HEALTHCARE WORKERS GUIDELINES

ON

RIFT VALLEY FEVER (RVF)

Developed by:
The National Institute for Communicable Diseases (NICD),
a division of the National Health Laboratory Service (NHLS)

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Table of content

Disclaimer

This guideline is intended for use by healthcare professionals. While the greatest care has been taken in the development of this document, the National Department of Health and the National Institute for Communicable Diseases (NICD) of the National Health Laboratory Services (NHLS) do not accept responsibility for any errors or omissions. All healthcare professionals should exercise their own professional judgement in interpreting and applying the information presented in this guideline.

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1. Introduction and situation update

A large Rift Valley fever (RVF) outbreak occurred in South Africa during 2010. At least 14 342 animal cases, including 8 877 animal deaths were laboratory-confirmed across 8 of the 9 South African provinces (i.e. all except for KwaZulu-Natal Province) from February to August 2010. During this period, the NICD-NHLS confirmed a total of 238 human infections, including 26 human deaths. However, these figures represent only the laboratory-confirmed RVF cases, and only symptomatic persons meeting the case definition underwent testing. It has been estimated that ≥80% of RVF infections are asymptomatic or unapparent, and our laboratory-testing strategy and case definition would not have detected such cases. Therefore, we cannot make inferences as to the true incidence of severe disease or calculate an accurate case fatality rate since we lack a reliable denominator.

Preliminary data suggests that approximately 82% of these cases worked within occupations where direct contact with animals frequently occurs. Furthermore, 94% of cases reported a history of direct contact with RVF-infected animals prior to onset of symptoms. Human infections via mosquitoes and raw (unpasteurised/uncooked) milk were noted infrequently.

A decline in RVF transmission was noted during the colder winter months of 2010. Nevertheless, there is much concern over a possible re-emergence of the outbreak in previously affected areas accompanying the recent seasonal increase in temperature and rainfall. Therefore, all healthcare workers must be aware of RVF and be vigilant for patients who meet the case definition, and in such instances submit specimens to the NICD-NHLS for laboratory testing.

2. What is Rift Valley fever?

RVF is a zoonotic mosquito-borne viral disease of domestic and wild ruminants that can cause severe disease in a small proportion of infected humans. The virus is from the family *Bunyaviridae* (genus *Phlebovirus*) and causes outbreaks of abortions and deaths of young livestock (predominantly sheep, goats and cattle). The disease occurs throughout Africa and Middle East Asia when exceptionally heavy rains favour the breeding of the mosquito vectors. In RVF outbreaks occurring in east or southern Africa, humans become infected primarily from contact with infected tissues of livestock or wild (game) animals, and less frequently from mosquito bites. The mosquitoes which transmit the virus (*Aedes* and *Culex* mosquitoes) are present in South Africa; however, these species generally prefer to feed on livestock outdoors at night.

3. Previous outbreaks of RVF in South Africa

Cases of human RVF infections generally occur in the context of major outbreaks of disease in sheep, cattle and goats characterised by abortions and deaths of young animals. Outbreaks occur at irregular intervals of years following heavy rains that favour breeding of the mosquito vectors of the causative virus, and can recur over a succession of unduly wet seasons, but may not be seen for decades during drier spells.

The last major outbreak of RVF on the interior plateau of South Africa occurred in 1974-76 during prolonged heavy rains. Since then, sporadic outbreaks and human infections have been documented within KwaZulu-Natal, the Kruger National Park, Limpopo, Gauteng, North West, and Northern Cape provinces. During 2008 and 2009, relatively small focal RVF outbreaks were observed across Mpumalanga, Limpopo, Gauteng and North West provinces. These outbreaks affected both domestic livestock and wildlife. A number of human infections were identified among individuals in direct contact with the affected livestock (incl. farmers, farm workers, and animal health personnel).

4. How is it transmitted to humans?

- Direct or indirect contact with the blood or tissues of infected animals (the most common route of transmission in South Africa). This may include:
    - handling of animal tissue during slaughtering, butchering or skinning of animals,
    - assisting with animal births,
    - conducting veterinary procedures, and/or
    - disposal of carcasses or foetuses.

- Less common modes of transmission include:
    - inoculation, for example via a wound from an infected knife or needle-stick injuries or contact with broken skin,
    - inhalation of aerosols produced during the slaughter/necropsy of infected animals,
    - bites of infected mosquitoes (most commonly *Aedes*), and/or
    - consuming raw (unpasteurised or uncooked) milk from infected animals.

- No human-to-human transmission has ever been documented.

Occupational groups such as herders, farmers and farm workers, abattoir workers and veterinarians/animal health workers are at especially high risk of infection.

