Rift Valley fever outbreaks and the Middle east: forecasting, surveillance and control
Outbreaks of Rift Valley fever in Africa 2006-2007

- Background on RVF
- The 3 times of the strategy to detect and control RVF outbreaks
  - Forecasting
  - Surveillance
- Outbreak control

Epidemic and Pandemic Alert and Response
Rift Valley Fever
the virus
Rift Valley Fever distribution, outbreaks and spread

Major Outbreaks

Countries/Areas at risk

Spread of RVF
Rift Valley Fever history

- 1912, description of the disease in livestock in Kenya.
- 1931, RVF virus isolated by Daubney in Kenya.
- Until 1977, known in South and East Africa with severe epizootic in animals. In Human was describe as a benign disease (dengue like). Until 1975 only one human death was reported.
 Rift Valley Fever history

Since 1977

- Egypt 1977: 600 deaths, 2,000 case hosp., 20,000 infect°
- Mauritania Senegal 87,
- Madagascar 90, Egypt 93,
- Enzootic in West and central Africa
- 1997-98, Somalia, Kenya and Tanzania (flooding)
- 2000, Saudi Arabia and Yemen
- 2006-07, Somalia, Kenya and Tanzania
- 2007-08, outbreak in Sudan, isolated case in Comoros
Rift Valley Fever

- Family Bunyaviridae, genus Phlebovirus, RNA virus
- Vector = mosquitoes
- BSL 4 or 3
- Incubation 2-6 days
- Zoonosis
- Case Fatality Ratio 1-20%
- Vaccines Animal & experimental vaccine in Human
- Treatment symptomatic and specific:
  - Red cells, platelets, rehydration, electrolytic balance, intensive care.
Rift Valley Fever

Structure of Bunyaviridae particle

L: RNA polymerase
N: nucleoproteins
G2: glycoprotein 2
G1: glycoprotein 1

L: Lipid envelope
M
S

80-120 nm

Epidemic and Pandemic Alert and Response
Rift Valley Fever: transmission

- **Transmission**
  - Most human infections due to direct or indirect contact with infected animal blood or organs (e.g. liver, spleen) (farmers, slaughtering house, veterinarians, etc…)
  - Laboratory infection frequent
  - No person to person transmission have been documented

- **Amplification**
  - Natural reservoir unknown
  - Amplification during epizootics in animal: cattle, sheep, goats, camels
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Rift Valley Fever: transmission
Rift Valley Fever: transmission

Veterinarians
Animal autopsy

Herdsmen milking animal

Epidemic and Pandemic Alert and Response
Rift Valley Fever: transmission
Rift Valley Fever

different ecotypes
different transmissions
Rift Valley Fever outbreak response, Sudan
Rift Valley Fever outbreak response, Sudan
Rift Valley Fever outbreak response, Sudan
Rift Valley Fever outbreak response, Madagascar
Rift Valley Fever outbreak response, Madagascar

March 2008, Carion: 50 human confirmed cases
All exposed to one Zebu
Rift Valley Fever outbreak response, Madagascar
Rift Valley Fever outbreak response, Madagascar

May 2008, Antananarivo, Casoumange: 2 human confirmed cases in the capital city, both exposed to seven Zebu
Rift Valley Fever: transmission

Breeding sites flooded (Dambos)

- Aedes
- Anopheles
- Culex

Domestics
Animals

Human

Epidemic and Pandemic Alert and Response
Rift Valley Fever outbreak response, Sudan
Rift Valley Fever: transmission

Irrigation scheme

Domestics Animals Traveling from affected zones

Domestics Animals

Anopheles
Culex

Anopheles
Culex

Human

Epidemic and Pandemic Alert and Response
Rift Valley Fever outbreak response, Sudan
Rift Valley Fever: transmission

Madagascar Rice irrigation system

Domestics Animals traveling from affected zones

Anopheles Culex, Mansonia

Domestics Animals

Anopheles Culex

Human

Epidemic and Pandemic Alert and Response
Rift Valley Fever
the disease
Rift Valley Fever in Human

- 98% cases are unnoticed or develop a mild disease
- characterized by a feverish syndrome with sudden onset, flu-like fever, myalgia, arthralgia and headaches. Hyperleucocytosis is followed by a leucopenia.
- Some patients develop a neck stiffness, anorexia, photophobia, nauseas and vomiting; in its early stages RVF can be mistaken for meningitis.
- These symptoms last in general from 4 to 7 days, after which the antibodies can be detected (IgM and IgG) as well as the disappearance of the virus in the blood
Rift Valley Fever in Human

- Pregnant women: vertical transmission have been reported in Saudi Arabia with fatal outcome in a newborn.

