



Preparing for a Crisis:
*Lessons Learned at Emory Before,
During, and After Ebola*

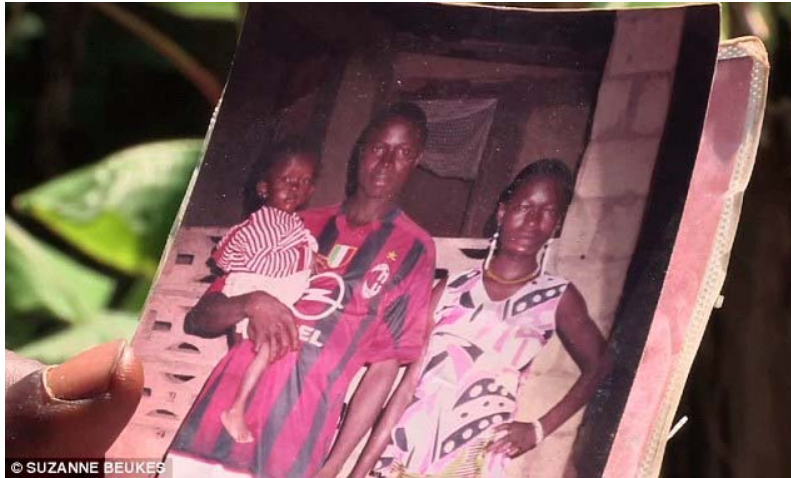
Jay B. Varkey, MD

On behalf of the
 **EMORY**
MEDICINE | Serious Communicable
Diseases Unit

Chapter 1
BEFORE EBOLA



The Story of Emile Meliandou, Guinea, December 2013



Photograph by Suzanne Beukes, UNICEF




The Story of Emile Meliandou, Guinea, December 2013




AM Saéz et al, EMBO Mole Med 2015


 The Story of Emile
Meliandou, Guinea, December 2013




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The Story of Emile Meliandou, Guinea, December 2013



Photograph by Suzanne Beukes, UNICEF



Spread of a “Cholera-Like Illness” Meliandou → Conakry, 12/2013 – 3/2014

Meliandou Village, Guéckédou

9 Deaths from Dec. 2, 2013, to Feb. 8, 2014
2 Deaths on March 26, 2014

First recorded cases of the outbreak

(S1) Child, 2 yr of age
Fever, black stool, vomiting
Onset Dec. 2, 2013; died Dec. 6, 2013

↓

(S2) Sister of S1, 3 yr of age
Fever, black diarrhea, vomiting
Onset Dec. 25, 2013; died Dec. 29, 2013

(S3) Mother of S1 and S2
Bleeding
Died Dec. 13, 2013

(S4) Grandmother of S1 and S2
Fever, diarrhea, vomiting
Died Jan. 1, 2014

(S5) Nurse
Fever, diarrhea, vomiting
Onset Jan. 29, 2014; died Feb. 2, 2014

(S6) Village midwife
Fever
Hospitalized in **Guéckédou** Jan. 25, 2014;
died Feb. 2, 2014

Dawa Village, Guéckédou

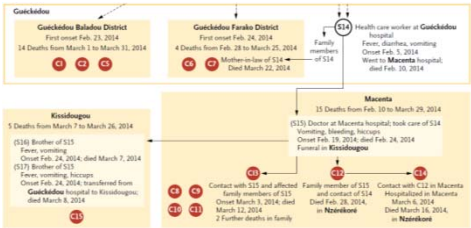
8 Deaths from Jan. 26 to March 27, 2014

(S7) Sister of S4, attended funeral of S4
Fever, diarrhea, vomiting, hemorrhage
Onset Jan. 20, 2014; died Jan. 26, 2014

