Transfusion and Ebola Virus Disease

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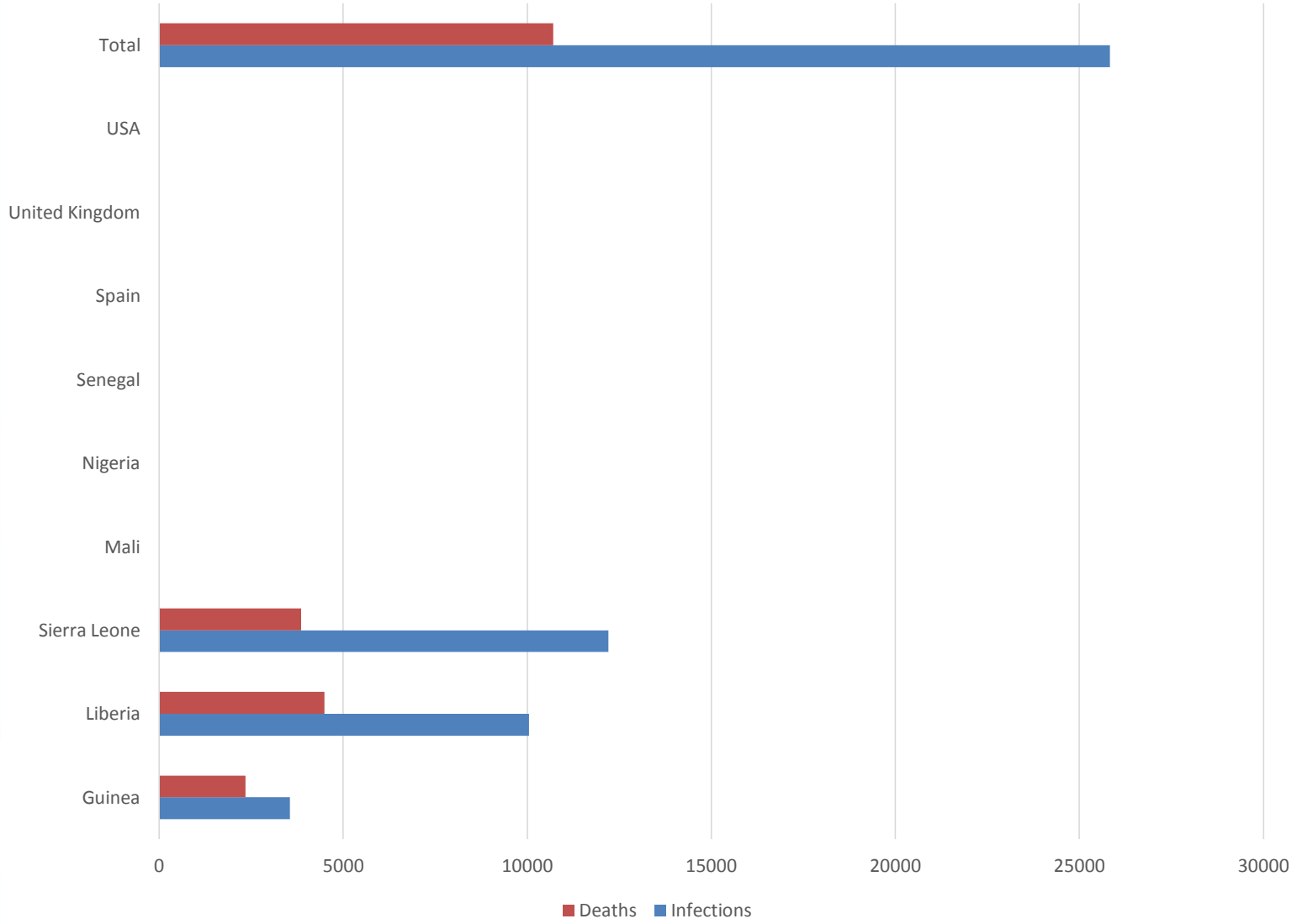
2014-15 Ebola Outbreak



