Forever the Unknown: The Lujo Virus Experience in Johannesburg

Prof. Adriano Duse, University of the Witwatersrand, South Africa

A Webber Training Teleclass

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Hosted by Paul Webber
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July 15, 2010

Some African Viral Hemorrhagic Fevers…

- Viral Hemorrhagic Fevers transmitted by mosquitoes
  - Yellow Fever
  - Rift Valley Fever
- Viral Hemorrhagic Fevers transmitted by ticks
  - [Crimean-Congo Hemorrhagic Fever]
- Viral Hemorrhagic Fevers transmitted by rodents
  - Lassa Fever
  - Other arenaviruses, e,g, Lujo virus
- Viral Hemorrhagic Fevers with bats as reservoirs
  - Ebola Virus Hemorrhagic Fever
  - Marburg Virus Hemorrhagic Fever

Wide Differential Diagnosis!

- Bacterial septicemia: streptococcal, staphylococcal, typhoid, gram-negatives (from meningococci to bacilli – common e.g. *S typhi* to unusual e.g. *Capnocytophaga*),
- Rickettsial infections: e.g. tick-bite fever
- Spirochetal infections: e.g. leptospirosis
- Parasitic infections: e.g. malaria
- Other viral infections: fulminant hepatitis A & B, systemic herpesvirus infections, hemorrhagic Varicella zoster, hemorrhagic measles, etc.
- Non-infective causes: neoplasia, drug sensitivities, anticoagulants, snake-bite, glue sniffing, traditional medicines, agricultural & industrial chemicals

General Principles 1:

- VHFs are an uncommon cause of fever & bleeding: need to always maintain high index of suspicion
- Laboratory confirmation takes time (in this outbreak: 12 Sept 08 > 10 Oct 08)
- Nosocomial transmission and outbreak amplification among HCWs of most (except RVF) African VHF agents is well-described
  - Failure to strictly adhere to barrier precautions: contact with infectious blood , (other) tissues, excreta and other body fluids
  - Sharps and splash injuries
  - Mechanical aerosolization of infectious particles

General Principles 2:

- All previously listed VHF agents are labile, lipid-enveloped RNA viruses & readily killed by simple disinfection: 2% clear phenolic (Hycolin); 1% Na-hypochlorite (bleach); ~ 1% peracetic acid
- Survival, particularly in blood samples, and blood and body fluid encrustations on medical devices & environmental surfaces is variable (days-weeks!)

General Principles 3:

- Adhere to simple & realistic IP&C precautions at all times
  - Then, tailor them to (inferred) knowledge of mode of transmission & biological behavior and characteristics of the infectious agent (or, if novel, an appropriate surrogate). Compile line-listing / an epidemic curve. ENSURE THAT DONNING/DOFFING OF PPE IS AS SIMPLE AS POSSIBLE!
- Do not de-escalate IP&C precautions on the basis of an initial negative RT-PCR; only do so when (i) a definitive diagnosis is reached, or (ii) patient is discharged, or (iii) patient is dead
- Beware of transient 'spontaneous improvement' noted in patient!

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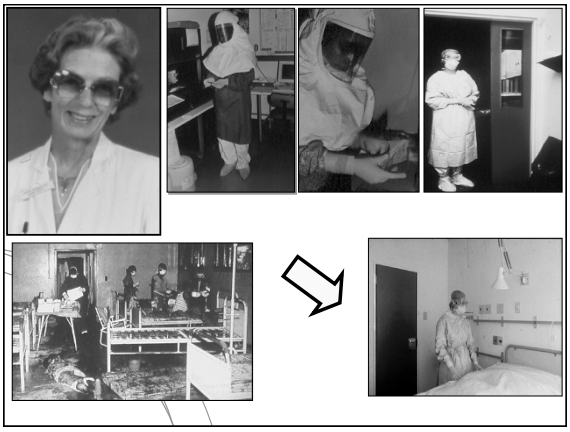

Disadvantages To Complex High-Level Containment Approaches:

- Systems may hinder patient care e.g. Racal respirators
- Personnel must be trained to function safely & effectively
- Expensive
- **NOT AVAILABLE TO PRIMARY & SECONDARY HCWs WHO ARE (OFTEN) THE FIRST TO HAVE CONTACT WITH A SUSPECTED VHF CASE**
- Paradoxically may increase the risk of exposure (parenteral & other).