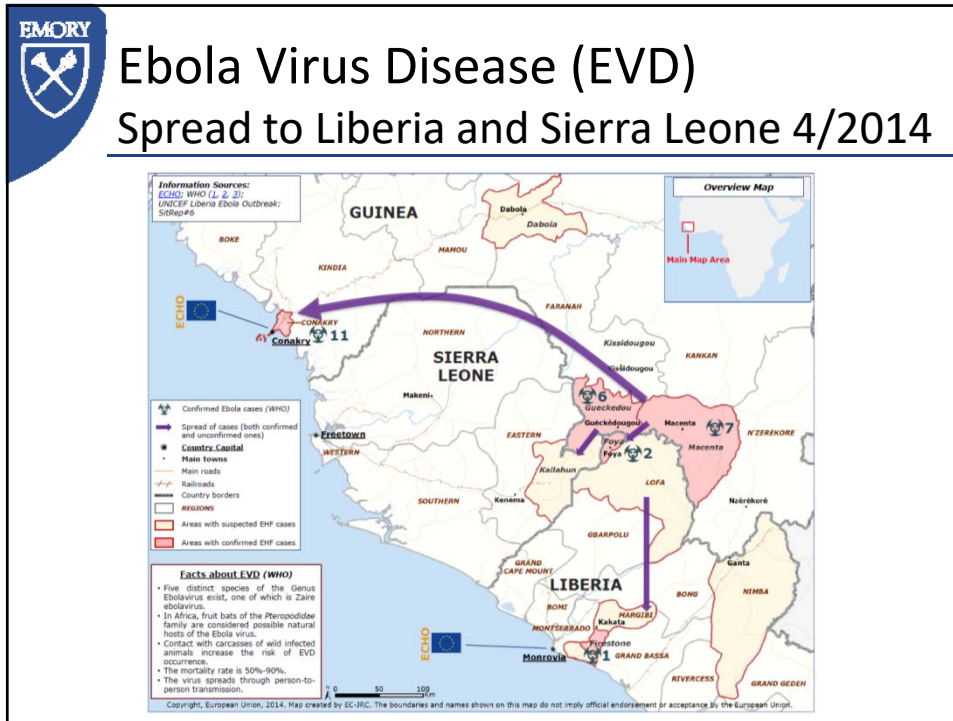
(S8) Attended funeral of S4
Fever, bleeding
Onset Jan. 25, 2014; died Jan. 30, 2014

↓

(S9–S12)
Onset Feb. 2–16, 2014; died Feb. 11–
March 5, 2014



S Baize, N Engl J Med 2014





ELWA ETU

Monrovia, Liberia 6/2014 – 7/2014



Photograph by Bethany Fankhauser, SIM



ELWA ETU

Monrovia, Liberia July 2014

- 40 patients with EVD treated
 - **39 of 40 died**



- July 22-23: 2 American humanitarians working in the ELWA ETC develop a fever....
 - Initially treated for malaria
 - **Laboratory testing confirmed Ebola Virus Disease**



Ebola Virus Disease and Emory

July 30, 2014

- Emory University Hospital was asked to receive the first patients with confirmed Ebola virus disease to be treated in the United States
- 2 American humanitarians had become infected while working in an ETU in Monrovia, Liberia
 - Patient 1: 33 yo male physician
 - Patient 2: 59 yo female medical missionary
- **Expected arrival time unclear but Emory was asked to be ready to receive the 1st patient within 72 hours.**

Chapter 2

DURING EBOLA



Woodruff Circle, Emory University July 30, 2014



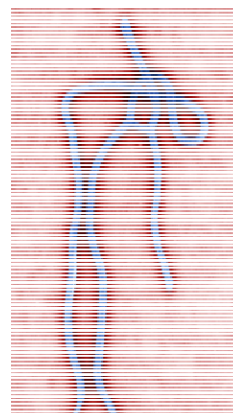
Woodruff Circle, Emory University August 2, 2014





Background: Ebola Virus

- Family Filoviridae
 - Two genera: *marburgvirus* and *ebolavirus*
- Enveloped RNA virus
- Five subtypes of Ebola virus
 - **Ebola (Zaire; EBOV)**
 - Sudan (SUDV)
 - Tai Forest (TAFV)
 - Bundibugyo (BDBV)
 - Reston (RESTV)
- No vaccines/treatments approved for humans
- Case-fatality rates of up to 50-90%