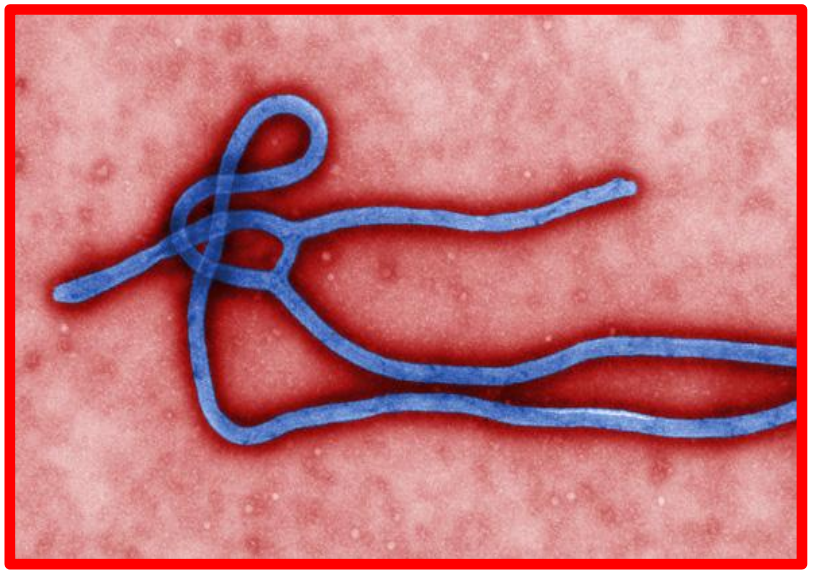
WHO

2014 Ebola Outbreak

Cola tree in Guinea, thought to be where the index patient was infected

Ebola virus

- Negative sense RNA virus of the Filovirus family
- Four strains
  - Zaire, Sudan, Cote d'Ivoire, Bundibugyo
- Incubation period is 2-21 days
- Infectiousness at disease onset
  - Contact with body fluids spreads disease



Ebola Virus Disease

- Clinical presentation
  - Fever
  - Fatigue
  - Loss of appetite
  - Vomiting
  - Diarrhea
  - Headache

- Very non-specific symptoms, which makes travel and contact history so important
- Diagnosis is usually through PCR testing, which is only performed in select labs

Ebola Virus Disease

Transfusion service recommendation

- Make sure your institution has a mechanism to alert laboratory staff when a specimen is collected from a high risk patient

Ebola and Blood Bank Testing

Categories of specimens

- Patient with febrile illness
  - Patients under investigation for EVD
  - Unknown or unsuspected EVD
- Patient without illness but high level risk
- Patient with confirmed EVD

Ebola and Blood Bank Testing

Transfusion Testing from Patients with Known EVD, considerations:

- Specimens highly infectious for weeks
  - J Appl Microbiol. 109(5): 1531-9
- Viral loads reported to be up to 10^8 per ml
- Infectious dose as few as 1 to 10 virions
  - JAMA 1997: 278,(5),399-411

CDC Guidance Summary for All Specimens

- To date, CDC considers the risk of acquiring EVD through laboratory testing to be low, but not zero risk.
- Some recommended measures to minimize the risk of laboratory transmission when testing patient specimens include
  - Limiting the number of staff engaged in testing
  - Evaluating and segregating equipment used for testing
  - Performing testing in a dedicated space.

CDC Guidance Summary for All Specimens

- Must follow OSHA blood borne pathogen standard
  - Appropriate PPE and following safety rules
- Each laboratory must perform their own risk assessment
  - Certified Industrial Hygienist (CIH) can be useful
- Adjust PPE requirements, practices and safety equipment controls, as needed

CDC Recommendation Summary for Laboratory Testing

- For persons under investigation of EVD, laboratory personnel need:
  - Gloves
  - Water-resistant gowns
  - Face protections using shields or goggles
  - Respirator
- Work in a class II Biosafety cabinet or behind a splash guard

Specimens from known Ebola patients

- Specimens should be secured and discarded in an appropriate fashion
- Specimens likely will be shipped to CDC
  - Category A
  - Packaged and shipped by qualified individual
    - certified in some way through Dept of Transportation
  - Likely will not be accepted by routine shippers
    - May cost thousands of dollars per shipment so batching is useful

Specimens from known Ebola patients

Specimens likely will be shipped to CDC

- If specimen is cultured and shown to contain Ebola, then the specimen becomes a select agent
  - Issue for split specimens unless you have a BSL4 lab and are registered to have Ebola in your possession
- Ebola RNA virus positive nucleic acid testing does not make specimen a select agent

CDC Recommendation Summary for Laboratory Testing

- Laboratories should consider using equipment with closed tube systems in which the specimen container stays capped during testing.
- Centrifugation can pose a risk of aerosolization.
- If centrifugation is necessary for testing, centrifuges should have sealed buckets or sealed rotors.
- After centrifugation, the sealed buckets or rotors should be opened inside a biosafety cabinet.