From Arishi et al, Ann Trop Paed, 2006; 26:251
Rift Valley Fever in Human

- 2% of the cases are serious with complications:
  - **Ocular form** (most frequent, around 2% of the RVF cases): chorioretinitis, temporary blindness. Patients reported blurred or decreased vision
    - Chorioretinitis appears between one and three weeks after the first symptoms.
    - Symptoms resolved spontaneously within 10 to 12 weeks from the onset of systemic symptoms.
    - Macular retinitis, paramacular retinitis, and optic atrophy are the most frequent causes of visual loss in RVF.
    - When the optic disc is affected, there is a permanent fall of vision (50% of cases).
    - The deaths are rare.
Rift Valley Fever in Human

- **Ocular form** (most frequent):
● 2 % of the cases are serious with complications:

● **Meningo-encephalic form**: intense cephalgias and meningitides. Loss of memory, hallucinations, confusion, disorientation, vertigo, convulsions, lethargy, coma.
  
  ● Appears one to four weeks after the first symptoms.
  
  ● Neurological complications can appear later (> 60 days).
  
  ● The deaths are rare.
  
  ● Severe or residual neurologic deficit is common sequelae.
Rift Valley Fever in Human

- **Meningo-encephalic form:**

  NEUROLOGICAL COMPLICATIONS:
  Ijara district, Kenya 2007

  NEUROLOGICAL COMPLICATIONS:
  Ifakara district, Tanzania 2007
Rift Valley Fever in Human

- 2% of the cases are serious with complications:

  - **Hemorrhagic icterus form**: 2-4 days after the beginning of the disease, the patient presents the signs of a hepatic attack engraves with icterus and hemorrhages: vomiting of blood, blood in the saddles, petechiae, purpura (rash caused by cutaneous bleedings), menorrhagia, bleedings from the gums and venipuncture sites, ecchymoses of the skin.

  - Death between day 3 and 6 post-onset.
  - Miscarriage
  - Viraemia up to 10 days.
  - CFR around 50%.
Rift Valley Fever in Human

- **Hemorrhagic icterus form:**

BLEEDING FROM THE GUMS:
Kosti, Sudan 2007

BLEEDING FROM NOSE:
Sinnar, Sudan 2007
Rift Valley Fever in Human

- Hemorrhagic icterus form:

ICTERUS AND CONGESTED CONJUNCTIVITIS:
Monaqil, Gezira State, Sudan 2007
Rift Valley Fever in Human

- **Hemorrhagic icterus form:**

  - HEMORRHAGIC ICTERUS form:
    - Saudi Arabia 2000
  - HEMORRHAGIC ICTERUS form:
    - Kenya 2007
RVF in Human: Treatment

- Symptomatic: replacement of the blood volume and components, red cells, platelets, rehydration, electrolytic balance, intensive care, +/- antibiotics and/or antimalarial drugs

- Contraindicated: aspirin

- Warning: Ribavirin was employed in the treatment of confirmed cases of RVF during the 2000 outbreak in Saudi Arabia without success (unpublished data)
○ Inactivated TSI-GSD-200 developed by the Salk Institute. Three subcutaneous doses (0, 7 and 28 days) of 0.5 ml. Shown to be safe and immunogenic in human studies. Testing of this vaccine in 598 at-risk laboratory personnel from 1986-1997 showed only minor side effects in 3% of all vaccinees and good long-term immunity at 12-year follow-up.

○ Experimental MP 12 live attenuated vaccine (1 dose) development by NIAID. Open-label, single dose, phase II study ongoing to assess the safety, immunogenicity, and genetic stability of RVF MP-12 vaccine in humans.

○ Clone 13 and R566 in development.
Rift Valley Fever

Clinic in Animal

Epidemic and Pandemic Alert and Response
Rift Valley Fever in Animal

- **Sheep** are more sensitive.

- **Lambs**: fever + anorexia and high CFR around 100%.

- **Adults**: fever, muco-purulent throwing, melaena and CFR around 20%.

- The abortions are frequent in pregnant females, abortion rate in herds can reach 85%.