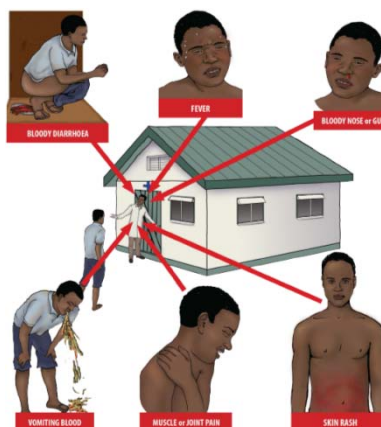


Cynthia Goldsmith/CDC



Background: Clinical Characteristics of EVD

- Acute infection starts as a non-specific febrile illness
 - Fever, severe headache, myalgias, malaise → **GI symptoms (SEVERE diarrhea and vomiting)**
 - May appear 2-21 days after exposure (8-10 days most common)
- Small vessel permeability
 - Dehydration AND edema
- Most death occur during the 2nd week of illness
- **Poor prognosis associated with**
 - **shock, encephalopathy, extensive hemorrhage (~30%), multi-organ system failure**

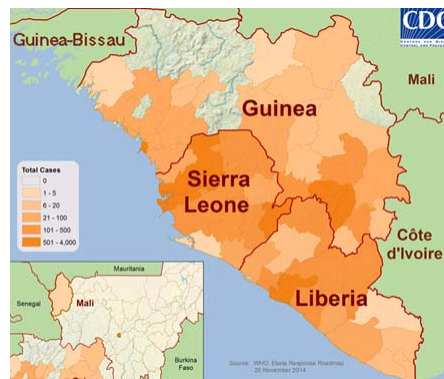


Developed by CDC



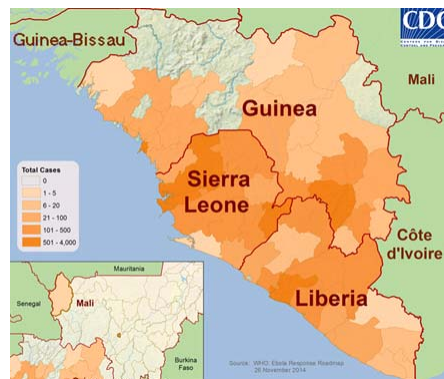
West Africa EVD Outbreak December 2013 – August 2014

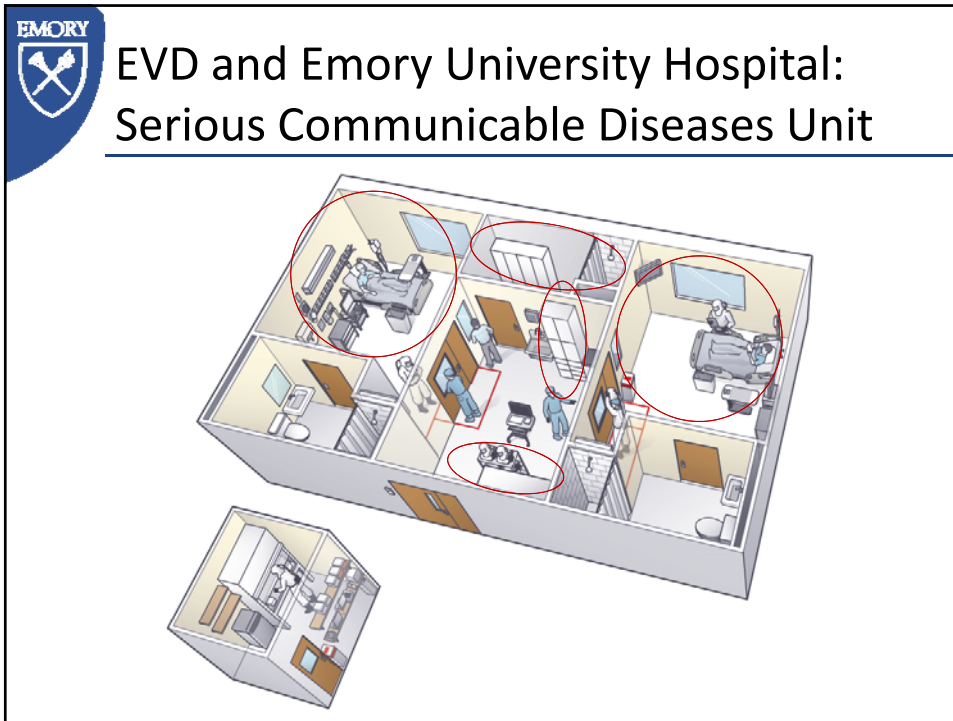
- **3,052 cases and 1,546 deaths** (as of 8/29/2014)
- Guinea
 - 648 cases
 - 158 deaths
- Sierra Leone
 - 1,026 cases
 - 331 deaths
- Liberia
 - 1,378 cases
 - 866 deaths
- Nigeria: 19 cases and 7 deaths