Ebola and Blood Bank Testing

Highly infectious waste considerations – CDC recommendations:

- Category A infectious substance (DOT: HMR, 49, CFR, Parts 171-180) for medical waste purposes
- Waste should be placed into leakproof containment in a rigid container
- Steam sterilization of waste or incineration, if available
- Coordinate/check with your medical waste contractor
- Sewer drainage ought to be ok, but need to check with local authorities

Ebola and Blood Bank Testing

- Practical issues in the blood bank:
  - Serofuge waste
    - Drain into container of bleach
    - Sinks: no handwashing and bleach daily

Ebola and Blood Bank Testing

- Practical issues in the blood bank:
  - Automated testing waste
    - Drain into container of bleach
    - 1:10 to 1:100 dilution of bleach should inactivate virus

Specimens from patients with known EVD: Emory and Nebraska Protocols

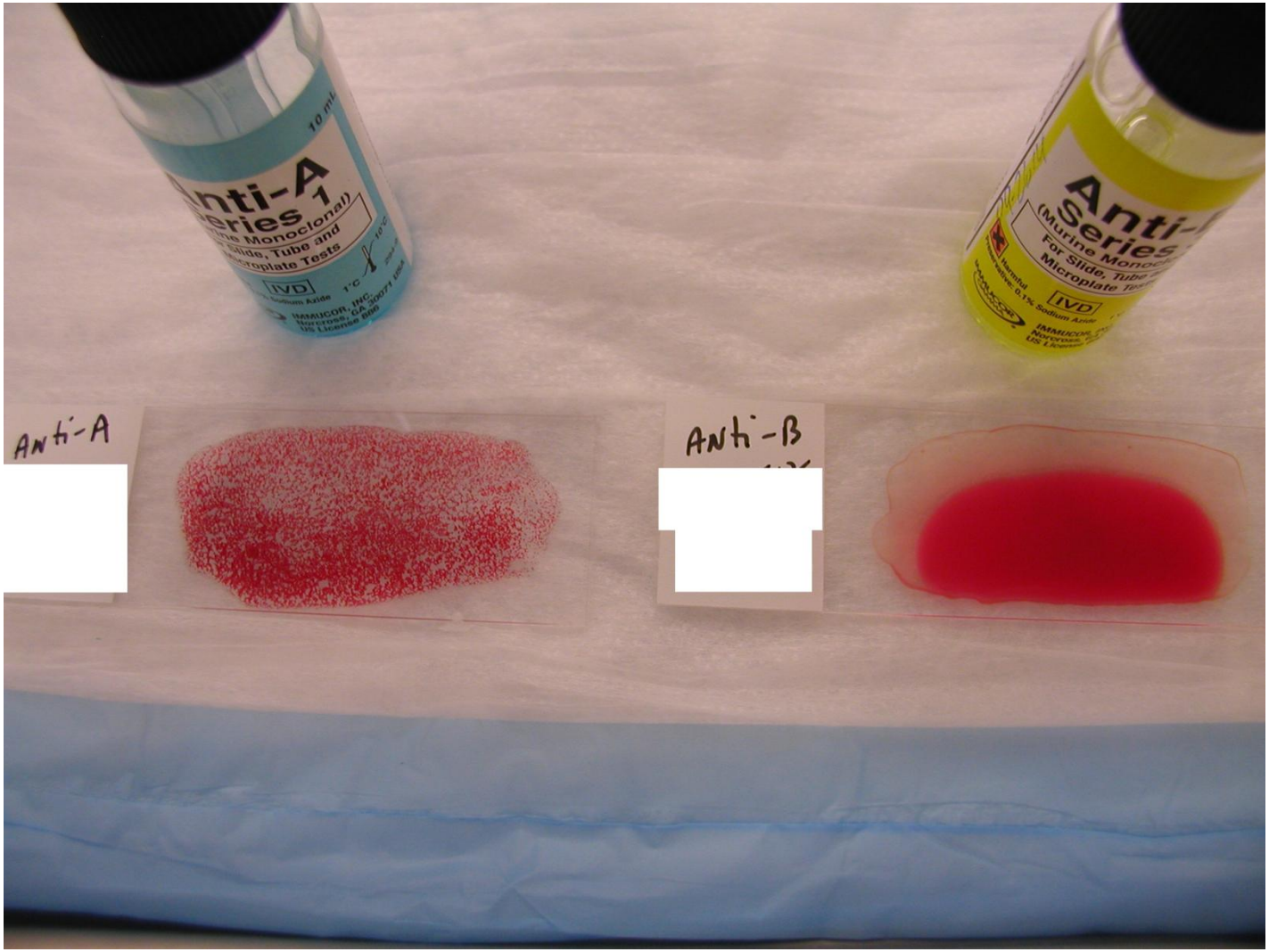
- For most routine labs, point of care testing platforms within Biocontainment Unit (BCU) are used
  - Does not include blood bank testing
- Testing that does not involve OPEN centrifugation or removal of specimen cap (i.e. on analyzers that access specimen through the cap) can be performed in the general laboratory

