IFPA international meeting in Cape Town December 2nd 2015

Akin Abayomi

Division of Haematology

Faculty of Medicine

Stellenbosch University

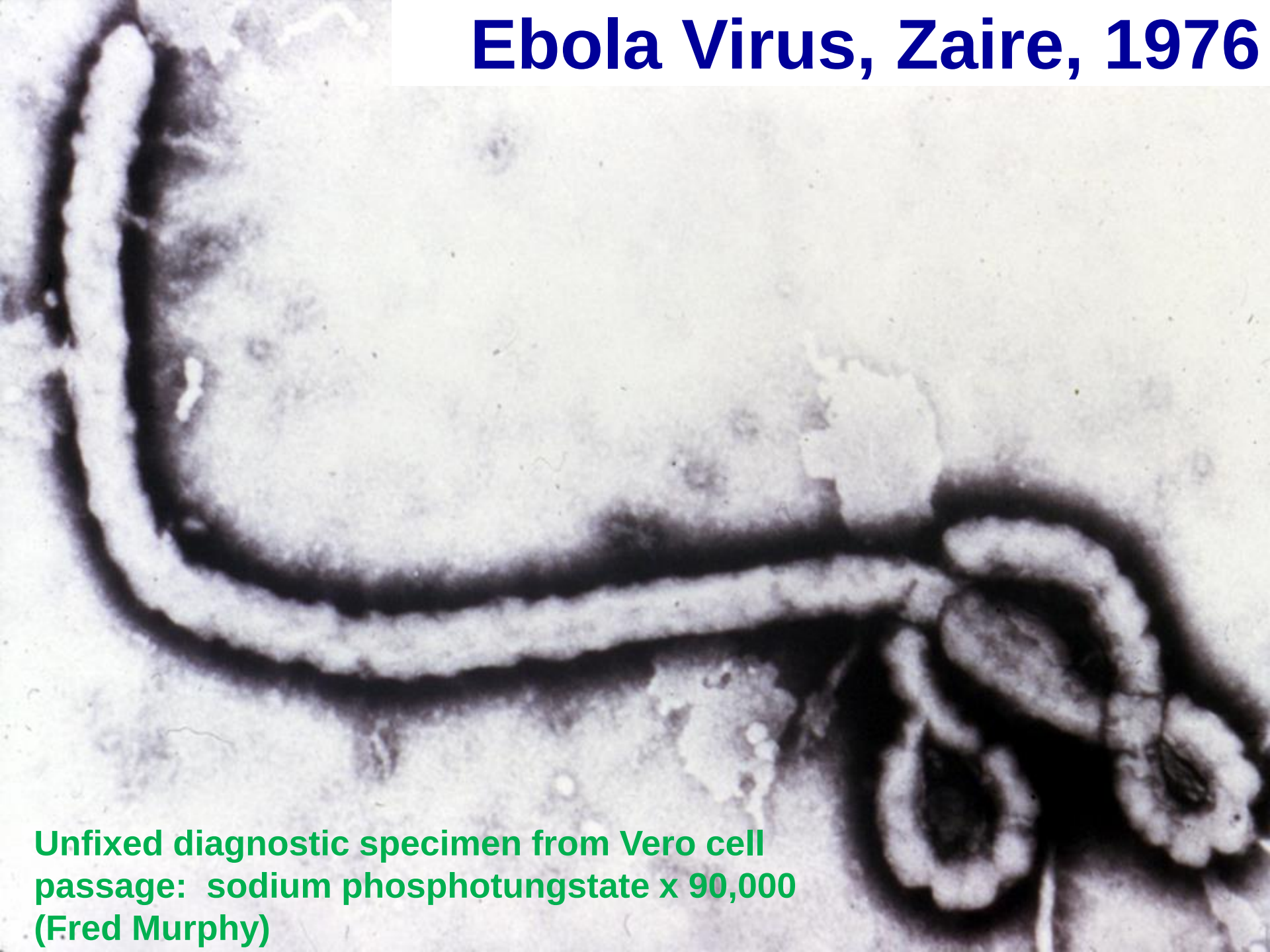
Convalescent Blood strategies in Public Health Crises caused by highly contagious Emerging Infectious Diseases.

WEST AFRICA EBOLA OUTBREAK MODEL and EXPERIENCE.

Tygerberg : 1,400 bed multi-disciplinary teaching hospital

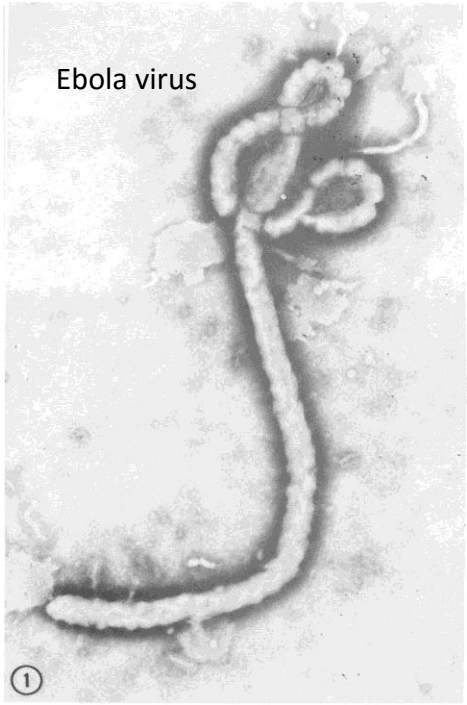


Ebola Virus, Zaire, 1976



Unfixed diagnostic specimen from Vero cell passage: sodium phosphotungstate x 90,000 (Fred Murphy)

FILOVIRUSES ARE THE MOST VIRULENT AGENTS OF AVHF.



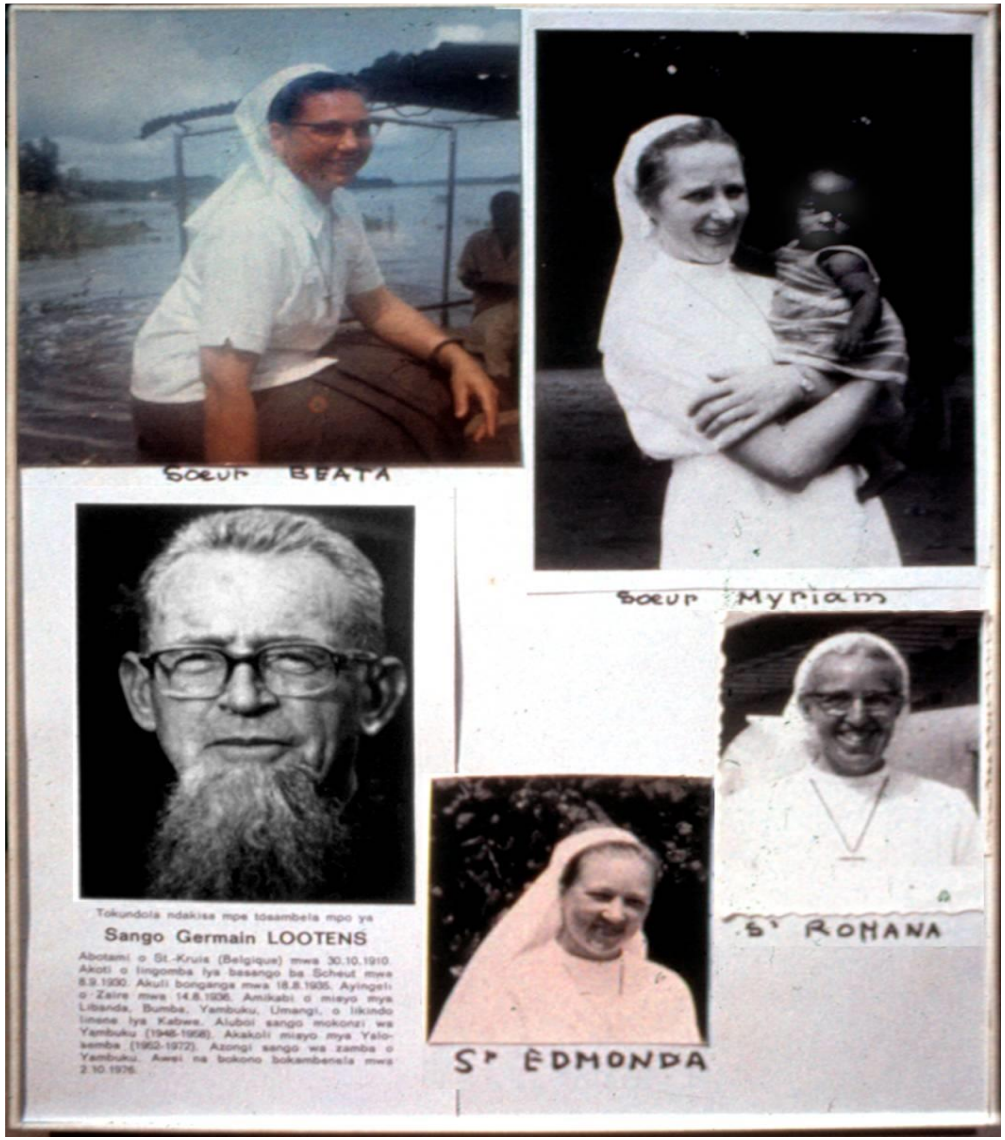
- MONONEGAVIRALES
  - FILOVIRIDAE
    - Ebola virus
      - Ebola Zaire Virus ZEBOV
      - Ebola Sudan Virus SEBOV
      - Ebola Côte d'Ivoire Virus CIEBOV
      - Ebola Bundibugyo Virus BEBOV
      - Ebola Guinea Virus GEBOV
    - Marburg virus