Ebola Virus Disease (EVD) December 2013 – June 9, 2016

- **28,616 cases and 11,310 deaths**
- Guinea
 - 3,811 cases
 - 2,543 deaths
- Sierra Leone
 - 14,124 cases
 - 3,956 deaths
- Liberia
 - 10,675 cases
 - 4,809 deaths
- **Sporadic cases since Fall 2015: Role of EVD Survivors?**
- Italy, Mali, Nigeria, Senegal, Spain, United Kingdom & USA: 36 cases and 15 deaths







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The Emory SCDU Team

- 21 ICU Nurses
- 5 ID Physicians



A group of seven healthcare professionals, including nurses and physicians, standing together. The nurses are wearing blue scrubs, and the physicians are wearing white coats. They are all smiling and looking towards the camera.



Clinical Care of EVD

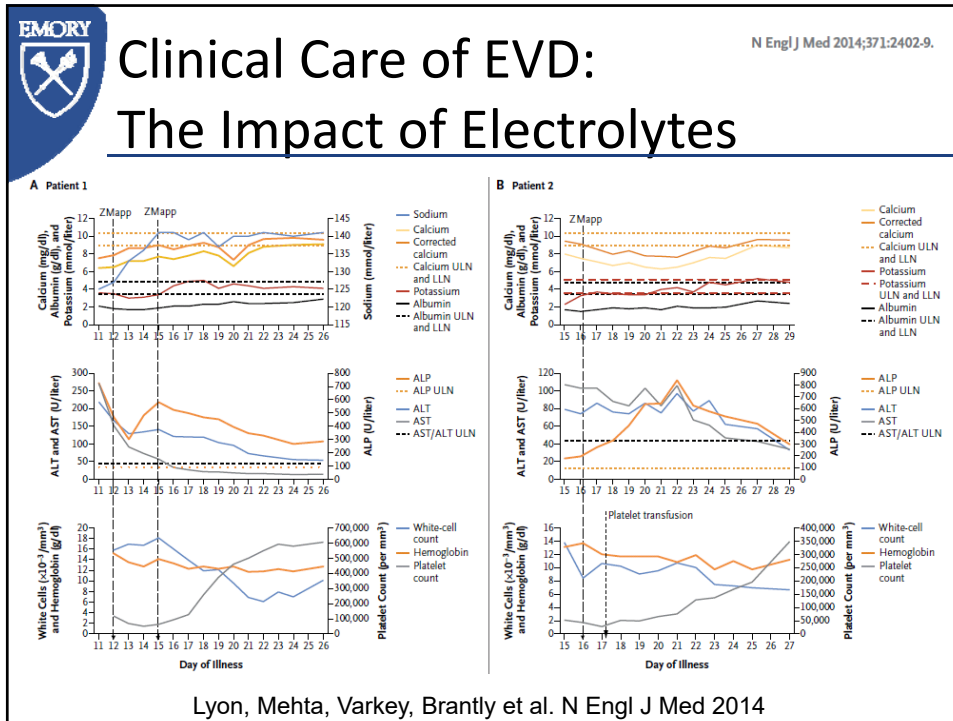
- **No Proven Therapeutics!**
 - Unclear availability of experimental agents
 - Limited safety or efficacy data in humans
 - BUT, Emory received SIGNIFICANT support and advice from CDC, FDA, and medical and scientific colleagues throughout the world