General Principles 4:

- Limit Staff exposure. (Ideally) dedicate senior, willing, and more experienced Staff as far as possible. Keep nursing shifts short (4 hours)
- Warn and educate all relevant personnel involved in HC delivery. Do not forget auxiliary services, including the laboratory
- Limit laboratory tests to the minimum & negotiate times of processing of samples
  - FBC, Hb, platelets, coagulation studies
  - LFTs: ALT & AST only
  - Blood cultures, CSF, & peripheral blood smears mandatory (& other, if indicated)
  - Serological and viral investigations
  - Other tests: discuss & arrange with Laboratory

General Principles 5:

- Set up a representative & suitably qualified outbreak response Team. Avoid: (i) impracticalities, (ii) multiple policies, and (iii) mixed messages – National, Regional and Local experts must all be on the same track
- Define and classify (high-, medium-, low-risk) and identify contacts (contact tracing) and monitor appropriately ('surveillance quarantine') - 21 days after last contact
- Implement social mobilization and education of general public and ACCURATE, HONEST, RESPONSIBLE information via the media – establish a hotline and an operations centre

General Principles 6:

- Continuously EVALUATE efficacy of IP&C interventions introduced – accept you may be wrong. Either way, criticism & judgment are inevitable!
- Beware of case definitions that are too wide and of denominators that are incorrectly defined. Does it all make biological & epidemiologic sense?
- Strict enforcement of port health regulations in patient transfer across international border is required
- Remember each outbreak has its own peculiarities: clinical; biological; personal vs. political vs. public health agendas; public health- related deficiencies, etc.

VHF Isolation Precautions In a Nutshell:

- Isolation of the patient (negative-pressure cubicles generally unavailable)
- Reinforcement of standard & contact precautions
- Enhanced VHF PPE – contact precautions to include aerosols, i.e. skin & mucous membrane protection
- Safe disinfection of spills, equipment & supplies (do not alter hospital cleaning & disinfection policies on basis of 'perceived' risk. Rather ensure that they are strictly enforced)
- Monitoring – from 'cradle-to-grave' of disposal of medical hazardous waste
- Thorough terminal cleaning and decontamination of patient's room, medical equipment used, etc.
- Safe **handling** (esp. 'last offices') and burial of corpses
- Education to family members & advice regarding sexual activity to patient & intimate partner

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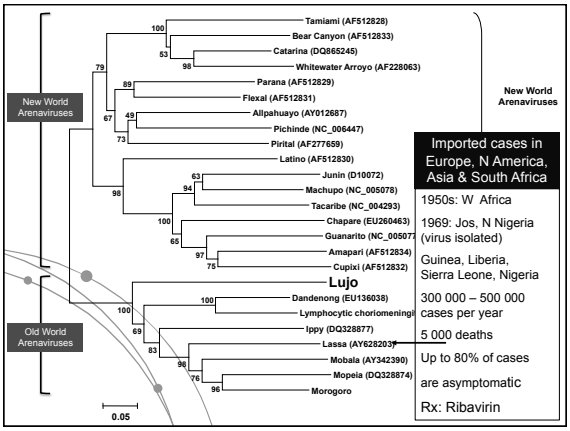
Arenaviruses:

- Negative-sense single stranded RNA viruses; most cause chronic infection in rodents (reservoirs) & excreted from urine; > 20 species identified
- Human transmission: from contaminated food / household items / ? dust; and contact with infected blood & body fluids
- Classified as: (i) Old World (prototype: lymphocytic chorio-meningitis (LCM) virus. Africa: Lassa fever; Ippy, Mobala & Morogoro - not pathogenic in humans; & (ii) New World arenaviruses. South America: e.g. Junin; Machupo, etc.



Courtesy:
Dr L Blumberg

On Sunday, 26 January 1969, Laura Wine died at the Bingham Hospital in Jos, Nigeria, the first recorded victim of a vicious new killer virus – Lassa Fever. Eight days later the nurse who had attended her, Charlotte Shaw, began to notice severe back and leg pains and a slight headache. Her temperature rose alarmingly quickly. A macular rash discoloured the skin of her face, neck and arms. Strange ulcers appeared in her throat, swellings, then a marked drop in blood pressure – in eleven days she, too, was dead. When another nurse, Penny Pinneo, developed similar symptoms shortly afterwards, it was decided to make ...