Ebola River Near Yambuku Hosp, Zaire 1976



Hospital Staff: 17

- **EHF 13**
- **Died 11**



From CDC slide set, 1977

The Belgian Missionary Hospital Staff

Haemorrhage vs GI features





Gingival bleeding

PHOTOS TAKEN IN CONGO 2003 ON EBOLA PATIENTS
(Courtesy Prof Jean-Jacques Muyembe)

“Ebola” a Category A pathogen

Category A pathogens are those organisms/biological agents that pose the highest risk to national security and public health because they can:

- **be easily disseminated or transmitted from person to person**
- **Result in high mortality rates and have the potential for major public health impact**
- **Might cause public panic and social disruption**
- **Require special action for public health preparedness**

Category “A” pathogen

Lassa

Rift Valley

Ebola

Marburg

Small pox

Anthrax

Pandemic Flu

Civil unrest and intense panic





Historical Distribution since 1976

Ebola virus epidemiology and ecology

Ebola outbreaks, year	Country	Nb Cases	Nb deaths	Origin
Yambuku, 1976	DRCongo	318	280	Unknown
Maridi, 1976	Sudan	284	151	Coton facory, insectivorous bats
Tandala, 1977	DRCongo	1	1	Unknown
Nzara, 1979	Sudan	34	22	Unkxnown
Côte d' Ivoire 1994	Côte d' Ivoire	1	0	Chimpanzee
Mekouka 1994	Gabon	52	31	Chimpanzee, Gorilla
Kikwit 1995	DRCongo	315	254	Unknown
Mayibout 1996	Gabon	33	23	Chimpanzee
Boué 1996	Gabon	60	45	Chimpanzee
Gulu 2001	Uganda	425	224	Unknown
Mekambo 2001=2	Gabon	65	53	Gorilla, chimpanzee, duiker
Mbomo Kellé 2001=2	Congo	59	44	Gorilla, chimpanzee, monkey
Kellé 2003	Congo	143	128	Gorilla, duiker
Mbandza Mbomo 2003	Congo	35	29	Monkey, duiker
Yambio 2004	Sudan	17	7	Monkey
Etumbi 2005	Congo	12	10	Unknown, wildlife?
Mweka 2007	DRCongo	264	185	Unknown, bats?
Bundibugyo 2007	Uganda	149	37	Unknown, bats?
Kaluamba 2008	DRCongo			
Isiro 2012	DRCongo			
Afrique de l'Ouest,2014				

ECOLGY of EBOLA

Animal source of Ebola outbreak eludes scientists



CARRIED AWAY Straw-colored fruit bats, *Eidolon helvum* (shown), and other bat species may have carried Ebola virus from Central Africa to West Africa, where the virus is now causing the largest-ever epidemic of the disease.

Labeled countries have had confirmed cases of Ebola.

Human outbreaks

2014-2015, as of March 4

23,963 total cases

9,806 deaths

MALI
SENEGAL
GUINEA
SIERRA LEONE
LIBERIA
NIGERIA

Earlier outbreaks

S. SUDAN
UGANDA
GABON
CONGO
CONGO REPUBLIC
SOUTH AFRICA

Mammals suspected of transmitting Ebola

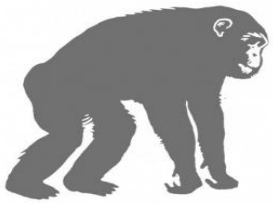
Fruit bats, which are often eaten as bush meat, are suspected of being the main hosts of the virus. A fruit bat was thought to have caused the recent outbreak in West Africa.



About one-third of Africa's **gorillas** have been wiped out by the disease.

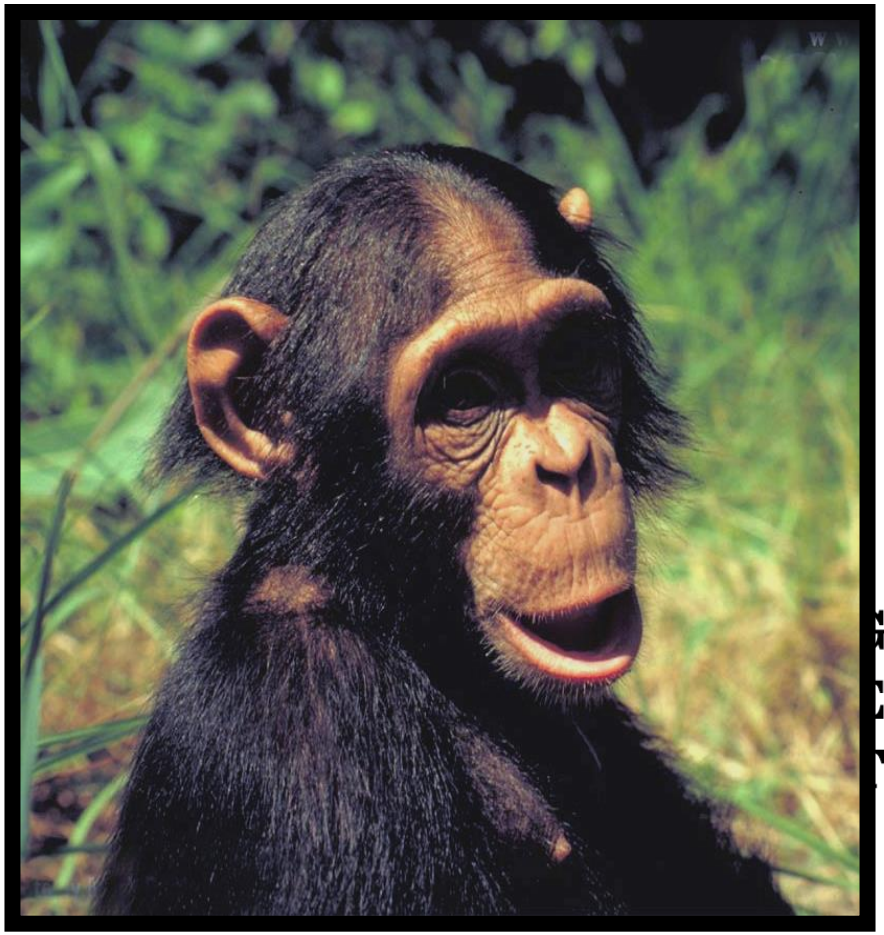


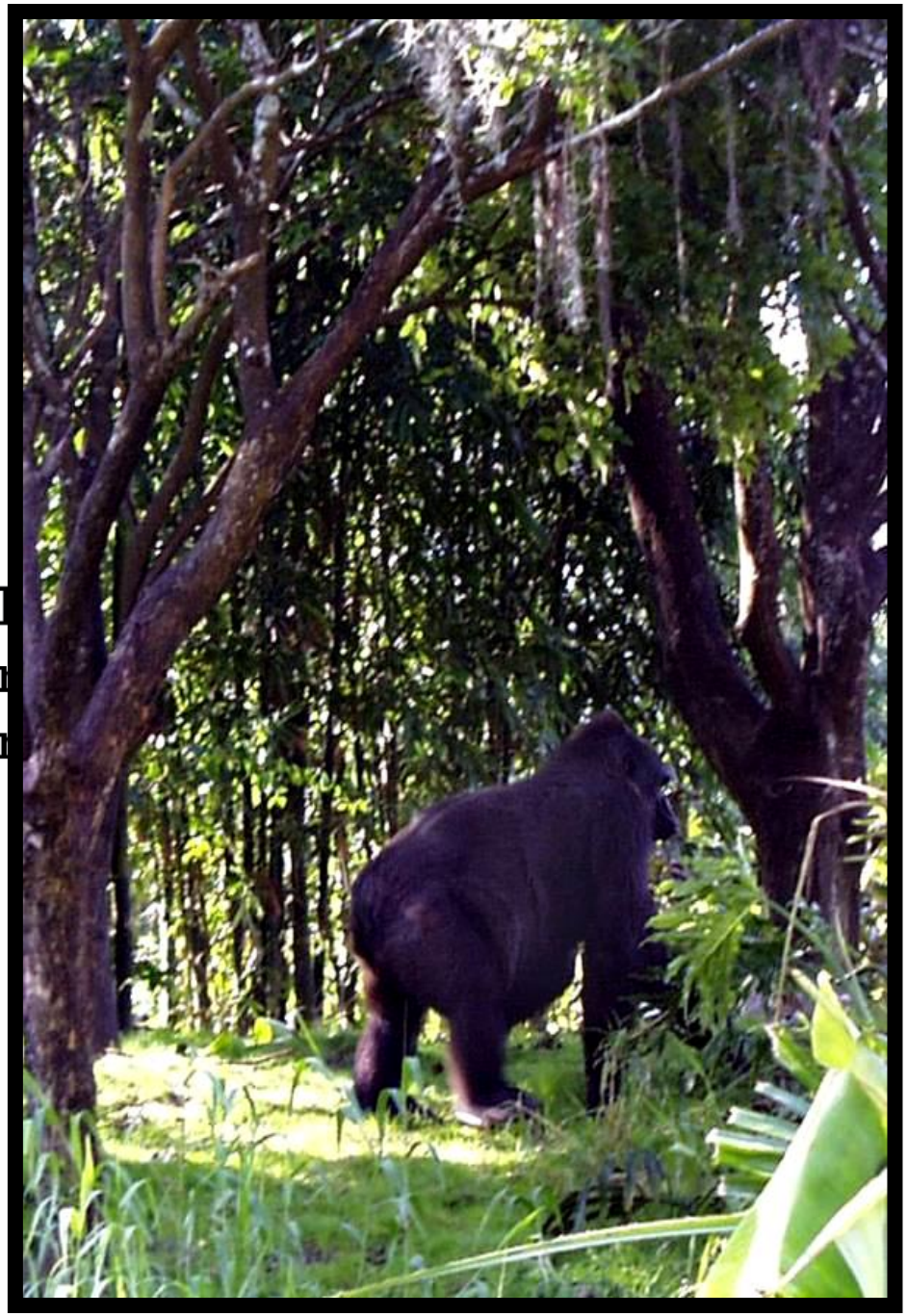
Infected **chimpanzees** can transmit Ebola to humans when they are eaten as bush meat.