- **Treatment is “Supportive Care”**
 - CDC Definition: “Providing IVF, balancing electrolytes, maintaining oxygen and blood pressure and treating other infections”
 - A Practical Definition: *“Keeping the patient alive long enough for them to develop the antibodies necessary to resolve Ebola viremia”*



Clinical Care of EVD: The Impact of Electrolytes

- Our patients had MARKED electrolyte abnormalities and nutritional deficiencies
 - Hypokalemia, hypocalcemia and hyponatremia
 - Required both intravenous and oral replacement
 - Required **significant** potassium replacement
 - Nutritional supplements (oral and parenteral)
 - **Laboratory testing for chemistries was critical to provide supportive care**



EMORY Ebola Virus Disease: Staff & Environmental Safety



- Personal Protective Equipment
 - Requires **Training & Competency**
- High viral load in EVD patients
 - **10⁸ virus particles/ml of fluid**
- Low infectious dose
 - **0.001 ml of blood**
- Frequent cleaning and disinfection **CRITICAL** for staff and environmental safety
- Environmental samples?
 - **NEGATIVE** by RT-PCR

Jelden et al Am J Infect Control 2015 and Varkey et al, SHEA 2015 Abstract 7227

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Ebola Virus Disease: Staff & Environmental Safety



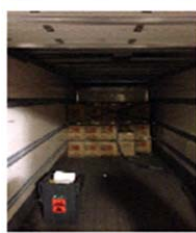
- All personnel required to enter twice daily temperature and symptom review into an online registry





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Environmental Safety: Waste Management

- Patient 1: Admitted for 19 days
- Patient 2: Admitted for 14 days
- Autoclaved **350** bags regulated medical waste
 - Total weight: 3,058 lbs**
- Packaged **218** boxes regulated medical waste
- 6 shipments of regulated medical waste were transported for incineration








“Emory EVD Patients #1 and #2”

	Symptom Onset	Admitted	Discharged
Patient #1	7/23/2014	8/2/2014	8/21/2014
Patient #2	7/22/2014	8/5/2014	8/19/2014



“Emory EVD Patient #3”

CNN
News Video TV Opinions More...

U.S.
World
Politics
Tech
Health
Entertainment
Living
Travel
Money

Name: Unknown


Age: Unknown

Organization: The World Health Organization has said a doctor working for the agency tested positive for Ebola on September 8.

Where he was infected: Sierra Leone

Where he is being treated: The man arrived at Emory University Hospital in Atlanta on September 9.


Current status: "We are still treating the patient with Ebola virus disease at Emory University Hospital, but we do not have a condition update," Emory representatives told CNN Monday. The HIPAA Privacy Rule prevents them from sharing any patient information without his permission.




Hospital Course

Experimental Treatments
 TKM-100802: Day 3-8
 Plasma: Day 8, 9, 11, 12, 14, 15

- Day 6: Severe gastroenteritis and hepatitis
- Day 9: Acute kidney injury and respiratory distress
 - Intubation and Mechanical ventilation
- Day 11: Cardiac arrhythmias and worsening acidosis
 - Continuous Renal Replacement Therapy
- Day 21: Extubated → Delirium
- Day 29: Improving mental status
 - Ambulates with assistance
- Day 35: Dialysis held
 - Blood tests **negative** for EBOV by RT-PCR
- Day 40: **Discharged home**
 - 30 lb weight loss, easy fatigability, proximal muscle weakness + unsteady gait → difficulty ambulating, word-finding difficulties



Kraft Clin Infect Dis 2015 and Connor J Am Soc Nephrol 2015



Follow-Up Visit: 11/14/14

Interval History:

- Ambulating up to 2 miles daily
- Occasional word-finding difficulty—markedly improved
- Gaining weight

- Hair loss, coming out in clumps
- Markedly decreased hearing (L > R)
- Low back pain (worse than baseline)
- Enthesitis: Bilateral Achilles tendons
- Occasional blurry vision bilaterally
 - transient, burning, lasts for few seconds, every few days
 - referred to Emory Eye Center for further evaluation

