Isles... combined!
Source: The Times Atlas

27 July 2014

- Nigeria reports first case.
- Eventually Nigeria has 20 cases, 8 deaths.

2 August 2014

- First US case: 33 y.o. physician, flown to Emory University Hospital, Atlanta, GA.
- 5 August 2014: 2nd American with Ebola flown to Emory, Atlanta.
- Both recover after receiving Zmapp, an experimental treatment.

8 August, 2014

- 1,711 cases, 932 deaths.
- WHO declares "Public Health Emergency of International Concern" (PHEIC).
  - The Head of State should declare a national emergency;
  - Health Ministers and other health leaders should assume a prominent leadership role in coordinating and implementing emergency Ebola response measures,
  - States should activate their national disaster/emergency management mechanisms and establish an emergency operation centre,
  - States should ensure that there is a large-scale and sustained effort to fully engage the community – through local, religious and traditional leaders and healers
  - It is essential that a strong supply pipeline be established to ensure that sufficient medical commodities, especially personal protective equipment (PPE), are available to those who appropriately need them, including health care workers, laboratory technicians, cleaning staff, burial personnel and others that may come in contact with infected persons or contaminated materials.
  - States should ensure funerals and burials are conducted by well-trained personnel,
  - States with EVD transmission should consider postponing mass gatherings until EVD transmission is interrupted.

Name change

- Fewer than 5% of people with Ebola have abnormal bleeding in 2014, hence the name of the illness causes by Ebola has been changed from Ebola Hemorrhagic Fever to Ebola Virus Disease.

16 September 2014

- Team dispatched by Guinean government to educate regarding Ebola is attacked; eight medical workers and journalists are killed.

25 September 2014

- Ill man with fever returned from Liberia goes to ER in Dallas, TX. He is sent home with antibiotics.
- 28 September 2014: he returns to the same hospital via ambulance, is admitted.

Forecasting: September 2014

- Both the CDC and WHO predict that without scale-up in interventions the current number of cases can double every 20 days. This is a catastrophic rate of spread.

- On Sept. 23, 2014, the CDC forecast that Ebola could infect 1.4 million people by the end of January, 2015.

6 October 2014

- First documented case of person-to-person transmission of Ebola outside Africa, in Spain.
- 10 October 2014: nurse who worked with ill patient in Dallas falls ill, is quarantined.
- 23 October, 2014: first documented case of Ebola in Mali.

November 2014

- CDC issued a complex and conditional matrix to guide monitoring and movement of persons with potential Ebola exposure. For asymptomatic individuals public health actions are dependent on 4 separate multi-criteria risk classifications.

17 November 2014

- Washington State Dept. of Health announced that eight hospitals in Washington have been designated as those that will provide care for patients with suspected or confirmed Ebola. In the Seattle area, these are UW Medical Center, Harborview Medical Center, and Valley Medical Center.

Investigational therapies

- ipZMapp is a combination of 3 different monoclonal antibodies that bind to the protein of the Ebola.
- Brincidofovir: a lipid-conjugated version of cidofovir—an oral nucleotide analog with broad-spectrum in vitro antiviral activity.
- Convalescent whole blood and plasma transfusions from patients who have recovered from Ebola.
- The efficacy of these treatments is unknown.

Vaccines

- Per the National Institutes of Health, the results of a Phase 1 trial of an EVD vaccine, cAd3-ZEBOV, have shown that the vaccine was well-tolerated and produced immune system responses in all 20 adult participants.

- African countries that will host phase 2 clinical trials of one of the leading candidate Ebola vaccines, ChAd3, have asked GSK, the manufacturer, for more information, which means the trials most likely will start in February 2015, the World Health Organization (WHO) announced [18 Dec. 2014].

- Some patients with exposure referred to Emory in Atlanta for experimental VSV (vesicular stomatitis vaccine). The doc at Emory who oversees that is Dr. Mark Mulligan.

CDC Guidance

- Guidance on Personal Protective Equipment to Be Used by Healthcare Workers During Management of Patients with Ebola Virus Disease in U.S. Hospitals, Including Procedures for Putting On (Donning) and Removing (Doffing)
- http://www.cdc.gov/vhf/ebola/healthcare-us/ppe/guidance.html

Northgate: Protocol and PPE

- “The Tub”
- Pod 2
- Adjacent to bin with white coats
- Protocol for MAs, providers, etc.