Red river hogs might be susceptible to the virus.

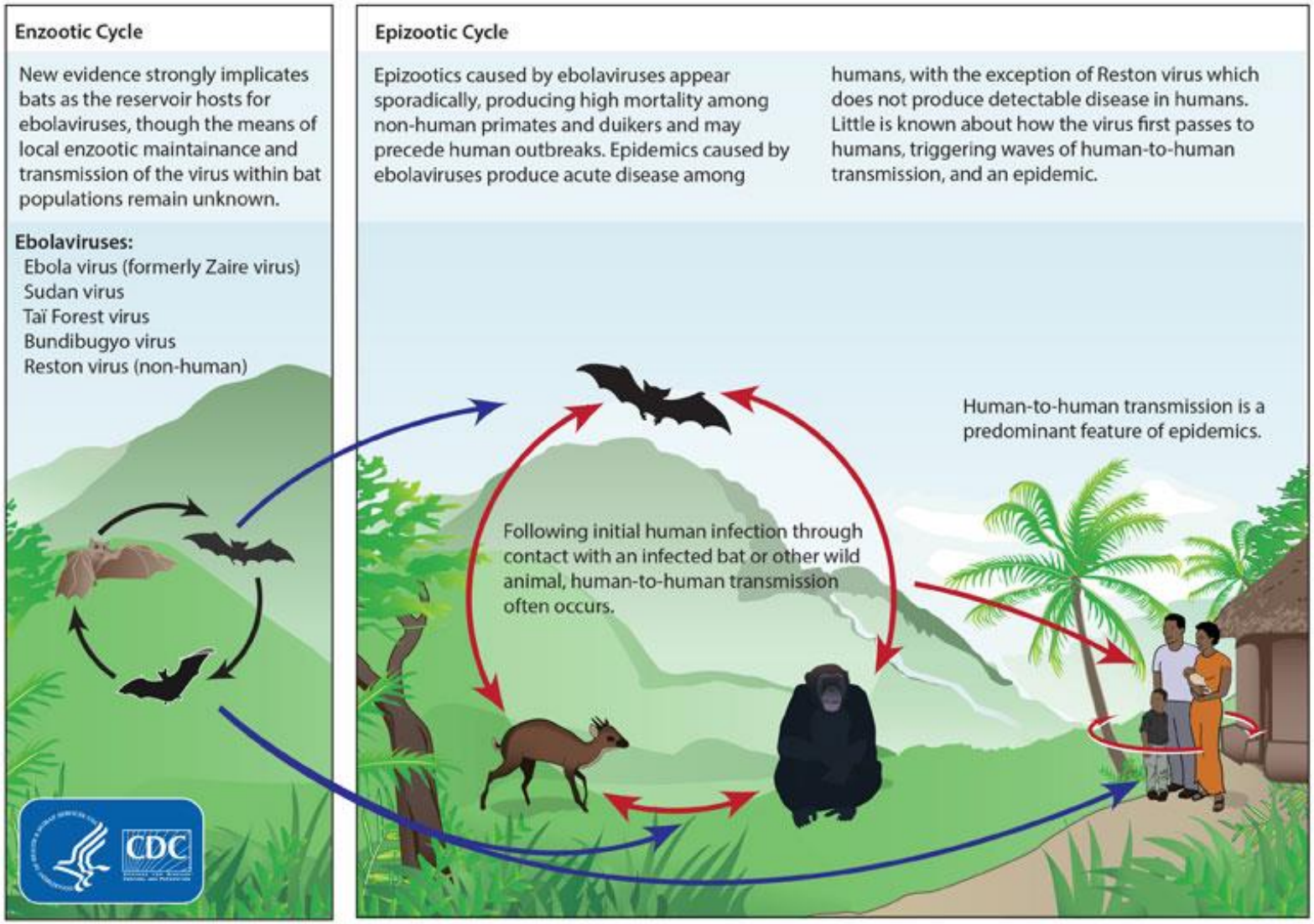






Ebola virus has killed thousands of great apes in the last few years. Outbreaks in the Congo have occurred over large areas, often centering on gorilla and chimpanzee habitat. (World Conservation Union)

Ebolavirus Ecology



This graphic shows the life cycle of the ebolavirus. Bats are strongly implicated as both reservoirs and hosts for the ebolavirus. Of the five identified ebolavirus subtypes, four are capable of human-to-human transmission. Initial infections in humans result from contact with an infected bat or other wild animal. Strict isolation of infected patients is essential to reduce onward ebolavirus transmission.

December 2013: Baize S et al. N Engl J Med 2014;371:1418-1425.