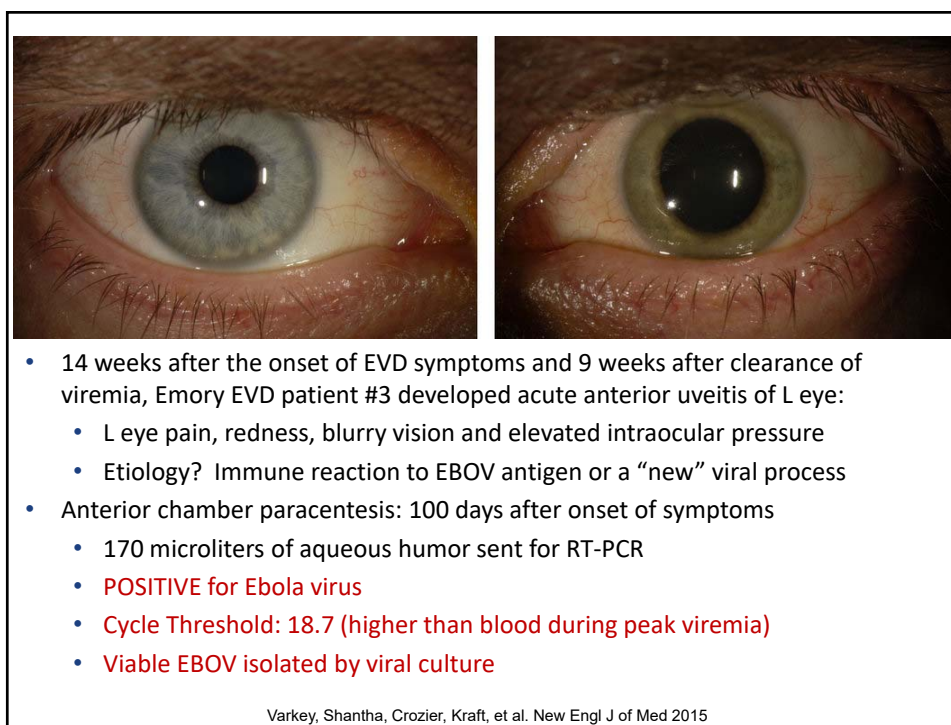
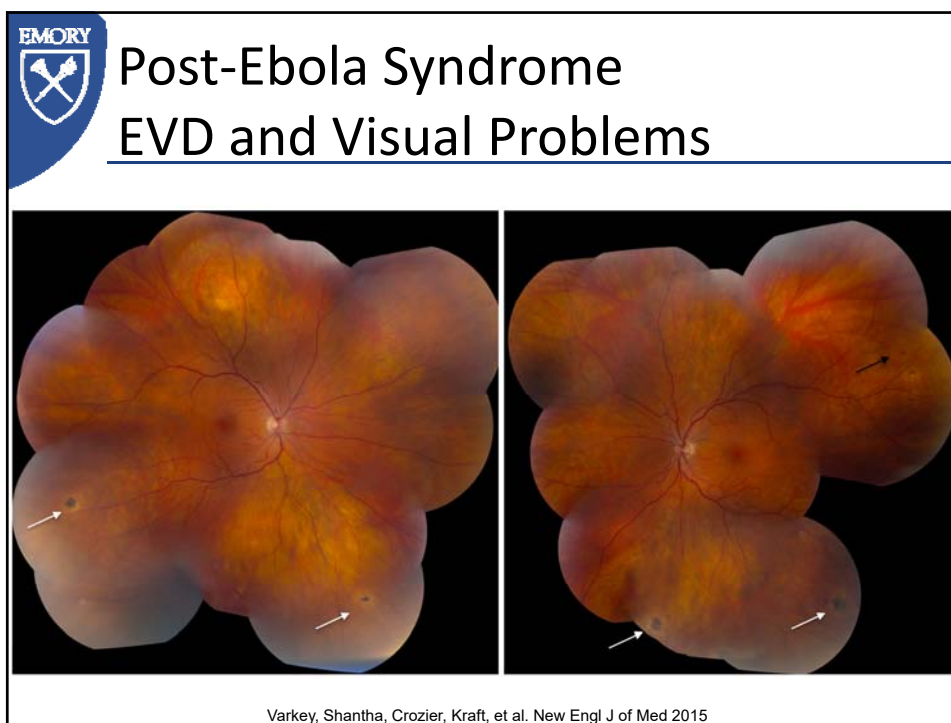
Chapter 3 AFTER EBOLA