If we see a patient with symptoms and potential exposure history

- Isolate patient.
- Notify Public Health—Seattle & King County
  - Communicable Disease Control
  - 206 296-4774
- Either we, or PH-S&KC, notifies CDC, for guidance regarding testing.
  - (770) 488-7100.

IMSuRT-West

- International Medical-Surgical Response Team.
- US federal team, based at Harborview Medical Center.
- One of 3 IMSuRTs in the US.
- A field surgical hospital, with surgeons and non-surgeon physicians, PAs, NPs, nursing staff, security, communications, logistics, etc.

7 deployments over the past decade

- 1) Hurricane Katrina: August 31-September 10, 2005. Operations at Louis Armstrong New Orleans International Airport.
- 2) Hurricane Katrina: February 21-28, 2006: Operations in tents adjacent to Charity Hospital, New Orleans.
- 3) Hurricane Ernesto, August 29-September 2, 2006. Based in Atlanta.
- 4) San Diego County wildfires, October 24-November 2, 2007. Based at Native American clinic near Temecula, California.
- 5) Presidential Inauguration, Washington DC, January 18-22, 2009. IMSuRT-West.
- 6) Haiti, post-earthquake, January-February, 2010. Chief Medical Officer at GHESKIO Field Hospital, Port-au-Prince, Haiti.
- 7) CDC Headquarters, Atlanta, GA; Dec. 1-14, 2014. Emergency Operations Center, Domestic Clinical Inquiries Unit, 2014 Ebola Response.


SANFORD

New Orleans Int'l Airport, 2005

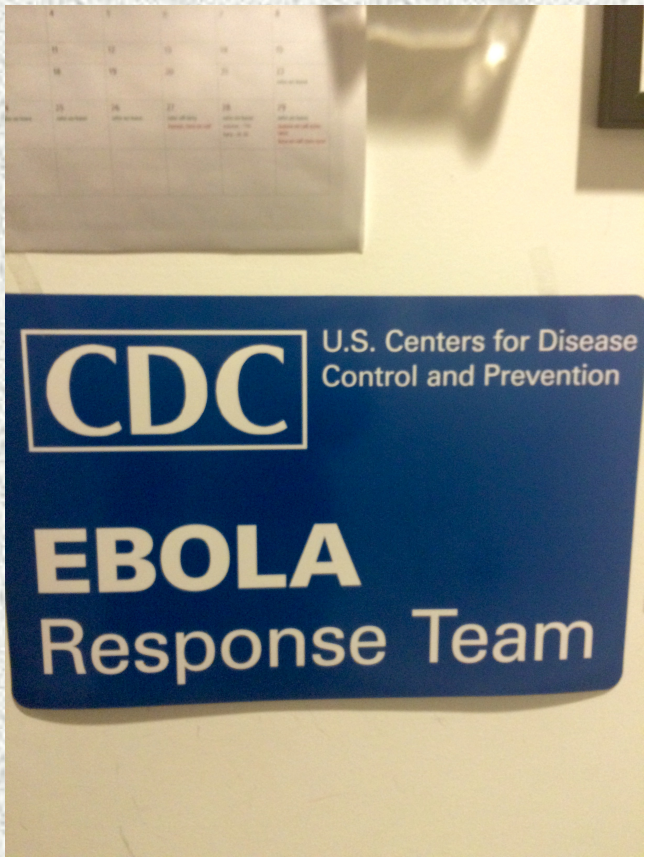

New Orleans
via
LEFT LANE
Airline Highway

Port-au-Prince, Haiti, 2010

IMSuRT-West deployment

- Domestic Clinical Inquiries Unit,
  Epidemiology Team,
  Epidemiology-Laboratory Task Force Section,
  Incident Management System for
  2014 Ebola Response. CDC.

- Mission: phone support:
  answering calls from
  physicians and health
  departments, regarding
  Ebola testing, isolation of
  patients, etc.