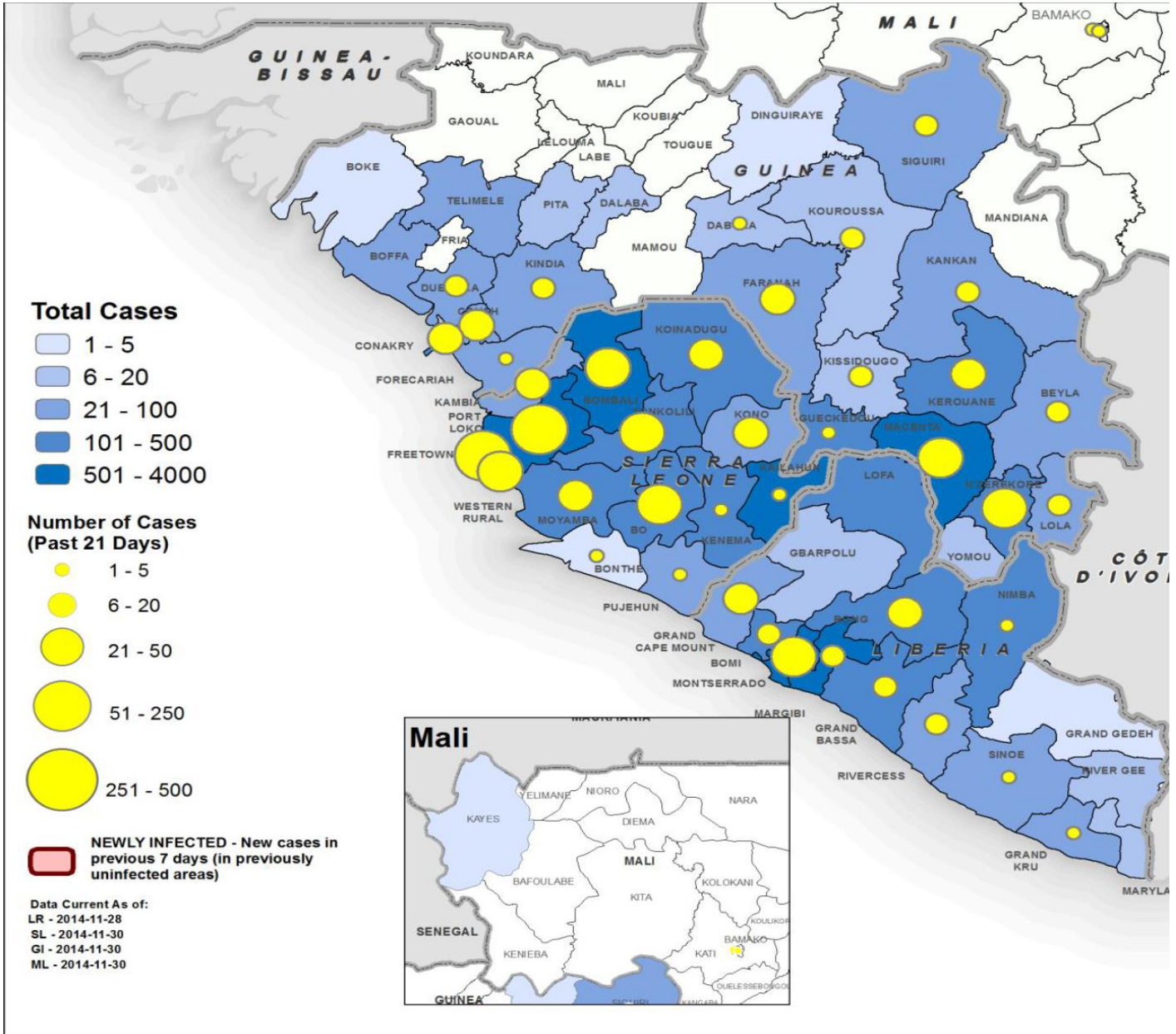


Mapping origin and the movement

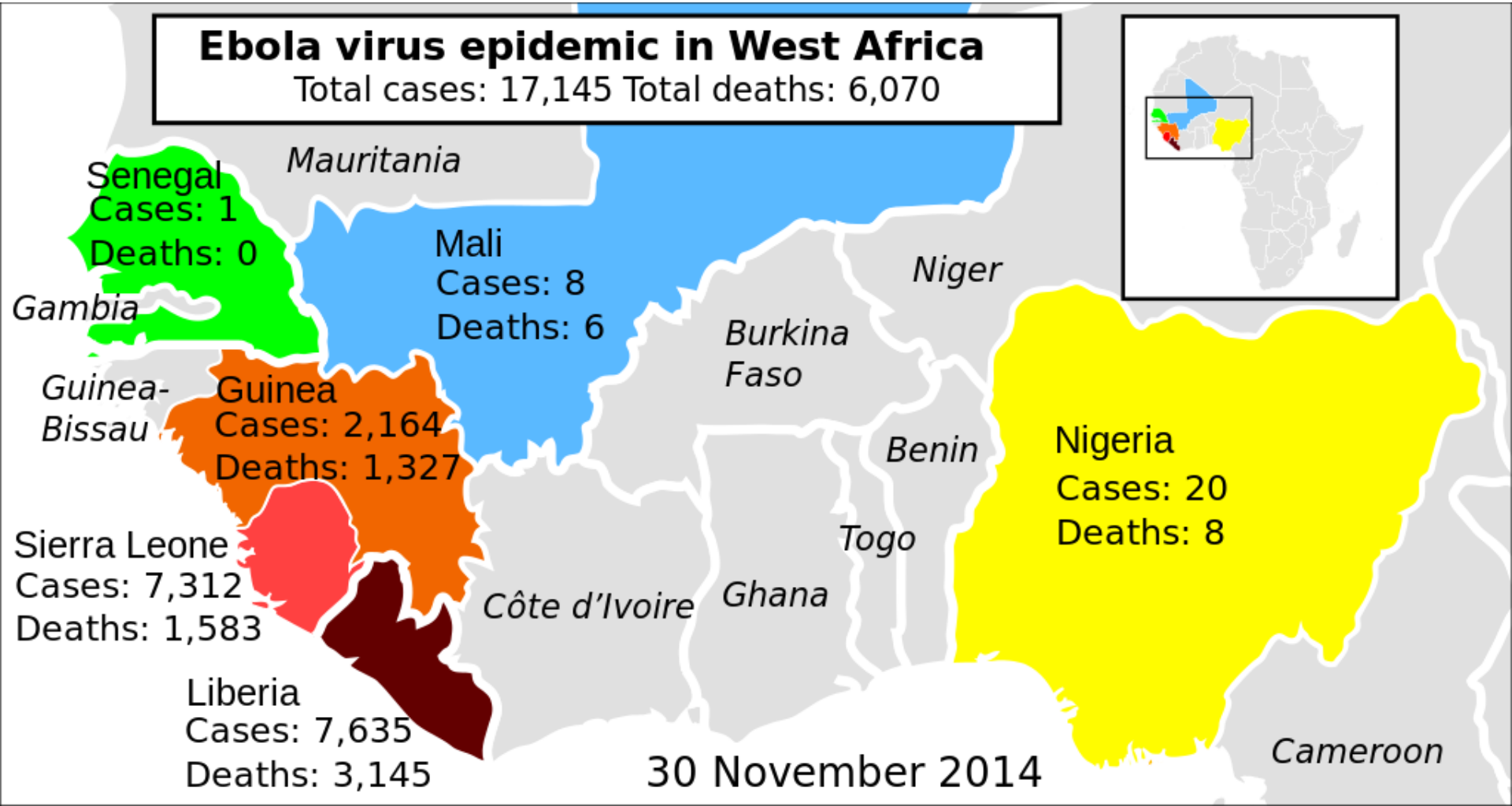
(Courtesy of PHE)



June 2014, large outbreaks in multiple locations in 3 countries.



Extent of spread of Ebola in West Africa alone by July 2014.



Lagos City





Lagos

- **Financial, Industrial and commercial nerve center of Nigeria**
- **Gate way into Nigeria : 1 international and 2 domestic airports. 2 sea ports**
- **Population is 23 million**
- **20 Local governments.**
- **3 have a density in excess of 100,000/km2**
- **3rd fastest growing city in the world**
- **Attained megacity status in 2000 when population exceeded 10 million**

Lagos City Metropolis 23 Million inhabitants.



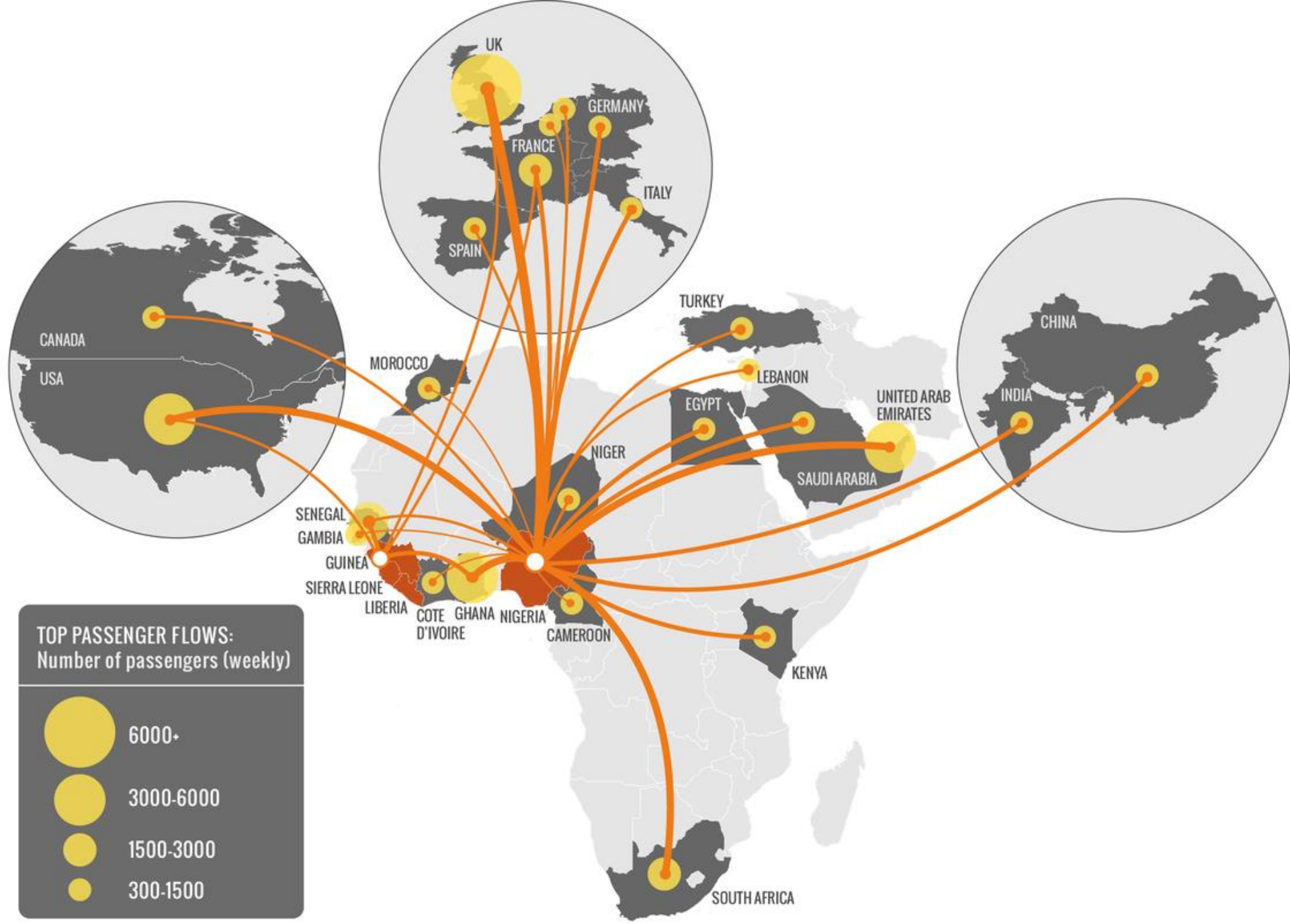
Ebola entry into Lagos

- **Index case entered Lagos on the 20th of July 2014 from Monrovia**
- **Index case demised on the 25th July and same day cremation was conducted.**
- **Primary contacts started presenting with acute symptoms soon after his demise**
- **900 primary and secondary contacts to identified in the first week**
- **Spread to one other major city**

Nigeria: 1 n 4 Africans is Nigerian. Population approaching 200 Million



About 12,000 people fly out of Nigeria daily to different corners of the globe, it could have had a devastating effect on the world if not rapidly contained.