- Epizootics can last 6 to 8 weeks.
Rift Valley Fever in Animal

- **Sheep**: ~20-30% mortality, abortions (up to 85%)
- **Cattle**: ~10-15% mortality, abortions
- **Goat**: ~5-10% mortality, abortions
- **Camel**: low mortality, low viraemia, abortions.
- **African Buffalo** (*Syncerus caffer*): experimental inoculation, survive, low viraemia, abortions
- **Other African ungulates**: antibodies, symptoms?

- Mortality depends on breeds, other health and stress factors.
- Infections of adult animals end in death if viremia high.
- Immature animals have higher viraemia and mortality.
- Abortion seems to be a complication of most viremic infections.
Rift Valley Fever in Animal

Epidemic and Pandemic Alert and Response
Rift Valley Fever in Animal

Hepatic Syndrome: vasculitis and necrosis of liver

Intestine: hemorrhages and petechia
RVF in Animal: vaccines

- Smithburn, MVP12. Lifelong immunity but only partially attenuated. Responsible for abortions.
- Inactivated vaccine is expensive and requires 2 injections for prime boost and booster every year.
- Real danger of needle propagation during mass vaccination operations
- Vaccination cost effective for exotic breeds
- Long term strategy possible in exotic breeds
RVF in Animal: vaccines

- Are RVF forecasting analysis good enough to drive cost effective vaccination strategies?
- Problem of availability of vaccine.
- Prospects of new vaccines clone 13 or R566
Rift Valley Fever
From forecasting to outbreak control
Rift Valley fever outbreak alert and response

Epidemic and Pandemic Alert and Response

- Animal outbreak
- Human outbreak

Number of Cases

TIME

Climate
Vegetation

Amplification

Human outbreak

Animal outbreaks
Rift Valley fever outbreak alert and response

- **Animal outbreak**
- **Human outbreak**

- **Late Detection**
- **Delayed Response**

- **First cases In Animals**

- **Amplification**

- **Control Opportunity**

**Epidemic and Pandemic Alert and Response**

[FAO logo]
[World Health Organization logo]
Rift valley fever outbreak alert and response

**Forecasting Readiness**

- Early Detection
- Mass Animal Vaccination

**Rapid Response**

- Amplification

**Control Opportunity**

Epidemic and Pandemic Alert and Response
Surveillance et contrôle de la FVR

1. Before
2. During
3. After

Epidemic and Pandemic Alert and Response
1. General strategy to MITIGATE RVF outbreaks

- RVF outbreaks are closely coupled with above normal rainfall periods and in East Africa, with the El Niño/Southern Oscillation (ENSO) event.

- **Forecasting**: forecasting models and early warning systems based on satellite images and weather/climate forecasting data for Rift valley fever have been successfully developed. They provide
  - accurate forecasting data that can predict emergence of RVF 2 to 4 months in advance

- **Animal Health**: efficient veterinary public health services capable of implementing emergency mass animal vaccination prior to the beginning of the epizootic.
1. General strategy to MITIGATE RVF outbreaks

- **Animal Health**: efficient veterinary public health services capable of implementing emergency mass animal vaccination prior to the beginning of the epizootic.

- Authorities to prepare in case of an epidemic:
  - Inform public / health education / **social mobilization**
  - Standard precautions in health care settings.
  - Heighten animal and human **surveillance + diagnostic**
  - Strengthen Human and Animal health collaboration

- Implement appropriate **vector control** program based on entomological surveys
2: General strategy to CONTROL RVF outbreak

- Establish **co-ordination** mechanism for response
- Inform public / health education / **social mobilization**
  - Restrict practices that promote transmission and source of infection
- **Partnership with media**
- **No Human-to-Human transmission** reported
  - Standard infection control practices.
  - Establish RVF ward or harm reduction strategy at home
  - Safe and Humane **case management**
  - Conduct safe funerals that allow the process of mourning.
  - Psychosocial support (patients, families, HCW).
2. General strategy to CONTROL RVF outbreak

- Establish active **surveillance** system
  - Identify new cases. Follow-up clinical complications (ocular, neurological, haemorrhagic)
  - Stop human source of infection: link with animal surveillance
- Implement appropriate **vector control** program based on entomological surveys
- **Animal Health**:
  - Restrict animal movement from epizootic areas to clean areas
  - Control slaughtering activities – at home, and in facilities
  - Do not vaccine in epizootic areas.
2. General strategy to **CONTROL RVF outbreak**