5. When should RVF be suspected as a cause of illness? Case definition & criteria for laboratory testing

A suspected case is defined as any person meeting **one or more** of the following criteria:

1. A person belonging to a high risk category and presenting with an influenza-like illness (which may include fever, myalgia, arthralgia or headache),
2. A person belonging to a high risk category and presenting with features of encephalitis, haemorrhage, hepatitis and/or ocular pathology (retinitis) ± fever, **OR**
3. A person with unexplained encephalitis, hepatitis or haemorrhagic illness residing in an area where RVF can potentially occur.

High risk categories include:

1. Recent close contact with livestock/game animals in or from RVF-affected areas, including:
    - Slaughtering and butchering (traditional or commercial),
    - Disposal of carcasses/foetuses,
    - Assistance with birthing or other animal husbandry activities resulting in exposure to animal blood and body fluids, and/or
    - Veterinary procedures and necropsies.
2. Residing in an area where RVF is known to occur or has the potential to occur, with a history of recent mosquito bites.
3. Consumption of raw (unpasteurised/uncooked) milk sourced from RVF-affected areas.

Note: other causes for these symptoms must be excluded where appropriate, to facilitate timeous treatment and appropriate infection prevention and control measures for other infections, including: malaria, Crimean-Congo haemorrhagic fever (CCHF) and tick-bite fever. Obtaining a thorough history including other signs and symptoms, recent travel, insect (e.g. tick) exposures, contact with livestock/game animals etc. will assist healthcare workers in narrowing the differential diagnosis.

6. What are the clinical features in humans?

Typically, illness is asymptomatic or mild in the vast majority of infected persons, with a small proportion experiencing severe disease. The true overall mortality rate following RVF infection is difficult to estimate given that case definitions and laboratory testing methods used in the various documented outbreaks differed significantly. Although the World Health Organization (WHO) Rift Valley fever fact sheet states an overall mortality rate of <1%, mortality rates noted in documented outbreaks range from <1% to 45%. The greatest number of laboratory-confirmed human cases in a single outbreak was recorded in the Saudi Arabian RVF outbreak during 2000, where the case fatality rate was 14.2%.

Mild illness

- The incubation period (interval from infection to onset of symptoms) for RVF varies from two to six days.
- Clinically, it presents as a fever with flu-like symptoms (including myalgia, arthralgia and headache).
- Some patients may also develop neck stiffness, sensitivity to light (photophobia), pain behind the eyes, loss of appetite and vomiting; in such patients the clinical presentation may be mistaken for meningitis.
- Symptoms of RVF usually last from four to seven days, after which time the immune response becomes detectable with the appearance of antibodies and the virus gradually disappears from the blood.

Severe illness

A small percentage of patients develop a much more severe form of the disease, which can manifest as one or more of the following complications:

- **Ocular disease (retinitis):** This may occur in up to 10% of infected patients. Onset of retinitis is usually one to three weeks after appearance of the first symptoms (which may be very mild or subclinical), and usually presents as painless blurred or decreased vision, or scotomata. It may resolve within 10 – 12 weeks with no sequelae. If lesions occur in the macula, up to 70% of patients will experience permanent loss of vision.
- **Meningoencephalitis:** The onset of meningoencephalitis usually occurs one to four weeks after the first symptoms (which may be very mild or subclinical) of RVF appear, and in some cases neurological complications can manifest >60 days after the initial symptoms of RVF. Clinical features may include: intense headache, loss of memory, hallucinations, confusion, disorientation, vertigo, convulsions, lethargy and coma. Although the mortality rate in patients who experience only this form of the disease is low, residual neurological deficit, which may be severe, is common.
- **Hepatitis:** This is characterised by markedly raised transaminase enzyme levels (ALT and AST), and may occur together with or precede other complications (e.g. haemorrhage or meningoencephalitis).
- **Renal failure:** Acute renal failure, characterised by elevated urea and creatinine levels, may be secondary to hypovolaemia, multiple-organ dysfunction, hepatorenal syndrome or possibly also direct virus-related injury.
- **Haemorrhagic fever:** Haemorrhagic manifestations appear two to four days after the initial onset of illness, and may present as haematemesis (vomiting blood), melaena (passing blood in the faeces), a petechial /purpuric rash or ecchymoses, bleeding from the nose or gums, menorrhagia, or bleeding from venepuncture sites. Thrombocytopenia is invariably present ± laboratory evidence of disseminated intravascular coagulation (DIC). Most cases also have evidence of hepatitis (markedly raised ALT and AST levels, or jaundice) which may precede the haemorrhagic state. The mortality rate of patients developing the haemorrhagic form of the disease is high (up to 65%).