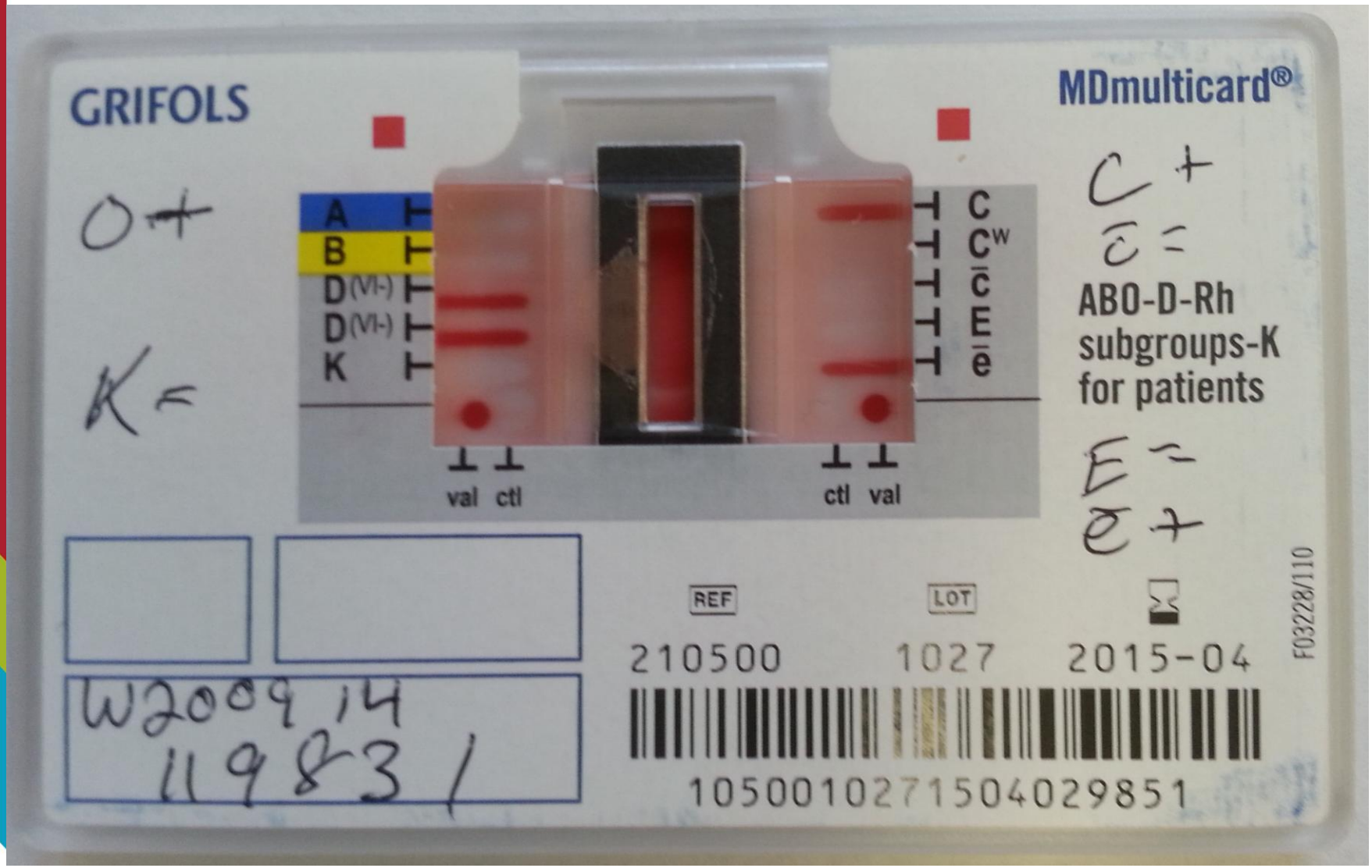
Specimens from patients with known EVD: Emory and Nebraska Protocols