NDMS (National Disaster Medical System) personnel

IMSuRT-West:

- Frances Lawson, MD: 2nd half of Nov., 2014
- Christopher Sanford, MD, Dec. 1-14, 2014

DMAT WA-1:

- Stephen Morris, MD: late November, 2014


CDC
U. S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
CENTERS FOR DISEASE CONTROL
AND PREVENTION
ARLEN SPECTER
HEADQUARTERS AND
EMERGENCY OPERATIONS CENTER


CDC Roybal Campus,
Atlanta, GA


CDC
EMERGENCY OPERATIONS
CENTER
AUTOMATIC
CAUTION
DOOR

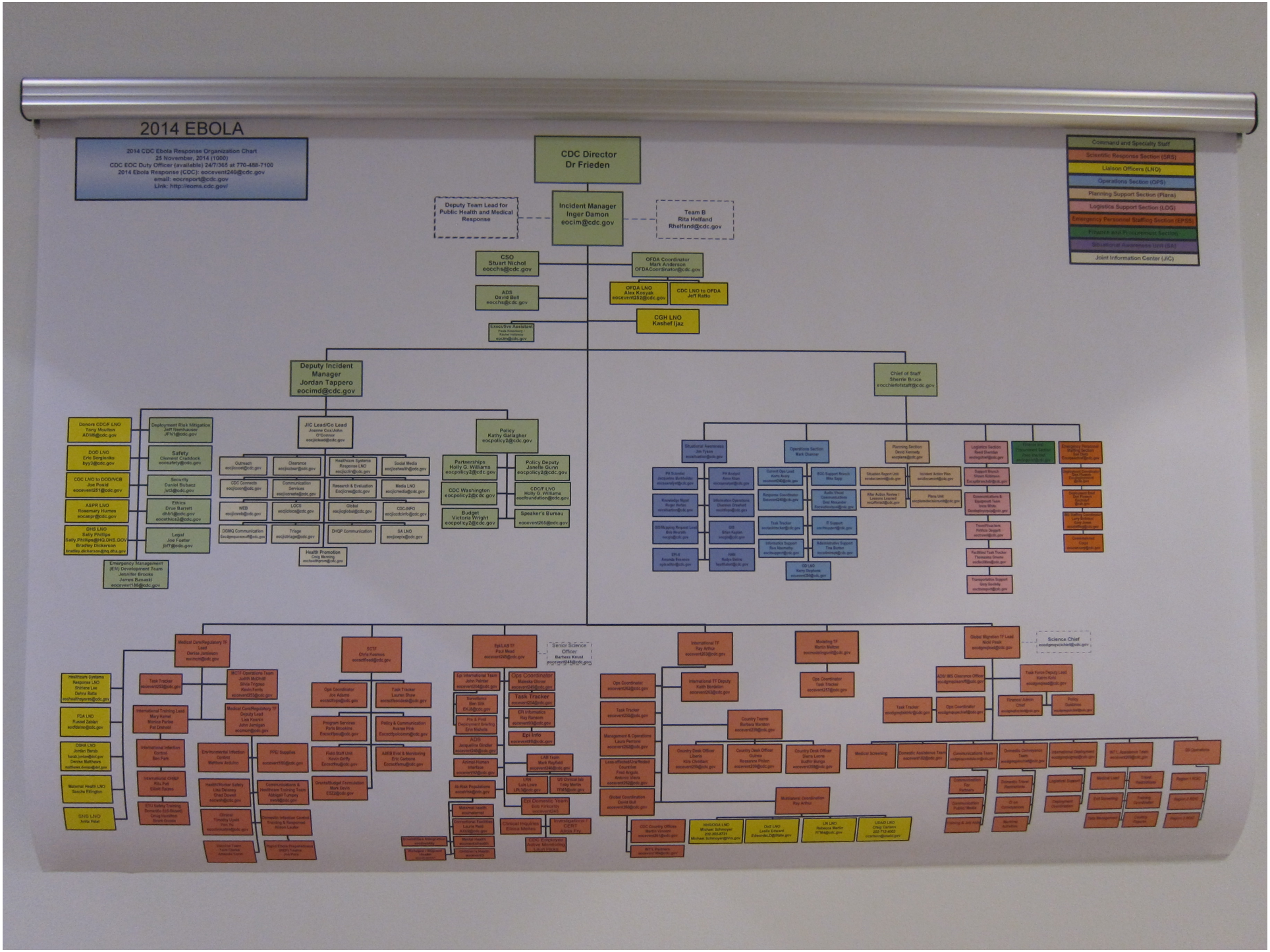
Main Control Room
Arlen Specter Headquarters and Emergency Operations Center
CDC Roybal Campus, Atlanta, GA