7. How is it diagnosed in the laboratory?

Live virus or viral nucleic acids may be detected in blood during the early phase of illness or in post-mortem tissue by RT-PCR or isolation in cell cultures or mice. Haemagglutination inhibition assay (HAI) and enzyme-linked immunoassay (ELISA) tests may confirm the presence of specific IgM and/or IgG antibodies to the virus. These tests are performed by the Special Pathogens Unit, NICD-NHLS.

8. Procedure following detection of a suspected case

Step 1: Notify the case

- RVF is a notifiable medical condition and should be notified to your local Department of Health.

Step 2: Collect specimens for laboratory testing

- All suspected cases of RVF should have TWO clotted blood specimens (either red top tubes or SST-gel tubes which usually have a yellow top) of sufficient volume (±5 ml each) taken for viral detection and antibody determination.
- The specimens should be packaged in accordance with the guidelines for the transport of dangerous biological goods (triple packaging using absorbent material) and transported directly to:

  The Special Pathogens Unit
  National Institute for Communicable Diseases (NICD)
  National Health Laboratory Service (NHLS)
  No. 1 Modderfontein Rd
  Sandringham, 2131
  Gauteng, South Africa
- ALL specimens should be labelled AND accompanied by a fully completed RVF suspected case investigation form (see page 6). These forms can also be faxed to the Special Pathogens Unit, NICD-NHLS, at +27-(0)11-882-3741
- Samples should be kept cold during transport (cold packs are sufficient).

The NICD-NHLS Hotline (✆082-883-9920) does NOT need to be contacted routinely for every case of suspected RVF. However, in the case of severely ill hospitalised patients where clinical advice is sought, or for whom laboratory testing needs to be prioritised and expedited, please call the NICD-NHLS Hotline (✆082-883-9920) which is a 24-hour service for all healthcare professionals countrywide. Please note that the NICD-NHLS Hotline is NOT a service for the general public, who should contact the Department of Health Hotline (✆ 086-136-4232) for any queries.

For RVF laboratory results contact the Special Pathogens Unit, NICD-NHLS, at +27-(0)11-386 6391 during office hours (07h30-16h00).

9. How is it treated? Is there a vaccine?

- No specific treatment is available for RVF; management comprises general supportive therapy.
- Early dialysis for patients with renal failure may improve outcome.
- Beware of and promptly treat nosocomial infections, particularly in critically ill patients.
- Ribavirin is NOT recommended for treatment of RVF.
- Moderate to high dose corticosteroids are NOT recommended as adjunctive therapy for RVF.
- Standard infection prevention and control precautions should be followed (refer to section 10); patients do not require isolation or barrier nursing. Human-to-human transmission has not been demonstrated.
- Follow-up of patients for at least 1 month after symptoms resolve is advised to monitor for possible development of ocular complications (retinitis in particular) or neurological complications.
- There are no human RVF vaccines registered in South Africa for use by the general public.

- Note: Should a patient present with a haemorrhagic fever where both RVF and CCHF are differential diagnoses, manage as possible CCHF until laboratory test results are available, i.e.:
  - Implement appropriate infection prevention and control measures (including isolation and barrier nursing);
  - Start treatment with ribavirin as soon as possible; and
  - Notify laboratory or NICD-NHLS hotline that specimens need urgent processing to ensure a rapid result.

10. Infection prevention and control in healthcare settings

Although no human-to-human transmission of RVF has been demonstrated, there is still a theoretic risk of transmission from infected patients to healthcare workers through contact with infected blood or tissues. Healthcare workers caring for patients with suspected or confirmed RVF should implement "Standard Precautions".

"Standard Precautions" define the work practices that are required to ensure a basic level of infection control, and are recommended in the care and treatment of all patients regardless of their perceived or confirmed infectious status. They cover the handling of blood (including dried blood), all other body fluids, secretions and excretions (excluding sweat), regardless of whether they contain visible blood, and contact with non-intact skin and mucous membranes. A two-page reminder with checklist can be downloaded at www.who.int/csr/resources/publications/EPR_AM2_E7.pdf

11. How can RVF be prevented?

Public health education and risk reduction plays a vital role in preventing human infections. Messages to the community, especially within affected areas should focus on:

- Avoiding high risk animal husbandry procedures and slaughtering practices through the use of gloves and other protective clothing, especially when handling sick animals.
- Avoiding the unsafe consumption of fresh blood, raw (unpasteurised or uncooked) milk or animal tissue. In outbreak regions, all animal products (blood, meat and milk) should be thoroughly cooked before eating. Slaughtering of sick animals for consumption should be discouraged during outbreaks.
- Personal and community protection against mosquito bites through the use of insect repellents (containing 30-50% DEET), insecticide-treated bed nets, and wearing of light-coloured clothing.