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Post-Ebola Syndrome

- Arthralgias and myalgias
- Abdominal Pain
- Extreme fatigue
- Anorexia
- Amenorrhea
- Parotitis
- Unilateral orchitis
- Hair loss
- Hearing loss
- **Visual problems**





Post-Ebola Syndrome EVD and Visual Problems

- Acute Infection
 - Bilateral conjunctivitis: Highly predictive
 - Subconjunctival hemorrhage (Rare: Blurry vision and blindness)

- Late complications may develop during convalescence
 - Incidence is unclear
 - Pathogenesis poorly understood
 - Immunologic reaction to persistent viral antigen OR
 - Direct lytic effect of active replicating virus?
 - Viable virus can persist in the immune privileged tissue of survivors
 - Semen
 - Aqueous humor
 - *Other ocular tissue?*
 - *Other CNS tissue?*
 - *Cartilage?*

Varkey, Shantha, Crozier, Kraft, et al. New Engl J of Med 2015



Emory EVD Patient #3: Surviving Ebola—Twice....

- Decreased visual acuity
- 20/15 → 20/60 → 20/200 → Hand motions

- Ocular hypertension → Severe hypotony


- Treatments:
 - Topical steroids
 - Topical atropine
 - Favipiravir (obtained by E-IND)
 - Periocular triamcinolone

- Current status?
 - *20/15 in 2015!*
 - Returned to Sierra Leone—established eye clinic for survivors



Epilogue
PREPARING FOR A CRISIS
Lessons Learned at Emory

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**Preparing for a Crisis:
Lessons Learned BEFORE Ebola**

- The Team: Build, Develop and Maintain
 - Nursing, Physicians, Laboratory, EVS
 - Administrative Support: Unit-Based and C-suite
- The Unit
- Training: Regular and Just-In-Time
- Coordination with Public Health

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Preparing for a Crisis: Lessons Learned DURING Ebola

- **Clinical Operations**
 - Maintain a Culture of Safety
 - Daily Huddle
- **Communications**
 - Internal
 - External

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Communication

- Primary goal: Educate and allay fears
- Audience: Internal AND external
- Key messages:
 - **We have expertise in serious infectious diseases**
 - **We are trained and prepared for these patients**
 - **We will protect our patients, our staff and our communities**
- Key principle: Act in the best interests of our patients
 - Maintain confidentiality and respect



Internal Communication

- Understanding the concerns of our hospital staff was critical
 - Twice daily town hall meetings
 - Email updates and FAQ website



- Maintaining honesty and confidence with our other patients
 - Letter given to all patients from CNO and CMO
 - Key leaders rounded on the wards to answer questions



External Communication

I'm the head nurse at Emory. This is why we wanted to bring the Ebola patients to the U.S.

These patients will benefit – not threaten – the country.



By Susan M. Grant August 6

Susan Mitchell Grant, RN, is chief nurse for Emory Healthcare.



Preparing for a Crisis: Lessons Learned AFTER Ebola

Favipiravir and Ribavirin Treatment of Epidemiologically Linked Cases of Lassa Fever

Vanessa N. Raabe,^{1,a} Gerrit Kann,^{2,a} Bruce S. Ribner,¹ Andres Morales,³
Jay B. Varkey,¹ Aneesh K. Mehta,¹ G. Marshall Lyon,¹ Sharon Vanairsdale,⁴
Kelly Faber,⁵ Stephan Becker,⁶ Markus Eickmann,⁶ Thomas Strecker,⁶
Shelley Brown,⁷ Ketan Patel,⁷ Philipp De Leuw,² Gundolf Schuettfort,²
Christoph Stephan,² Holger Rabenau,⁸ John D. Klona,⁷ Pierre E. Rollin,⁷
Anita McElroy,⁷ Ute Ströher,⁷ Stuart Nichol,⁷ Colleen S. Kraft,^{1,9,a} and Timo Wolf,^{2,a}
for the Emory Serious Communicable Diseases Unit^b