**International Organizations**
- Inform member states FAO, WHO and OIE.
- +/- WHO recommendations on travel (IHR 2005)
- +/- OIE recommendations on animal trade
3. General strategy to AFTER RVF outbreaks

- To announce the end of the epidemic and ensure follow-up with press coverage.
- To evaluate outbreak management
- To work out an end of the outbreak report
- To file outbreak documents in archives
- To go back to surveillance activities of the pre-epidemic phase
  - Monitoring of the climatic data
  - Monitoring of the human and animal epidemics
Rift Valley Fever Forecasting
HoA climatic and ecological conditions and RVF outbreak sites Sept 2006 to May 2007

Mapping of the RVF human case locations shows that

- 64% of the cases were reported in areas at risk within the RVF potential epizootic area,
- 36% were reported in areas not thought to be at risk of RVF activity
Madagascar climatic and ecological conditions and RVF outbreak sites Sept 2007 to May 2008

- Red: RVF Risk Area
- Green: RVF Potential Epizootic Area
- Yellow: Outbreak identified as Non-Risk
- Blue: Outbreak identified as Risk

Epidemic and Pandemic Alert and Response
Rift Valley Fever forecasting limitations (1)

- when should FAO WHO Alert the countries?
  How to interpret RVF monthly risk maps:
  only 1 big outbreak (2006-07) in 7 years

- Could model framework be improved with good field data, soil type, elevation, vector ecology maps...

- models are mapping risk for Arbovirus emergence (not only RVF)
Rift Valley Fever forecasting limitations (2)

- model apply well in East and South Africa, more difficult in West Africa

- RVF warning given 2 months in advance
  BUT we need a 6 month period between Forecasting Alert and outbreak to allow mass animal vaccination
Rift Valley Fever Surveillance
RVF 2007 Horn of Africa outbreaks

Kenya, Somalia, Tanzania: >100,000 estimated cases, 923 reported cases including 234 deaths
Rift Valley Fever surveillance

- Animal RVF surveillance: weak to very weak. Need to recognize and declare
- Human surveillance: sentinels?
- GLEWS, GPHIN at international level
- Laboratory confirmation needed
- Who want to declare to OIE, FAO and/or WHO?
Rift Valley Fever
Outbreak control
Rift Valley Fever outbreak control

**Animal Health**

- Need a good immunity and safe RVF vaccine, available before outbreaks
- A better understanding of RVF disease and its epidemiology in animals
Rift Valley Fever outbreak control

**Human Health**

- RVF standard infection control practices: consider as a blood born pathogen. Blood safety, injection safety, uninterrupted supply.

- Early clinical diagnosis for early treatment: field guidelines for RVF clinical diagnostic (signs, symptoms, biochemistry, haematology, patient history).

- SOPs for treatment of different forms of RVF

- Need for new antiviral drugs
Rift Valley Fever outbreak control

**Human Health**

- RVF standard infection control practices: consider as a blood born pathogen. Blood safety, injection safety, uninterrupted supply.

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- Treatment for the different forms of RVF

- Need for new antiviral drug

Epidemic and Pandemic Alert and Response
Rift Valley Fever outbreak control

Social Mobilization

- The social and cultural aspects are usually underestimated or neglected when they are key. The support of medical anthropology is highly beneficial.
Rift Valley Fever outbreak control

FADIANA NY MIKITIKA NY "RA SY NY TAOVANKENA" RAHA TSY MISY FIAROVANA
Rift Valley Fever outbreak control

La fièvre de la vallée du Rift, « mieux vaut prévenir que guérir ! »

La fièvre de la vallée du rift a été identifiée à Mayotte sur le bétail. Cette maladie peut être transmise à l’homme. Chez l’homme, la maladie est souvent inapparente. Dans le cas contraire, les symptômes s’apparentent à ceux de la grippe. Il peut cependant exister, rarement, des formes plus graves, hémorragiques, oculaires ou neurologiques.

Comment se transmet la fièvre de la vallée du Rift ?
- au contact du bétail infecté
- par ingestion de viande mal cuite et de lait cru ou caillé
- par piqûre de moustique

Que faut-il faire pour se prémunir de cette maladie ?
- Pour les personnes pratiquant des abattages de zébus, de chèvres ou de moutons,
  - se protéger : port de masques, lunettes et gants
  - Assurer une meilleure saignée des animaux : suspendre les carcasses et les nettoyer avec de l’eau potable
  - Se laver les mains avec du savon

- Pour l’alimentation,
  - bien cuire la viande
  - faire bouillir le lait
  - Ne pas consommer le lait caillé

- Pour les piqûres de moustiques,
  - éliminer les lieux de ponte
  - éviter les piqûres de moustiques

Le Préfet communiqué
Rift Valley Fever outbreak control

Vector Control

● What's New?