EXIT
Admin Help Desk
553-7550
2014 Ebola Response


MetLife
Polio OPS
553-7605
2014 Ebola Response
Epidemiology
Polio Policy
553-7584
DELL

The CDC response

- Over 750 people working fulltime on Ebola: about 170 in Africa, and over 500 in Atlanta, others at quarantine stations at airports in US.


2014 EBOLA
2014 CDC Ebola Response Organization Chart
25 November, 2014 (1000)
CDC EOC Duty Officer (available) 24/7/365 at 770-488-7100
2014 Ebola Response (CDC): eocevent240@cdc.gov
email: eocreport@cdc.gov
Link: http://eoms.cdc.gov/
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Dr Frieden
Deputy Team Lead for Public Health and Medical Response
Incident Manager
Inger Damon
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Team B
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Command and Specialty Staff
Scientific Response Section (SRS)
Liaison Officers (LNO)
Operations Section (OPS)
Planning Support Section (Plans)
Logistics Support Section (LOG)
Emergency Personnel Staffing Section (EPSS)
Finance and Procurement Section
Situational Awareness Unit (SA)
Joint Information Center (JIC)

Daily update:

- Every weekday there was a detailed approx. 100 slide PowerPoint presentation with updates on CDC activities broadcast to all CDC employees working on Ebola.

Signs on bulletin board in our conference room.

- Don’t miss the case.
- Overcommunicate.

Procedure:

- We would receive a call. If traveler had both symptoms potentially consistent with Ebola, and potential exposure, we'd recommend testing for Ebola, and would generate a PUI (person under investigation) number, and a risk categorization.

The CDC has defined two levels of monitoring: active, and direct active.

- Active monitoring, supervised by state or local public health authorities, means that the at-risk individual reports measured temperatures and symptoms consistent with Ebola on a daily basis to the public health authorities.
- Direct active monitoring entails a public health authority directly observing the at-risk person at least once per day to review symptoms status and monitor temperature. Public health authorities should also discuss work, travel, take public conveyances, and to take place in congregate activities, e.g., to attend religious services.

For example

- 32 y.o. male. Now at Massachusetts General ER.
- Was in Liberia.
- 102° fever.
- Didn't have any significant exposures while in Liberia; not a HCW; didn't attend funerals.
- Didn't finish course of doxy for malaria prophy.
- Malaria test positive.

- Issued a PUI (person under investigation) #
- Risk categorization: "Low but not zero risk."
- Initial PCR for Ebola negative.
- But—was done before 72 hours of symptoms.

- Encourage workup for other causes of fever, including influenza.
- Protocol: check temperature every 12 hours x 21 days.
- If he defervesces on antimalarial, probably won't repeat Ebola PCR at 72 hours.

70 y.o. man in Florida.

- Was in Mali, returned to Atlanta on 11/24. Notes three days of inc. temp and dry cough. Has history of bronchitis; feels this is his usual attack of bronchitis. Called his pulmonologist, got rx for Levaquin and clinda. Advised to go to hospital; pt refused, says he'll go in the morning. He prefers Baptist Hosp. as it's closer to his house; told Jackson or U. Miami better (bigger).

CDC employees

- Three CDC employees in Sierra Leone in vehicle for hours with symptomatic driver later found to have Ebola, positive test.
- Follow temperature.
- No PUI issued unless they become symptomatic.
- Involve occupational health.

39-year-old CDC employee

- Returned to Thailand from Guinea, has now developed URI symptoms, plus nausea and vomiting.
- Not a medical worker; no known exposures
- Thai officials decided to begin contact tracing although the CDC did not recommend that they do so.

Seattle, WA

- 53-year-old man returned from Mali.
- Returned to Seattle November 23.
- No known exposures there—didn't go to any funerals, wasn't around sick people, etc. Developed a sore throat then fever to 100.6° and upper respiratory symptoms. His two-year-old has similar URI sx.
- He's in the ER at Harborview.