- Externally decontaminated specimens
  - Transported securely to BSL3 lab or tested directly within the BCU
  - Aerosol-producing procedures done in BSL-3 lab containment
    - Slide agglutination typing
    - Experimental (RUO) tests such as antigen typing using the Grifols MultiCard

Specimens from patients with known EVD: Emory and Nebraska Protocols

- At this time, screening for irregular RBC antibodies is not performed, and universally compatible blood products are selected for patients with EVD
- Low risk of hemolysis (~0.5%)
  - Immunohematology 2012;28:39–44
- Risk of hemolysis due to irregular RBC antibodies may be reduced with antigen-matched units


Anti-A
Anti-B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Transfusion Therapy for Ebola patients

RBCs
- O negative, (consider K-negative or antigen matched)

Plasma
- AB or type compatible

Convalescent Plasma
- Would consider incompatible transfusion
- Anti A or Anti B titers

Platelets
- AB or type compatible

Transfusion Therapy for Ebola patients

Administration of blood product

- Once issued to BCU, no return
- Transfused using standard tubing/filter set and standard transfusion policy with regard to monitoring of patient and their vital signs
- Uncrossmatched RBCs transfused slowly at first

Specimens from patients with known EVD: Nebraska Protocols

Special Report

An Integrated Approach to Laboratory Testing for Patients with Ebola Virus Disease

Peter C. Iwen, PhD, D(ABMM),[1,3] Jodi L. Garrett, MT(ASCP)SM,[4] Shawn G. Gibbs, PhD,[2] John J. Lowe, PhD,[2] Vicki L. Herrera, MS,[3] Anthony R. Sambol, MA,[3] Karen Stiles, MT(ASCP)SM[CM],[3] James L. Wisecarver, MD, PhD,[1,4] Kathryn J. Salerno, MT(ASCP),[4] Samuel J. Pirruccello, MD,[1,4] Steven H. Hinrichs, MD.[1,4]*

Lab Med Fall 2014;45:e146-151

Nebraska Ebola Method Public Course can be found at http://www.unmc.edu/publichealth/news/ebola-community.html

Specimens from patients with known EVD: Emory Protocols

Special Report

Laboratory Test Support for Ebola Patients Within a High-Containment Facility

*Charles E. Hill, MD, PhD,[1] Eileen M. Burd, PhD,[1] Colleen S. Kraft, MD,[1] Emily L. Ryan, PhD,[1] Alexander Duncan, MD,[1] Anne M. Winkler, MD,[1] John C. Cardella,[2] James C. Ritchie, PhD,[1] Tristram G. Parslow, MD, PhD[1]**

Lab Med Summer 2014 45:e109-e111

Emory Ebola Preparedness Protocols can be found at http://www.emoryhealthcare.org/ebola-protocol/ehc-message.html

Questions?

EVD and convalescent plasma

August 2, 2014 – First patient arrived at Emory to be treated for Ebola Virus Disease