● Integrated approach

● When?
Rift Valley Fever outbreak control

**Laboratory**

- In the field support Animal surveillance and Human case management

- Support establishment of Regional reference laboratories and National lab capacities:

- Support international reference laboratories WHO-CC, FAO and OIE.
Rift Valley Fever outbreak response, Sudan

- **Laboratory:** NAMRU-3 was deployed in Kosti (PCR) for 5 days and in Khartoum (IgM by ELISA) for 7 days. NAMRU-3 confirmed 16/47 human cases in Kosti and Khartoum labs.
Rift Valley Fever
Lessons Learnt
Outbreaks of RVF from forecasting to control

- Need for an integrated approach and more collaboration between MoH, MoA, Vet Services (animal data)

- **Forecasting.** Several RVF Alerts send to countries and Regions

  \[\Rightarrow\] RVF outbreaks forecast (2003, 2006, 2007) BUT

  - Only some countries take appropriate measures, prepare outbreak response team and vector control program

  - Need for a more systematic way of sharing forecasting maps with countries (web site is not enough)

  - Alert message is not enough \(\Rightarrow\) Forecasting field team.

  - Need to improve forecasting model (knowledge in ecology, Indian Ocean Dipole, database of outbreaks, generating risk maps, bioclimatic zones...)

Epidemic and Pandemic Alert and Response
Outbreaks of RVF from forecasting to control

- **Surveillance**: need a better animal surveillance based on stronger veterinary services, national laboratory capacities

- **Animal Vaccination strategy**: safe, immune, available before outbreaks. Need Vet Services able to implement mass vaccine campaigns

- **New vector control** approach?

- **Case management and treatment**: need for new antiviral drugs
Outbreaks of RVF from forecasting to control

International: at global level OIE FAO and WHO do have a common strategy, from Forecasting to Outbreak response:

- need for SOPs for RVF from forecasting to outbreak containment: One Health, One Message
- preparedness guidelines for occupational health (e.g. how to protect slaughtering house personnel in different technology settings)
- field lab for human + animal health / outbreak response
Outbreaks of RVF from forecasting to control

Rainfall Prediction from APCC

Multi-Model Probabilistic MME for Precipitation

- Increasing rainfall
- Reduce rainfall

Forecast Method: GAMS
Anomaly fields are displayed
Hindcast Period: 1983 to 2002

© APEC Climate Center created: 08/16/07

Epidemic and Pandemic Alert and Response
Outbreaks of RVF from forecasting to control

Adapted from Tebaldi et al. (2006), in Bilan des changements climatiques, groupe d’Expert intergouvernemental sur l’évolution du climat (GIEC), Rapport 2007, groupe de travail 1
Outbreaks of RVF from forecasting to control

Precipitation increase + dry days increase = RVF epidemiology may change

Adapted from Tebaldi et al. (2006), in Bilan des changements climatiques, groupe d’Expert intergouvernemental sur l’évolution du climat (GIEC), Rapport 2007, groupe de travail 1
Thank You

Ministry of Health and Ministry of Agriculture Kenya
Ministry of Health and Ministry of Agriculture Madagascar
Ministry of Health and Ministry of Agriculture Somalia
Ministry of Health and Ministry of Agriculture Senegal
Ministry of Health and Ministry of Agriculture South Africa
Ministry of Health and Ministry of Agriculture Sudan
Ministry of Health and Ministry of Agriculture Tanzania

Bob Swanepoel, NICD; Assaf Anyamba, NASA/GFSC; Tom Ksiazeck and Pierre Rollin, CDC Atlanta; Nilesh Buddha WHO Sudan, Maalim Dabar WHO Kenya, H ElBushra EMRO, JM Reynes IP Madagascar,…

KEMRI-CDC in Nairobi, Kenya; NAMRU-3 in Cairo, Egypt; Institut Pasteur Sénégal;
Institut Pasteur Madagascar; NICD South Africa;

Médecins Sans Frontières

World Animal Health Organization (OIE), Paris, France.