12. How are outbreaks prevented or mitigated?

Prevention of RVF outbreaks primarily relies on the prevention of infection in livestock through vaccination. Several veterinary (animal) vaccines are available in South Africa. Other ways in which to mitigate the spread of RVF involve control of the vector and protection against their bites. Larviciding measures at mosquito breeding sites are the most effective form of vector control if breeding sites can be clearly identified and are limited in size and extent. During periods of flooding, however, the number and extent of breeding sites is usually too high for larviciding measures to be feasible.

13. Where can I get more information?

- Regular updates and these guidelines are available through the NICD-NHLS website (www.nicd.ac.za).
- Questions from the general public can be directed to the Department of Health hotline:
  - 0861-DOH-CDC (0861-364-232)
- Additional information on RVF is available on the following website references:
  - World Health Organization. Rift Valley Fever. www.who.int/mediacentre/factsheets/fs207/en/.
  - Centers for Disease Control. www.cdc.gov/ncidod/dvrd/spb/mnpages/dispages/rvf.htm.

RIFT VALLEY FEVER (RVF) SUSPECTED CASE INVESTIGATION FORM, 2011

To be submitted with all requests to NICD-NHLS for human RVF testing. Or fax to 011 882 3741.

PATIENT DETAILS			
1. SURNAME, FIRST NAME:			
2. AGE/DOB:		3. GENDER: ☐ MALE ☐ FEMALE	
4. CONTACT NUMBER:			
5. OCCUPATION:		6. NAME OF FARM:	
7. TOWN:	DISTRICT:	PROVINCE:	
CONSULTATION/ADMISSION DETAILS			
8. NAME OF THE CLINICIAN:		9. CELL/TEL NUMBER:	
10. FACILITY NAME:			
11. DATE OF FIRST CONSULTATION: DD / MM / YYYY			
12. ADMITTED TO HOSPITAL? ☐ Y ☐ N If yes, DURATION OF HOSPITAL ADMISSION (days)?		13. REQUIRED ICU CARE? ☐ Y ☐ N If yes, DURATION OF ICU CARE (days)?	
CLINICAL DETAILS ON FIRST PRESENTATION/ADMISSION			
14. PAST MEDICAL HISTORY: UNDERLYING ILLNESS? ☐ Y ☐ N … If yes, WHAT? IMMUNOSUPPRESSION? ☐ Y ☐ N … If yes, GIVE DETAILS?			
15. DATE OF ONSET OF RVF ILLNESS? DD / MM / YYYY			
16. SYMPTOMS (tick all that apply): ☐ FEVER ☐ MYALGIA ☐ ARTHRALGIA ☐ FATIGUE / MALAISE	☐ LOSS OF APPETITE ☐ NAUSEA ☐ VOMITING ☐ ABDOMINAL PAIN ☐ NECK STIFFNESS	☐ HEADACHE ☐ OCULAR PAIN ☐ PHOTOPHOBIA ☐ BLURRED VISION ☐ LOSS OF VISUAL ACUITY	☐ CONFUSION ☐ HAEMORRHAGE If yes, SITE/S:
17. EXAMINATION ON PRESENTATION (tick all that apply): ☐ FEVER (≥ 38°C) ☐ SHOCK (↓BP)	☐ DEHYDRATION ☐ JAUNDICE ☐ PALLOR	☐ MENINGISM ☐ CONFUSION ☐ RETINITIS	☐ HEPATOMEGALY ☐ ABDO TENDERNESS ☐ RASH
☐ **18. HAEMORRHAGE** If yes, tick sites that apply:	☐ EPISTAXIS ☐ HAEMATEMESIS ☐ MELAENA	☐ MENORRHAGIA ☐ PETECHIAE BLEEDING FROM VENEPUNCTURE SITES	☐ BLEEDING ELSEWHERE? Specify:
19. LIST OTHER CLINICAL FINDINGS?			
CLINICAL PROGRESSION			
20. CLINICAL PROGRESSION TO DATE? ☐ UNEVENTFUL RECOVERY or ☐ DEVELOPED COMPLICATIONS ... If developed complications, tick all that apply: ☐ ELEVATED TRANSAMINASE LEVELS (AST, ALT) ☐ LIVER FAILURE ☐ RENAL FAILURE ☐ THROMBOCYTOPENIA ☐ HAEMORRHAGE ☐ RETINITIS ☐ ENCEPHALITIS			
21. OUTCOME: ☐ ALIVE ☐ DIED … If yes, DATE OF DEATH?			
22. EXPOSURE (tick all that apply)			
☐ CONTACT WITH ANIMALS/ TISSUES ☐ DRANK UNPASTEURISED MILK ☐ CONSUMED ANIMAL MEAT NOT SOURCED FROM RETAIL OUTLET ☐ MOSQUITO BITES	DATE OF EXPOSURE? DD / MM / YYYY DESCRIPTION OF EXPOSURE:		