Rift Valley fever outbreaks in Africa and Middle east: forecasting, surveillance and control

RVF Workshop

P. Formenty and S. De la Rocque – 27 January 2009
Cairo, Egypt

Epidemic and Pandemic Alert and Response
Rift Valley fever outbreaks

● Background on RVF
● The 3 times of the strategy to detect and control RVF outbreaks
  ● Forecasting
  ● Surveillance
  ● Outbreak control
Rift Valley Fever

the virus
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 described as a benign disease (dengue like). Until 1975 only one human death was reported.
Rift Valley Fever history

Since 1977

- Egypt 1977: 600 deaths, 2000 cases 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, Sudan, Comoros, Madagascar
- 2009, Madagascar

Epidemic and Pandemic Alert and Response
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

Lipid envelope

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

80-120 nm
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…)

Mosquito bites: *Aedes caballus, A. theileri, A. circumluteolus, Culex pipiens, Eretmapodites spp.*

Laboratory infection frequent

No person to person transmission has been documented

**Amplification**

Amplification during epizootics in animal: cattle, sheep, goats, camels
<table>
<thead>
<tr>
<th>Genus (Subgenus)</th>
<th>Species</th>
<th>Locality (year)</th>
<th>Reference</th>
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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, 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)

Domestics
Animals

Aedes

Anopheles - Culex

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

Anopheles Culex

Domestics Animals

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

Domestics Animals

Anopheles Culex, Mansonia

Human

Anopheles Culex

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, nausea 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):

  BILATERAL BLINDNESS: Ijara district, Kenya 2007

  OCULAR RVF: MACULAR SCARRING
  From Madani et al, CID, 2003;37:1084
Rift Valley Fever in Human

- 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)
RVF in Human: Vaccines

- 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 Animals
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
- Are veterinary services capable of implementing safely mass vaccination campaigns?
Rift Valley Fever
From forecasting to outbreak control
Rift Valley fever outbreak alert and response

- Animal outbreaks
- Human outbreaks

Time

Number of Cases

Climate
Vegetation

Amplification

Animal outbreaks

Human outbreak

Epidemic and Pandemic Alert and Response
Rift Valley fever outbreak alert and response

- Animal outbreak
- Human outbreak

First cases in Animals

Amplification

Late Detection

Delayed Response

Control Opportunity

Number of Cases

0 10 20 30 40 50 60 70 80 90

Time

-40 -35 -30 -25 -20 -15 -10 0 5 10 15 20 25 30 35 40

Epidemic and Pandemic Alert and Response

FAO

World Health Organization
Rift valley fever outbreak alert and response

Forecasting Readiness

Early Detection

Rapid Response

Control Opportunity

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

1. Before
2. During
3. After
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 develop. 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

- 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

RVF Potential November 2006

- RVF risk areas
- RVF endemic regions
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.
Sudan climatic and ecological conditions and RVF outbreak sites May to November 2007

Mapping of the RVF human case locations shows that:
● 50% of the cases were reported in areas at risk within the RVF potential epizootic area,
● 50% were reported in potential epizootic areas not thought to be at high risk of RVF.
Madagascar climatic and ecological conditions and RVF outbreak sites Sept 2007 to May 2008

- RVF Risk Area
- RVF Potential Epizootic Area
- Outbreak identified as Non-Risk
- 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 forecasting: general pathway

El Nino / IOD

Rainfall

Vegetation growth + floods

Vector population increase (from primary focal areas)

Increased RVF circulation in animals

Implication of other vectors

Vector dispersal

Animal movements

Full extent of the RVF epizootic
Rift Valley Fever forecasting: questions?

- Climate-based risk forecast
- NDVI-based risk forecast
- Flood-map based risk forecast
- Wind-based dispersion risk forecast
Rift Valley Fever forecasting: questions?

Outbreaks / animal cases, human cases?
- Primary cases or Secondary cases?

Vector distribution?
- Some vectors implicated in maintaining RVF in inter-epidemic periods
- Some vectors implicated in epizootic conditions
- Is this homogeneous across Africa, or are there regional variations?