August 5, 2014 – Second patient arrived at Emory

August 19, 2014 – Second patient discharged

August 21, 2014 – First patient discharged

Both received Zmapp and supportive care

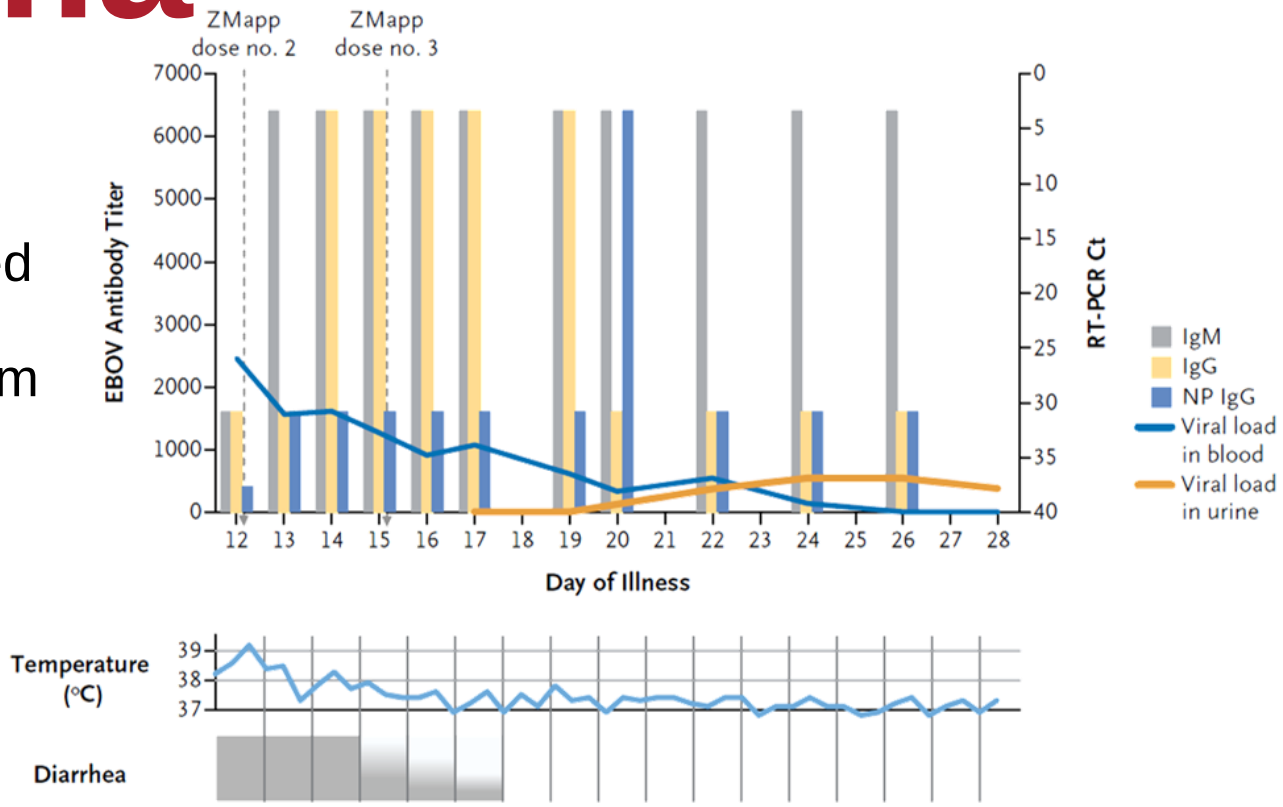
N Engl J Med 2014; 371:2402-2409

Convalescent Plasma

Thursday September 4th, 2014 (Opening day of NFL)

Convalescent Plasma

- In 1995, 8 patient received whole blood transfusion from survivors of EVD and 7 survived



Mupapa K. *J Infect Dis* 1999; 179(Suppl 1), S18-23
Lyon GM NEJM 2014;371:2402-2409

CP

- Wrote an IRB and contacted FDA for emergency Investigational New Drug exemption to collect plasma from survivors of Ebola Virus Disease and to transfuse that plasma into patients currently ill with EVD

- Significant unknowns
  - Blood type of recipient
  - Dose to collect
  - Testing to be done on plasma