Lassa Fever: The High Price Of Poor Medical Practice

- 1989: 2 hospital outbreaks in Imo State (southern central Nigeria) **BMJ 1995;311:857-859**
  - Among 34 cases: 20 patients, 6 nurses, 2 surgeons, 1 physician, son of a patient (65% mortality)
  - Most cases exposed in hospitals (attack rate in one hospital 55%)
  - Both hospitals inadequately equipped & staffed, with poor medical practice: parenteral drug rounds with sharing of syringes fuelled the epidemic; staff infected during emergency surgery and during health care delivery

The Novel Old-World Arenavirus ('Lujo' v) Outbreak in RSA: September-October 08:

- Nosocomial outbreak following transportation of primary case from Zambia to South Africa
- Epicenter: Private hospital in Sandton, Gauteng
- Primary case: Safari tour agent (1)
- Secondary cases: Paramedic (2), nurse (3), cleaner (4)
- Tertiary case: Nurse (5)

Case Definitions:

Suspected case :

- Acute onset of documented fever (an oral temperature ≥38 ºC, or axillary temperature of ≥37.5º C)

AND

- Has a history of direct/close contact with one of the confirmed arenaviral cases in the current cluster (in the 21 days after the onset of illness in these cases)

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Case Definitions:

- Probable case:
  - A suspected case
  - History of a direct contact with one of the confirmed arenaviral cases, PLUS ONE OR MORE of the following:
    - Thrombocytopenia - presence of small skin and mucous membrane hemorrhages (petechiae) OR a platelet count of 150-100X10 / L, AND/OR
    - Raised transaminases: AST ≥100 u/l & ALT ≥ 100 u/l, AND/OR
    - Organ (or multi-organ) failure
    - Evidence of bleeding

Case Definitions:

A confirmed case is determined by definitive positive laboratory tests for Arenavirus, as confirmed and reported by the NICD & collaborating partners

Summary Of Case Histories:

- Primary case (Case 1)
  - 33-year-old female
  - Safari-booking agent resident in Lusaka
  - Arrived at a Sandton private hospital in South Africa (air-evacuated) for medical care on 12 September 2008
  - Critically ill, with diagnosis of (& treated for) African tick-bite fever (eschar noted on R foot)
  - Died 14 September 2008
  - Source of infection undetermined

Case Histories - Secondary Cases:

- Case 2
  - 33-year-old male; Paramedic
  - Cared for primary patient (1) during air evacuation
  - Performed procedures such as nebulization, suctioning & manual ventilation of patient
  - A second paramedic (admitted for observation at the Sandton private hospital), responsible for ambulance transport of patient from airport to the hospital, stated that his colleague wore 'minimal' PPE & had described soiling with patient excreta on his forearms as he delivered care during air evacuation
  - Admitted on 27 September 2008 and died 2 October 2008

Case Histories - Secondary Cases:

- Case 3
  - 34-year-old female
  - Nurse
  - Cared for primary case (1) in intensive care unit
  - Nature of contact uncertain but had attended to, and cleaned the body of, primary case (1)
  - Admitted to a private hospital (Sir Albert Medical Centre) on 1 October 2008 and died on 5 October 2008

Case Histories - Secondary Cases:

- Case 4
  - 38-year-old female
  - Hospital Cleaner
  - Performed terminal cleaning of ICU room of primary case (1)
  - Cleaning *allegedly* involved spray washing of walls
  - Went to 2 public facilities (first, seen at CHBH and subsequently admitted to Leratong Hospital) then transferred and admitted to CMJAC VHF isolation unit on 5 October 2008
  - Died 6 October 2008

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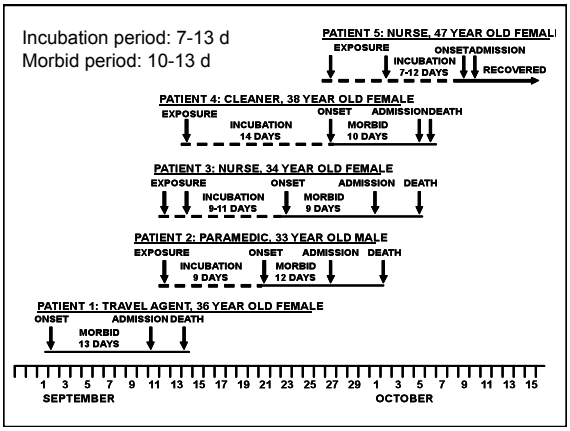
Case histories - tertiary case:

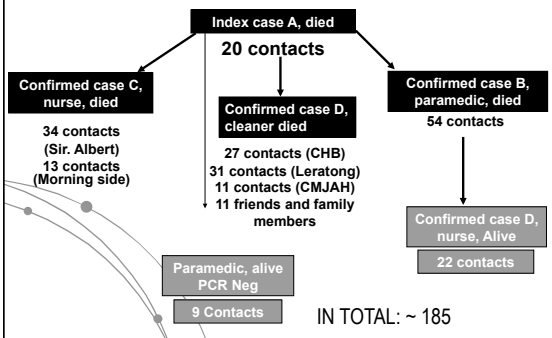
- Case 5
  - 47-year-old female
  - Nursing sister
  - Cared for paramedic (2)
  - Involved in traumatic insertion of central venous catheter
  - Became ill on 9 September 2008 and admitted to the Sandton private hospital on the 10 September 2008
  - Condition serious but stable
  - Treated with first oral then IV ribavirin
  - Discharged on 2 December 2009. Only survivor!

Exposures:

- Paramedic (2): was witnessed to have turned the primary case (1) without gloves in a Zambian hospital, prior to air evacuation - PIV dislodged & several drops of blood fell onto bed-sheet
- Cases 1-4: initially managed without special PPE (gloves donned when blood samples were collected and plastic apron worn) – HCWs & cleaners were potentially exposed to contaminated bedding, excreta & vomitus
- No known needle-stick / splash injuries were recorded
- Only case 5 was managed with full PPE , after which no further cases occurred

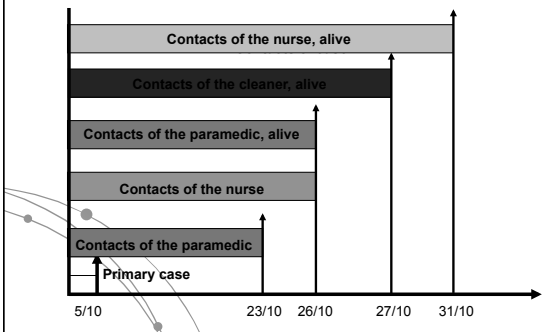


Chain Of Transmission:



IN TOTAL: ~ 185

Follow- up Of Contacts (n~185):



Functions Of The IP&C Team:

- Development of case & contact definitions & case assessment forms
- IP&C policy formulation
- IP&C audits of all facilities where suspected/confirmed cases were seen / admitted
- Assessment of suspected cases
- Manning of the VHF Ward at CMJAC
- Education about arenaviruses & training in correct use of PPE: Port Health, EMS personnel, HCWs & Laboratory personnel (> 1024 p)
- Counseling
- Distribution of PPE
- Monitoring of contacts at CMJAH & NHLS laboratories
- Laboratory biosafety
- Waste disposal audits

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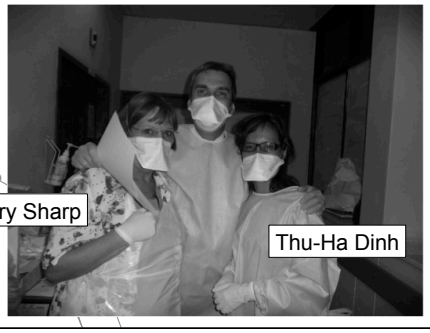
The Core Team:



Gerry Sharp

Thu-Ha Dinh

Tyvek oversuit / surgical scrub suits with impervious gowns & disposable balaclavas

Double-gloving

N95 respirators

Goggles/visors

Impervious overshoes

" I am sure that what any of us do, we will be criticized either for doing too much or for doing too little …. If an epidemic does not occur, we will be glad. If it does, then I hope we can say …. that we have done everything and made every preparation possible to do the best job within the limits of available scientific knowledge, **[>*AGD: availability of resources*<]** and administrative procedure."

US Surgeon General Leroy Burney, Meeting of the Association of State and Territorial Health Officers, August 28, 1957

THANK YOU !

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