UK
GERMANY
FRANCE
ITALY
SPAIN
CANADA
USA
MOROCCO
TURKEY
LEBANON
EGYPT
UNITED ARAB EMIRATES
SAUDI ARABIA
NIGER
CHINA
INDIA
SENEGAL
GAMBIA
GUINEA
SIERRA LEONE
LIBERIA
COTE D'IVOIRE
GHANA
NIGERIA
CAMEROON
KENYA
SOUTH AFRICA
TOP PASSENGER FLOWS:
Number of passengers (weekly)
6000+
3000-6000
1500-3000
300-1500

Commissioner of Health, Lagos State, Nigeria. Dr. Jide Idris. Mastermind of containing the Lagos outbreak and co- founder of a research led research Consortium to try novel approaches to containment.





GET

Global
Emerging Pathogens
Treatment Consortium

GET

Help
Logistics
Infrastructure
Mobilised
Experts
Support
Samples
Healthy



GET was conceptualized in July 2014

Two of GET's Priority actions

- **Africa Regional Ebola Conference**
  - **Lack of a harmonized response**

- **Convalescent blood strategy**
  - **No known treatment**

Convalescent plasma containing hyper immune globulin in infectious epidemics

- Possibly the only treatment that can be of value in a public health emergency with a pathogen for which there is no known treatment and which is spreading at alarming rates with high fatality

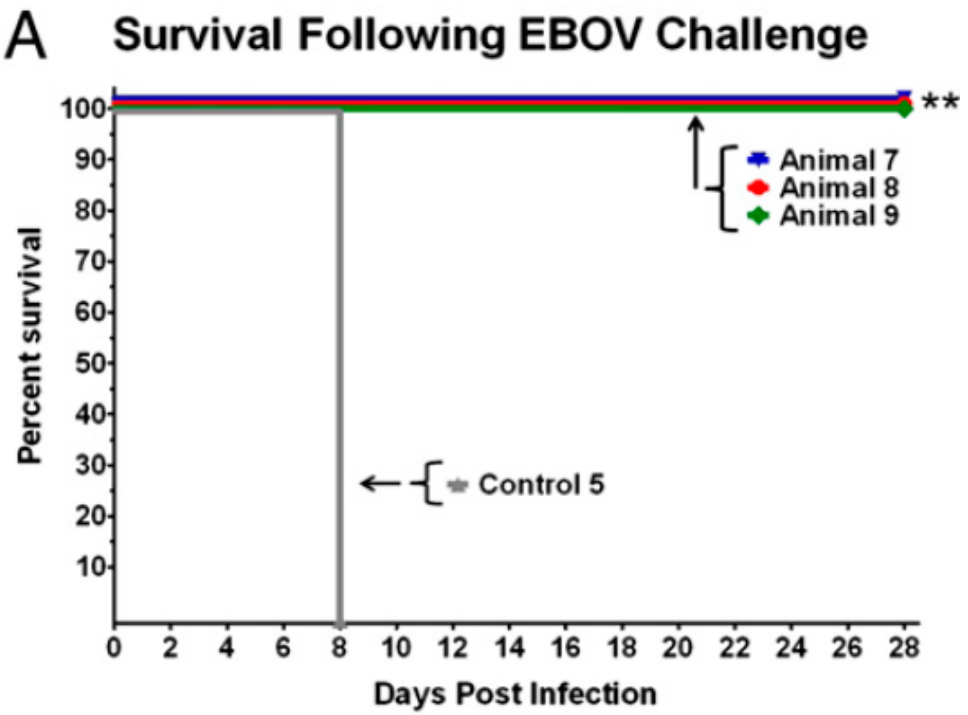
- Some precedent in Ebola and other EID

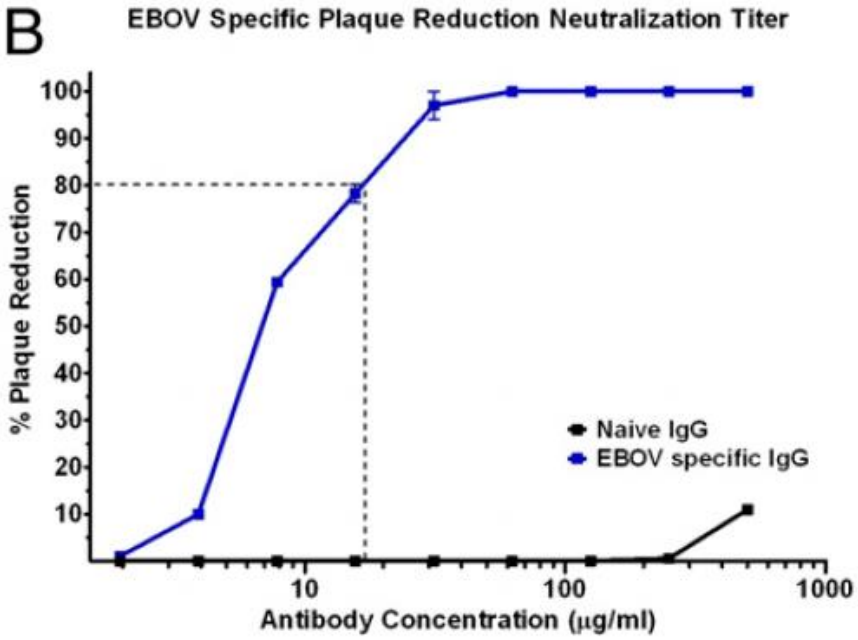
Treatment of EHV with convalescent blood

Patient	Time Onset/date transfusion	CC of blood received	Outcome
1	7	400cc	alive
2	11	150cc	Alive
3	13	150cc	Alive
4	9	250cc	Alive
5	15	250cc	Alive
6	13	250cc	Alive
7	11	450cc	Alive
8	8	450cc	Dead

Treatment of Ebola haemorrhagic fever with blood transfusions from convalescent patients was carried out in Kikwit, 1995

Dye et al. 2012. USAMRIID BSL4 AF. Plasma protects NHP from Ebola exposure.





First African Voices conference on Ebola. Dakar Jan 2015

- High level meeting: GET/RARS/WATER
- Representatives of all MOH in ECOWAS
- WAHO/WHO/UN/MSF/WFP/
- Regional scientists
- Health care providers in the hot zone
- Survivors
- Press


EBOLA
SUR LA VOIX ET LE LEADERSHIP
L'EVALUATION DES TRAITEMENTS
DU VIRUS EBOLA EN A
19-20 JANV
KING FAHD PALACE
OSIWA


Forum
19-20 JANVIER 2015
KING FAHD PALACE • DAKAR, SÉNÉGAL


Forum

Dakar Declaration on Ebola

Full text and conference report:

www.getafrica.org



AFRICAN VOICE AND LEADERSHIP MEETING TO ACCELERATE THE EVALUATION OF POTENTIAL TREATMENTS AND VACCINES FOR EBOLA IN WEST AFRICA

Dakar, Senegal, January 19-20, 2014

Resolution 1

- **Accelerate the evaluation of promising treatment options and vaccine candidates against EVD and other emerging and re-emerging highly infectious pathogens.**

- **There is an urgent need to facilitate and fast track the evaluation of the use of EVD survivors' plasma as therapeutic option.**

- **Generate a capability to collect plasma and develop the biotechnological capacity to fractionate plasma for domestic use in Africa.**

Total as of October 2015

- **28,000 reported cases**
- **11,000 reported deaths**
- **14,000 survivors**

Post Ebola Syndrome

- **Myalgia and joint pains**
- **Lineage cytopenia: particularly Red Cells**
- **Insomnia**
- **PTSD**
- **Neurological features**
- **Sanctuary site reactivation**