- SCU activation March 2016
 - Successful care of a patient with Lassa Fever



EMORY
MEDICINE

Serious Communicable
Diseases Unit


- | | | | |
|---|--|---|--|
| <ul style="list-style-type: none"> • Emory Nursing • Toni Ash • Chris Barnes • Jason Calhoun • Lauren Chapman • Tracey Daye • Haley Durr • Shunasee Evans • Janice Gentry • Jan Ginnane • Susan Grant • Chris Haynes • Carolyn Hill • Dustin Hillis • Crystal Johnson • Jessica Loomis • Josia Mamora | <ul style="list-style-type: none"> • Laura Mitchell • Susan Mitchell • Jill Morgan • Nancy Osakwe • Jacqueline Owen • Sarah Piazza • Kristina Shirley • Jodi Siddens • Carrie Silas • Jason Slabach • Elaina Tirador • Donnette Todd • Sharon Vanairsdale • Pharmacy • Amir Emamifar • Susan Rogers | <ul style="list-style-type: none"> • Health & Safety • George Golston • Sean Kaufman • Patricia Olinger • Sean Olinger • Kalpana Rengarajan • Scott Thomaston • Infection Control • Connie Bryant • Betsy Hackman • Regina Howard • Marolyn Jones • Environmental Services • Jeff Broughton • Brian Frisle • Robert Jackson • Jerry Lewis | <ul style="list-style-type: none"> • Emory Medical Labs • Nicole Brammer • Juli Buchanan • Eileen Burd, PhD • John Cardella • Brenda Eaves • Crystal Evans • Charles Hill, MD • Krista Hostetler • Karen Jenkins • Maureen Lindsey • Jordan Magee • Randall Powers • Emily Ryan, PhD • Occupational Health • Emily Beck • Paula Desroches |
|---|--|---|--|

EMORY MEDICINE | Serious Communicable Diseases Unit

- **Administration**
 - Robert Bachman
 - Bill Bornstein
 - John Fox
 - Bryce Gartland
 - Anne Adams
 - Dee Cantrell
 - Mary Beth Allen
 - Nancye Feistritzter
 - Jen Goodman
 - Ira Horowitz
 - Chad Ritenour
- **Communications**
 - Vince Dollard
 - Melanie De Gennaro
 - Nancy Seideman
 - Holly Korschun
 - Janet Christenbury
- **Pastoral Care**
 - Robin Brown-Haithco
 - Miranda Lynn Gartin
 - Erica Gerald-Washington
 - Rhonda James-Jones
 - Donald Miller
 - Dan Stark
- **EUH Security**
 - Linda Scott-Harris
 - James Cain
 - Roderick Davis
 - Tyrone Johnson
 - Tyrone Pickett
 - Anthony Shaw
 - Tenina Truesdale
- **Emory Nephrology**
 - Michael Connor
 - Harold Franch
- **Emory Critical Care**
 - Jim Blum
 - Matthew Klopman
 - Ricky Matkins
 - Kathy Schwock
 - Francis Wolf
 - Kathy Stack
 - Joel Zivot
 - Laureen Hill
 - Cathy Meechan
 - Paul Meechan
 - Jon Sevransky
 - Viranuj Sueblinvong
 - Seth Walker
- **Emer Med / CEPAR**
 - Alex Isakov
 - Sam Shartar
- **Grady EMS**
 - Wade Miles
 - Aaron Jamison
 - John Arevalo
 - Gail Stallings
- **Emory Infectious Diseases**
 - **Bruce Ribner**
 - **Sonia Bell**
 - Colleen Kraft
 - G Marshall Lyon
 - Aneesh Mehta
 - Rachel Friedman
 - Vince Marconi
 - Colleen Kelley
 - Mark Mulligan
 - Carlos Del Rio
 - Phyllis Kozarsky
 - Monica Farley
 - David Stephens
- **Logistics**
 - Gentrice McGee
 - Porcia Jones

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Our Patients and Their Families



EVD survivors will help us prepare for the next crisis....



Our Patients and Their Families



EVD survivors will help us prepare for the next crisis....



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MEDICINE

Serious Communicable
Diseases Unit

THANK YOU!