Risk area is dynamic
- Focal in inter-epizootic period
  - Starts from areas that combine abnormal vegetation growth and floods
  - Artificial flooding through irrigation practices (semi-permanent vector breeding areas)
- Expands during epizootic period, because
  - New vectors may become implicated
  - Animals movements, migrations
  - Vectors may move over some distances
Rift Valley Fever forecasting: questions?

At which spatial scale are we mapping the risk
- Focal areas where it would start should the next abnormal rain arrive?
- Large Areas where it would spread in epizootic conditions?
- Potential epidemic mask <-> statistic map of probability of occurrence

Temporal scale
- What are the operational expectations?
- What is technically feasible: Forecasting: 6 months?

Spatial
- How can we deal with the uncertainty in spatial definition of the epidemiological data themselves?
- What is the resolution at which dissemination of risk mapping outputs is appropriate given:
  - Animal and Vector movements
  - Intervention and needs of end-users: MoH, MoL, MoA.
Rift Valley Fever Model

- Statistical models are very prone / data availability
- Inclusion of rainfall <-> temporal resolution of products and risk ranking
- primary outbreak sites and RVF mask

Probability of suitability

- NOAA AVHRR -
  - MIR
  - LST
  - NDVI
  + DEM
  as predictors (NO rainfall!).

Epidemic and Pandemic Alert and Response
Rift Valley Fever Surveillance
RVF 2007 Horn of Africa outbreaks

Kenya, Somalia, Tanzania: >100,000 estimated cases, 923 reported cases including 234 deaths
Cases of RVF in Kenya, meeting inclusion criteria, by Province and onset of symptoms, December 2006 – March 2007 (n = 607 cases).
Rift Valley Fever, Tanzania 2007

Cases of RVF in Tanzania, by date of onset of symptoms (estimated for 104 cases) and Region, January to April 2007 (n = 333 cases).
Rift Valley Fever, Sudan 2007-08

Cases of RVF reported in Sudan, by date of reporting from week 48/2007 to week 4/2008 (n = 738 cases).

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<th>Week of onset</th>
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Cases: 738, Deaths: 230, CFR: 31%

MoAR report to OIE

Joint Investigation MoAR, MoH, FAO, WHO

20 December Eid Al-Adha festival

First Rumours Human cases

White Nile, Sennar, Gazeera
Cas de FVR rapportés à Madagascar, par date de début des symptômes du 1er Janvier 2008 au 1er Mai 2008, (n = 72 cas confirmés).

- Cas confirmés
- Carion (50 cas confirmés)
- Ambongamarina (87 cas suspects)
- Mandialaza (149 cas suspects)

Premier cas Homme RVF+ Mandialaza

Premier cas Homme RVF+ Taolagnaro

Presse décès Animaux-Homme Mandialaza

Déclaration OIE

Déclaration OMS

Joint FAO/OMS

Epidemic and Pandemic Alert and Response
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

The Citizen 28 March 201
WELCOME CUSTOMER THAT IS THE RVF MEDICINE.

The Citizen 28 March 201
WELCOME CUSTOMER THAT IS THE RVF MEDICINE.

The Citizen 28 March 201
WELCOME CUSTOMER THAT IS THE RVF MEDICINE.

The Citizen 28 March 201
WELCOME CUSTOMER THAT IS THE RVF MEDICINE.
Rift Valley Fever outbreak control

Animal Health

● Need a good immunity and safe RVF vaccine, available before outbreaks

● Good Vet services able to implement safe mass vaccination campaigns

● A better understanding of RVF disease and its epidemiology in animals (Bird and al., JoV 2008, Multiple virus lineages sharing recent common ancestry were associated with a large Rift Valley Fever outbreak among livestock in Kenya during 2006-07)
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

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" RAILA TSY MISY FIAROVANA
Le Préfet communique

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 prévenir 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 faire 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

République Française
Rift Valley Fever outbreak control

Vector Control

- studies to understand vector capacity to transmit RVF virus and its implication in animal and human epidemiology
- New vector control strategies?
- Integrated approach
- When?

Epidemic and Pandemic Alert and Response
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.

RT-PCR pos.

RT-PCR neg.
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. RVF 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)
  - 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

Precipitation intensity

(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

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Médecins Sans Frontières

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