Stop
EBOLA
I Made It
EBOLA
Champion
SAFE
BLOOD
I Made It

Clinical Aspects of Ebola Virus Disease

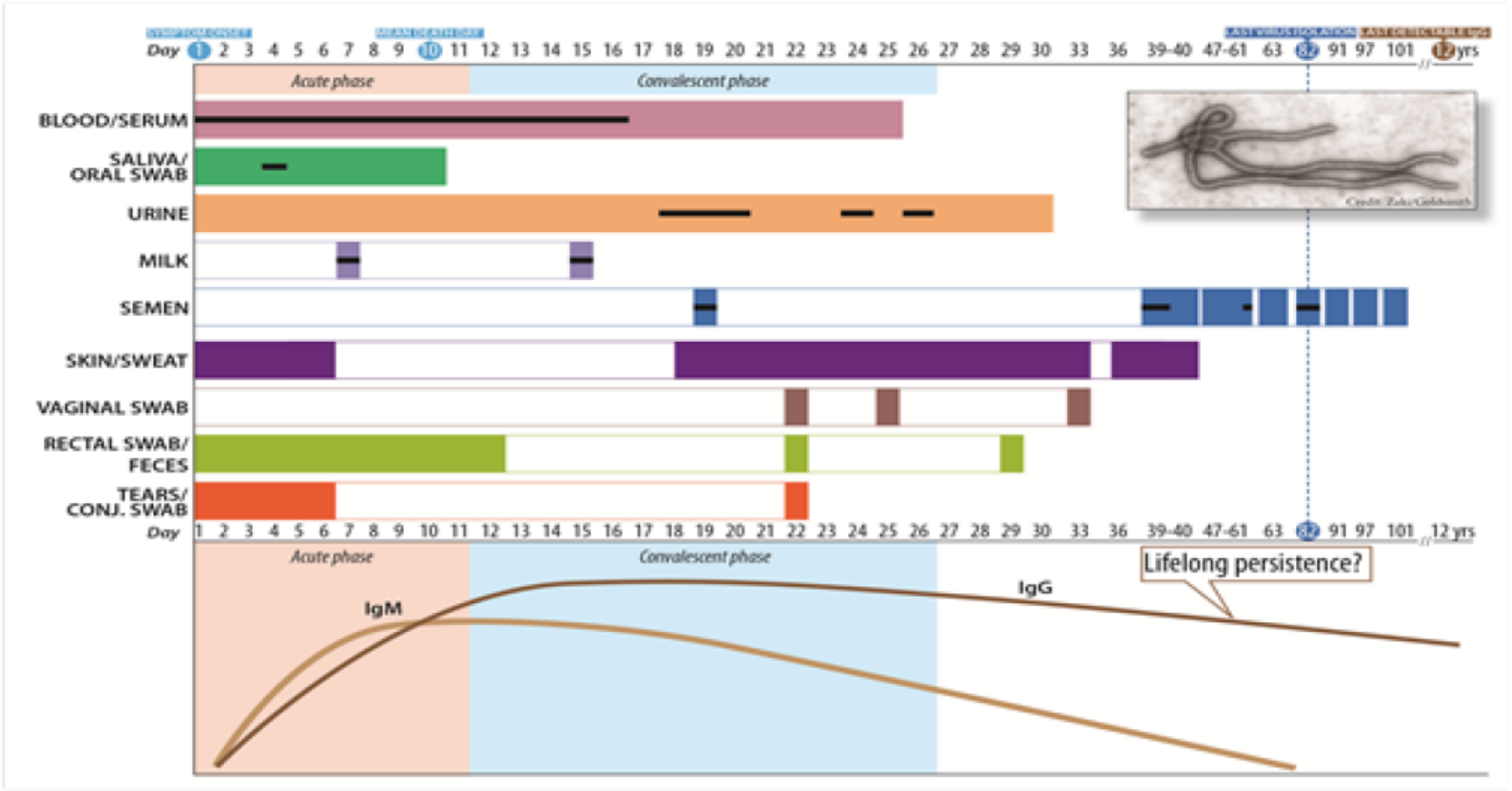
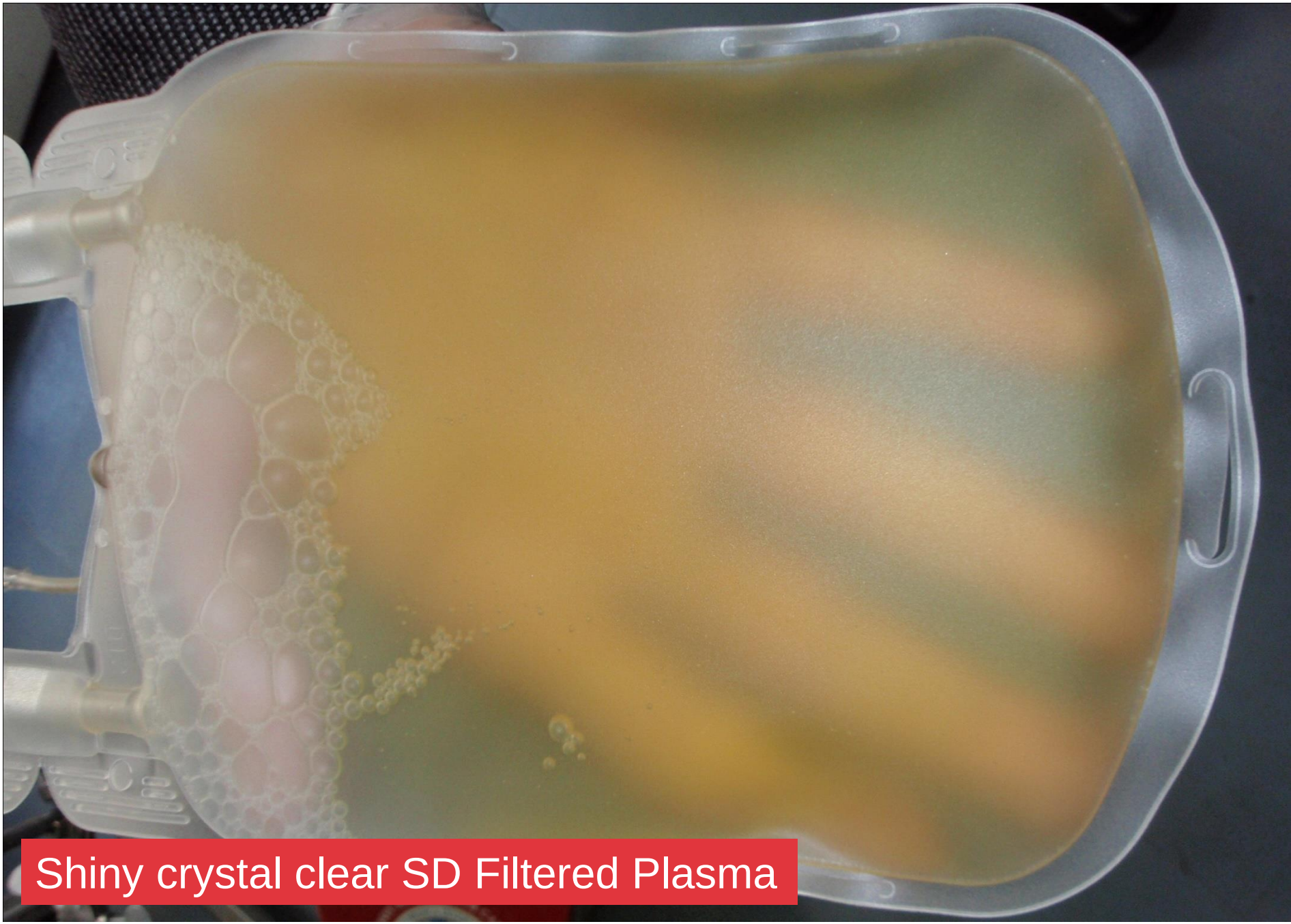


Figure 2. Ebola virus shedding in body fluids. Colors=PCR positive. Bars=culture positive.

Source: Pierre Rollin/CDC


Shiny crystal clear SD Filtered Plasma

There was a complete absence of plasmapharesis or fractionating capacity in the region.

Infrastructure and capacity building for plasmapharesis during an infectious public health crises is not the right time.

Hope Mobiles

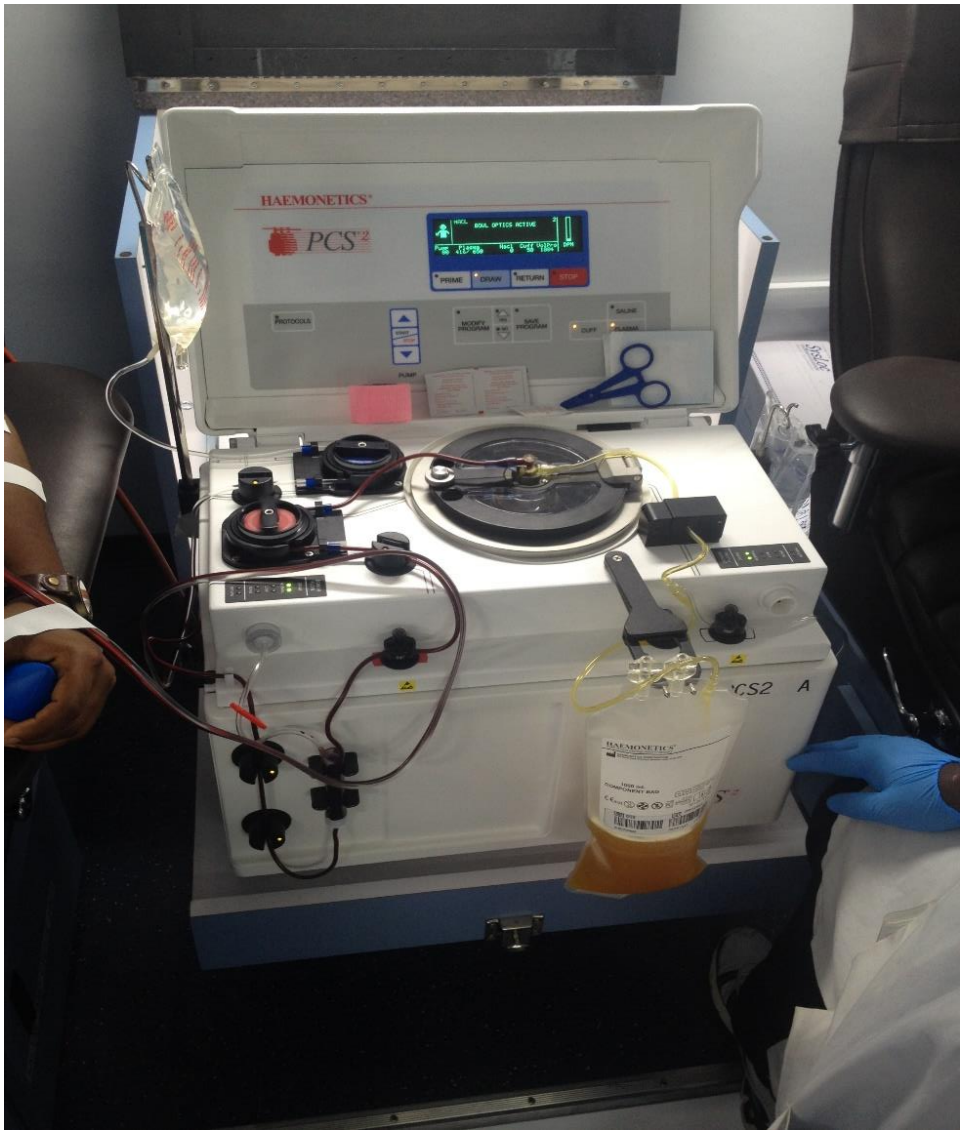








The Inside of a Hope Mobile



CERUS Intercept Illuminator and viral in activator



Antanov Airline carrier, took the Cargo to West Africa.