CP

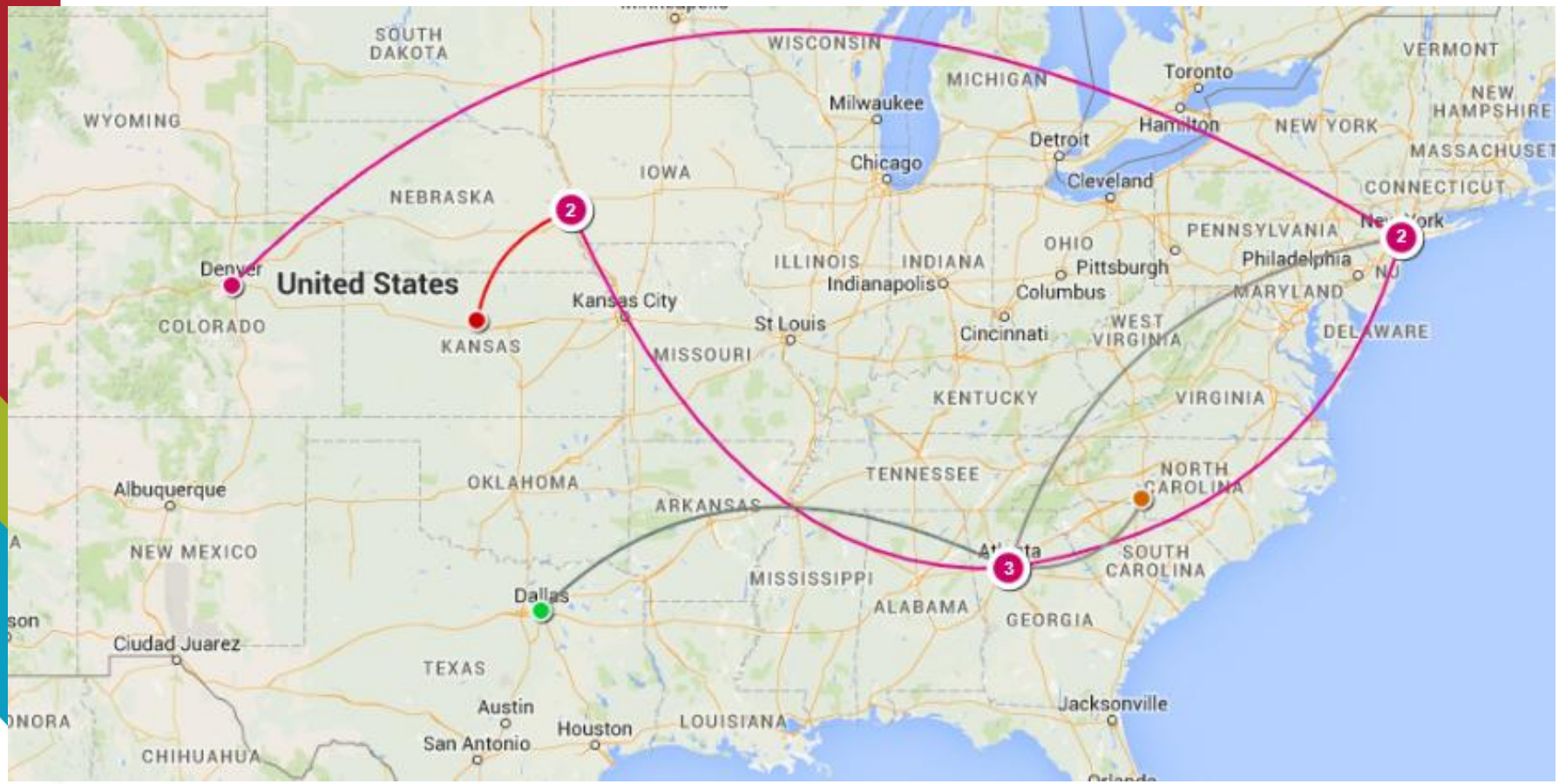
- Dr. Kent Brantly was contacted and was flown to Omaha on September 5, 2015, the same day Dr. Sacra was admitted for treatment of EVD
- Collected 1000 mL of plasma using apheresis

CP

- All routine infectious disease testing for blood donors was performed
- Plasma was transfused on September 6, 2014 without complication
- Dr. Sacra discharged on September 25, 2014

- Protocol was repeated for another patient admitted at Emory University

CP



Courtesy of Dr. Anne Winkler

CP - Currently

- The current NIAID trial may consider convalescent plasma as a treatment arm in the future
- Trials using convalescent plasma are underway in Africa

Summary

- EVD disease was treated in the USA for the first time
- EVD presents unique challenges for the laboratory and can serve as a model for other highly infectious emerging diseases
- Each laboratory must perform a risk assessment and develop policies and procedures to keep patients and staff safe
- The transfusion service may be called upon to provide convalescent plasma