Americans are bad at geography.

- We informed callers that Guinea-Bissau, Republic of Equatorial Guinea, Papua New Guinea, Guyana, and French Guyana are not Guinea.

Challenges

- The final decision to test for Ebola was not made by the CDC, but by local health personnel.
- Local health personnel would not always tell us when they tested.
- Local health personnel would sometimes test to allay staff anxiety.
- Media would appear and this would stress local health personnel.

Challenges (cont.)

- Some medical personnel elected to test outside the CDC network of labs
  - Laboratory Regional Network (LRN); 55 labs in 43 states in the US (as of 31 January 2015).
- E.g., the BioFire test for Ebola. Approved by the FDA on an emergent basis; it is unlike the usual PCR Ebola test done by the CDC.

Challenges (cont.)

- Intense media coverage is a kook magnet.
- Scattered reports in ERs of people claiming to have been in West Africa when they weren't.
- Within CDC, Division of Global Migration and Quarantine can liaison with the Dept. of Homeland Security, and access flight manifests.

Challenges (cont.)

- Lack of data regarding duration of transmissibility in semen, breast milk.
- PCR has been positive in seminal fluid for up to three months after the resolution of clinical symptoms, but positive signal in PCR doesn't necessarily mean infectivity. There's a suggested recommendation that men abstain from sex or use condoms for three months after the resolution of symptoms; recommendations for women and sex, or nursing, have not yet been established.

MMWR (Morbidity and Mortality Weekly Report), released Dec. 5, 2014

- Clinical Inquiries Regarding Ebola Virus Disease Received by CDC—United States, July 9-Nov. 15, 2014. During that interval the CDC received queries on 650 persons thought to be at potential risk for Ebola. Of those, 61 (9%) were tested; four of the tests were positive. Interestingly, 490 of the potential patients with Ebola had neither been to a country with known Ebola transmission nor had contact with someone with Ebola.

- The CDC Emergency Operations Center continues to provide 24/7 consulting services for U.S. health care providers seeking assistance in evaluating patients who potentially have Ebola.
- Phone number: (770) 488-7100.

Diagnosis

- Negative PCR test result for Ebola, before 72 hours of symptoms have elapsed, may represent a false negative.

- A negative test 72 hours or later after symptom onset is reliable (as is a positive test obtained at any time).

A few caveats:

- Not symptomatic = not contagious.
- In cases of Ebola, symptoms worsen each day.
- GI sx usually occur around d. 3-6, post onset of sx.

Cases in the US:

- Total: 10. (6 evacuated to the US from other countries; 4 first diagnosed in the US; 2 contracted in the US; 2 deaths; active cases: 0).

Fatality rate in the US

- 20%
- This suggests that aggressive treatment, including IV fluids, markedly decreases the mortality rate.

Risk factors for death in patients with Ebola

- Increased age, bleeding, additional symptoms suggesting organ dysfunction, and fever on admission. The fatality rate for patients under age 21 is 57%; for those aged 45 and older: 94%. The higher the temperature at admission to hospital, the more likely patients are to die from Ebola.

mid-January 2015

- The tide appears to be turning. Per WHO: Guinea reported its lowest weekly total of new confirmed Ebola virus disease (EVD) cases since the week ending 17 Aug 2014. Case numbers remain low in Liberia, with no confirmed cases nationally for the final 2 days of the week ending 11 Jan 2015, and the lowest weekly total of confirmed cases since the 1st week of June 2014. Sierra Leone has now reported a decline in case incidence for the 2nd week running and recorded its lowest weekly total of new confirmed cases since the week ending 31 Aug 2014.

28 February, 2015

- Cases: 23,948 (total suspected, probable, and confirmed).
- 14,347 (confirmed)
- Deaths: 9,729.
- Future epidemic curve: unknown.

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- Prescott J, et al. Post-mortem stability of Ebola virus. *Emerging Infectious Diseases* DOI: 10.3201/eid2105.150041 (2015). http://wwwnc.cdc.gov/eid/article/21/5/15-0041_article
- WHO timeline:
  - http://www.who.int/features/ebola/storymap/en/

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