VOLGA DNEPR
Volga-Dnepr
Волга Днепр




KOTERBA
OMAHA WORLD-HERALD

Capacity over several months

- **Liberia**
- **Guinea**
- **Sierra Leone**
- **Nigeria**
- **All sites have a plasmapharesis unit, stocks of ECP and indigenously trained staff on both plasmapharesis and viral reduction steps**

Massive Community Engagement

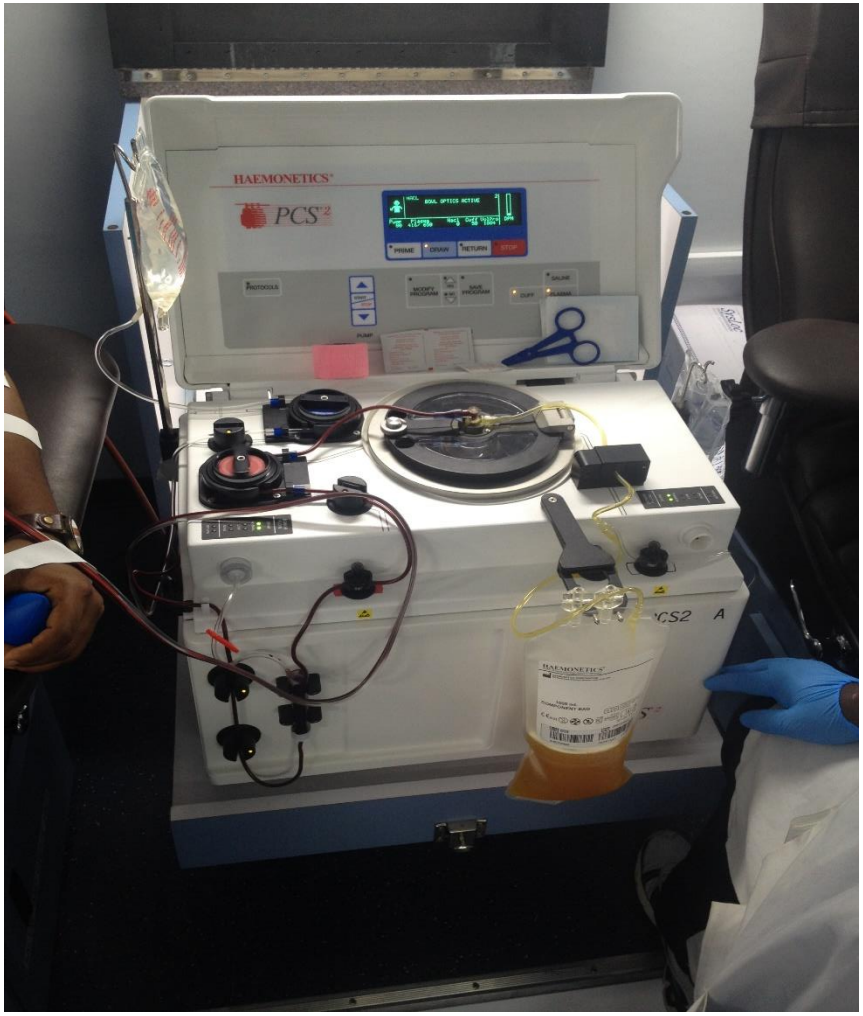




Sierra Leone






HAEMONETICS
PCS2



Ebola Treatment Unit in Freetown





Liberia ELWA2 Hospital site of the first ECP pilot study. (CRO ClinicalRm)



Ebola Treatment Center Donka - MSF





CERSU viral inactivation technology:




HELMER
-30.8°C
FREEZER #2
Freezer Temperature Log


Helmer

Clinical Trials ECP finally Began after the peak of the outbreak:

- Sierra Leone had a convalescent blood study running
- Liberia started but had to close due to lack of patients
- Guinea accrued just over a hundred patients
- Sierra Leone similarly started but had to stop

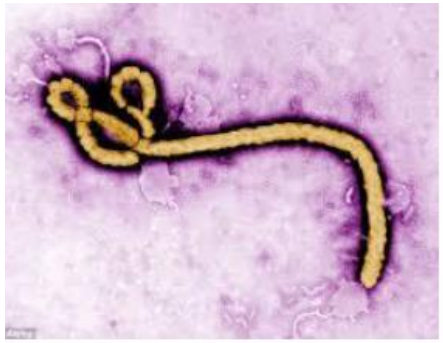
Sierra Leone Convalescent Whole Blood Study

Chief Investigator:
Professor Sahr M. Gevao, Consultant Hematologist,
Ministry of Health and Sanitation, Government of Sierra Leone

Clinical Trial of Convalescent Blood in the Management of Ebola Virus Disease (EVD)
COBED

	NUMBER	DATE
FINAL VERSION	Version 1.0	28th October,2014

CLINICAL TRIAL PROTOCOL
Protocol Number: MOHS-WBT001





Emergency evaluation of convalescent plasma (CP) for Ebola Viral Disease (EVD) in Guinea

Johan van Griensven, MD MMED MSc PhD on behalf of the **Ebola_Tx consortium**

Institute of Tropical Medicine

Methodology (1)

- Study design
  - Non-randomized comparative study
- Study population
  - Confirmed EVD of all ages + pregnant women
  - Exclusion Criteria: Contra-indication/Futility
- Study intervention
  - Total 400-500ml (2 x 200-250ml units of CP – 2 donors)
  - As per WHO guidance
    - No EBOV titre (neutralising activity) results required before use
    - Conduct retrospectively/during implementation

Methodology (2): primary objective

- To assess if CP + SC improves the 14 day survival of patients, compared to SC alone; 20% absolute decrease in mortality
- The control group comprises of patients treated with SC alone
  - (a) Initial phase controls: optimized standard care is given until convalescent blood therapy available.
  - (b) Concurrent controls: non-availability of suitable CP: SC alone.
- Allocation to intervention determined by availability of compatible CP

Methodology (3): secondary objectives

- To compare 30 day survival
- The relationship between Ebola antibody levels in donated CP and
  - survival
  - changes in levels of viral RNA (pre/post)
- Safety
- Feasibility including safety risks in health care providers

DONORS

131 donors visits

117 plasma donations

85 donations with qualified plasma



PATIENTS

102 enrolled

- 10 CP + favipiravir
- 92 for primary analysis
  - **89** treated with CP
    - ✓ 9 < 15 years; 3 < 1 year
    - ✓ 7 pregnant women



Outcomes.

- **Convalescent blood trial in Sierra Leone:**
  - **Data still being analyzed but there is a suggestion that patients that received whole blood demonstrated a reduced Ebola viral load cf controls**
- **Liberia: No data because of lack of patients**
- **Guinea: Data still being analyzed**

In Summary. What to do in the heat of a pandemic situation, with an pathogen that has no treatment:

- Set up biobanking
- Attempt to harvest convalescent plasma
- Adopt rapid clinical trials with relaxed ethics
- Promote and encourage in-epidemic genomic studies to create ideas about possible drug options

Modern Technology must be deployed early in an outbreak

- **Sequencing Technology must be an integral component of a hit squad that arrives early at a pandemic threat location.**

  Convalescent plasma fractionating technology be initiated early.

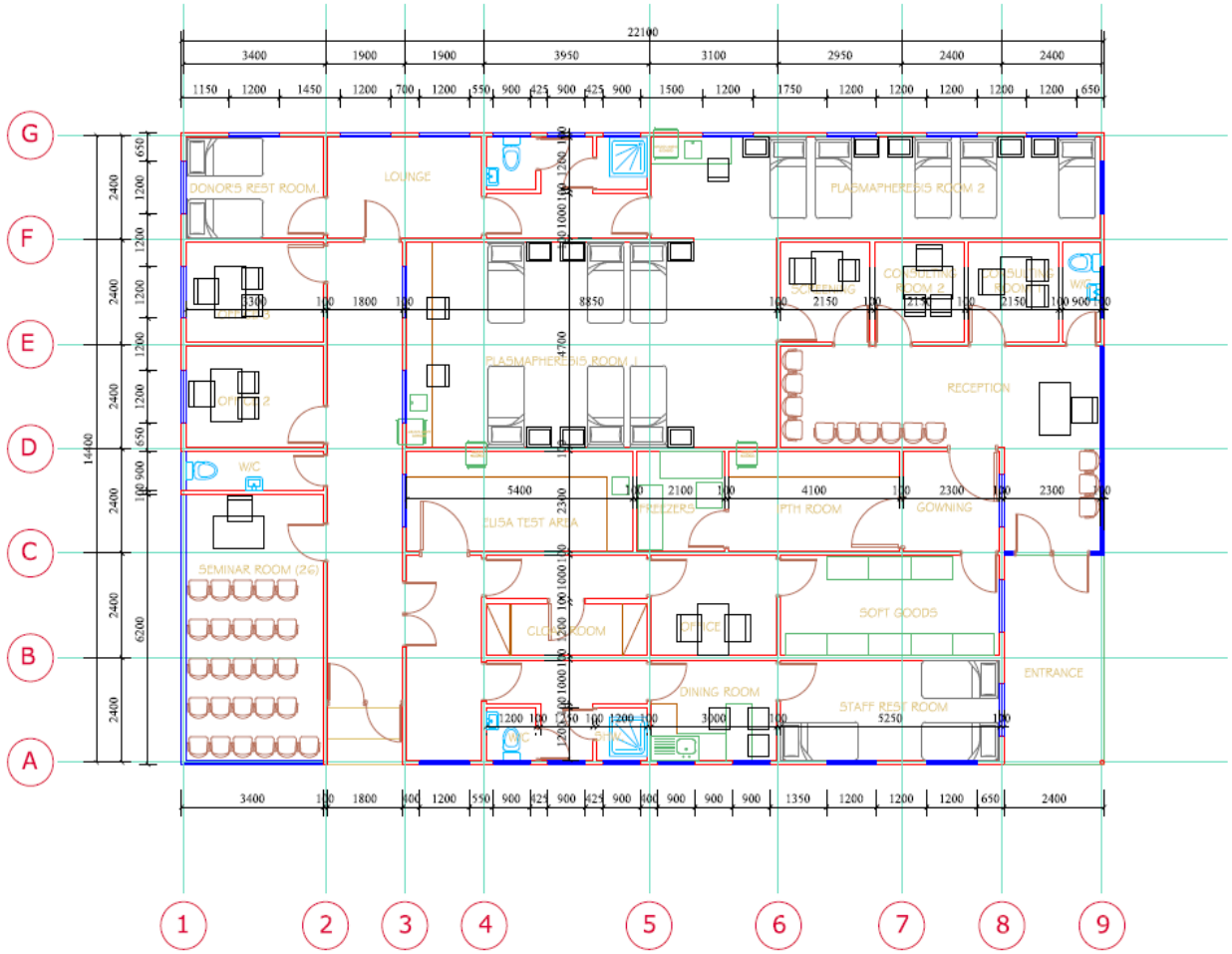
Outcomes of the Ebola outbreak in sub-Sahara Africa (SSA)

- **Plasmapharesis awareness**
- **Plasmapharesis infrastructure**
- **Plasmapharesis skills**
- **Trigger the discussion on a plasma product strategy fro SSA**
- **All sites now have stocks of ECP**

The future:

- **What Plasmapharesis and fractionating strategy should SSA adopt moving forward**
- **What lessons did we learn from the Ebola outbreak and the use of Convalescent Plasma Model.**
- **How do we respond to public health crises caused by EID using HIG**

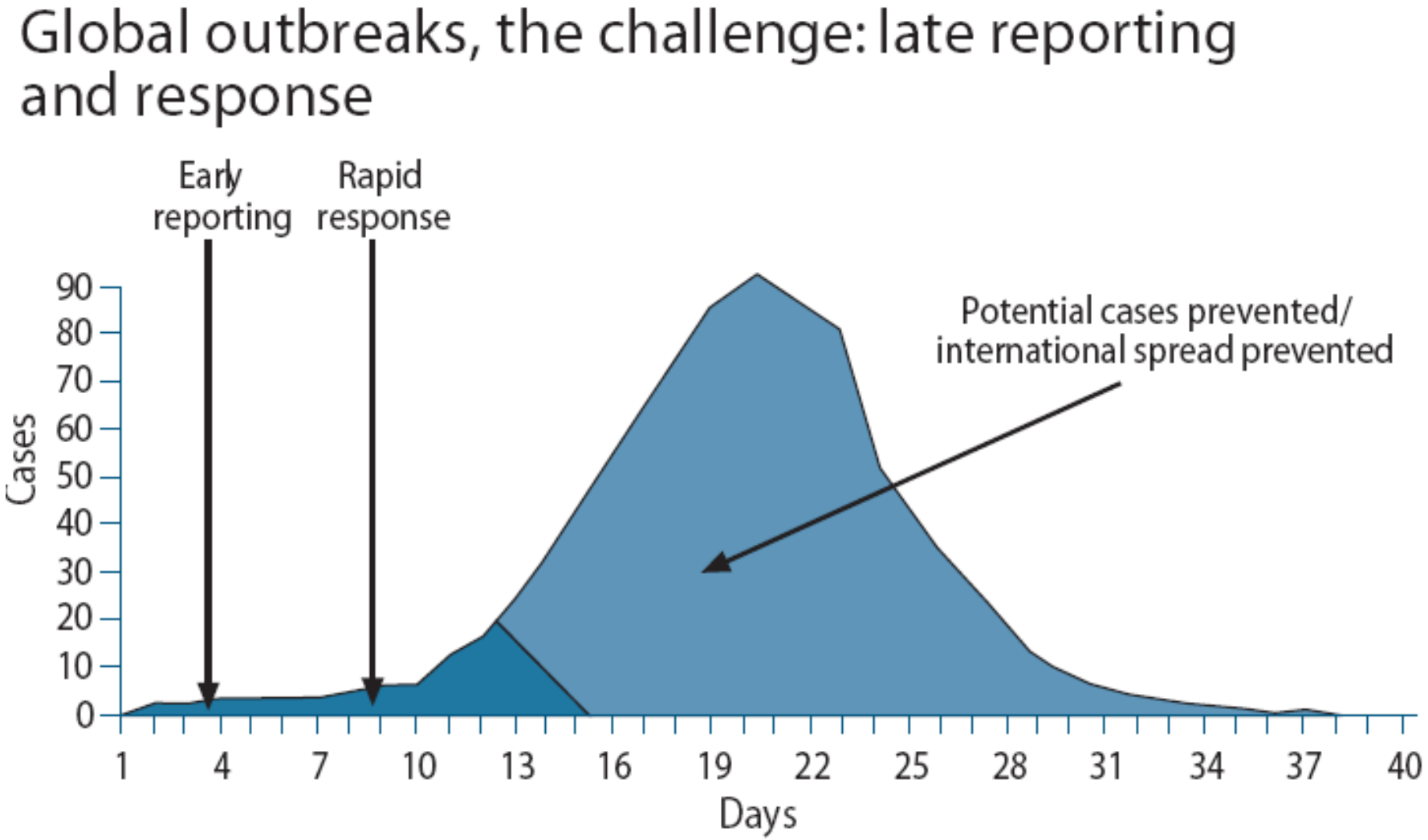
10 bed Plasmapheresis Unit designed for Lagos



job title	date	drawing title	drawing no	
PROPOSED LABORATORY FOR EBOLA CONVALESCENT PROJECT; MAINLAND HOSPITAL, YABA, LAGOS.	NOVEMBER, 2014	PLASMAPHERESIS BUILDING	EBL/AR/01/04	DEUX PROJECT LTD. 261A CORPORATION DRIVE, DOLPHIN ESTATE, IKOYI, LAGOS tel. 01-2694414, 4033. e-mail: tech@metrong.com
	scale 1:100 / drawn LANRE		revision no A B C	

Prevention and Early Rapid response profile: WHO, The World Health Report 2007.

A Safer Future: global public health security in the 21st century



Thank you.

Akin Abayomi
abayomi@sun.ac.za

GET Global Emerging Pathogens Treatment Consortium

NATIONAL HEALTH LABORATORY SERVICE

UNIVERSITEIT STELLENBOSCH UNIVERSITY

WEST AFRICAN TASK FORCE FOR EMERGING & Re-EMERGING INFECTIOUS DISEASE OUTBREAK

Acknowledgements

- **All the hard working volunteers of GET, now too many to mention**
- **GATES Foundation, Jim Greenbaum and Paul Allone**
  Foundation for Hope Mobile Unit Donations
- **Outpouring to the Nations or generous philanthropic Support**
- **Sierra Leone MOH Whole Blood Study**
- **Ebola Treatment Consortia ITM**

Consortium































ITM (consortium leader/sponsor)

Methodological aspects
LSHTM
University of Oxford
University of Liverpool

Laboratory
Université Aix-Marseille
Institut Pasteur/INSERM

Blood transfusion
Guinean Transfusion Service
EFS
Belgian Red Cross - Flanders
Laboratoire Ebola – Donka
Maferyniah Center
INRB – Prof Muyembe
Antropologists
MSF - WHO/ISARIC



GET support Team on ground in Sierra Leone



Thank you for your attention

Join GET:

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