NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES
Division of the National Health Laboratory Service

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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Practice number: 5200296

Table of contents

Disclaimer iii
Acknowledgements iii

1. Introduction and situation update 1
2. What is Rift Valley fever? 1
3. Previous outbreaks of RVF in South Africa 2
4. How is it transmitted to humans? 3
5. When should RVF be suspected as a cause of illness? Case definition and criteria for laboratory testing 3
6. What are the clinical features in humans? 4
7. How is it diagnosed in the laboratory? 5
8. Procedure following detection of a suspected case 5
   - Step 1: Notify the case 5
   - Step 2: Collect specimens for laboratory testing 5
9. How is it treated? Is there a vaccine? 6
10. Infection prevention and control in healthcare settings 6
11. How can RVF be prevented? 6
12. How are outbreaks prevented or mitigated? 7
13. Where can I get more information? 7

Rift Valley fever (RVF) suspected case investigation form, 2020 8

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

There has been substantial rainfall for December 2019 and January 2020 in Free State, Gauteng and KwaZulu-Natal (KZN) provinces. KZN is cumulatively above normal (~ +200mm) rainfall, while Free State is still in deficit (~ -100mm). The south-western region of the Central Karoo of the Western Cape that was affected by ongoing drought until 2019, received significant rain relief in early 2020. Almost 80% of the Northern Cape (NC), particularly the western parts of NC, are still seriously affected by drought. There has been below-average rainfall forecast for most of the Eastern Cape. Based on predictions by SA Weather Service reported 20 December 2019, there is significant uncertainty on the expected rainfall conditions for the rest of the summer period.

The most recent outbreak of Rift Valley Fever (RVF) for South Africa was in 2018, detected on a single farm in the Jacobsdal area of Free State, South Africa. A total of 250 sheep deaths/abortions were documented and laboratory-confirmed on 16 May 2018. Subsequently, eight human cases were laboratory-confirmed to have recent RVF infection amongst ten human samples submitted for testing from 22 people of the farm.

A widespread RVF epidemic occurred in South Africa in 2010-2011 with more than 14,000 animal cases recorded in 8 of 9 provinces. During this period the National Institute for Communicable Diseases, National Health Laboratory Services (NICD-NHLS) confirmed a total of 278 human cases, of which 25 were fatal. Data from epidemiological investigations suggested that approximately 83% of these cases worked within occupations where direct contact with animals occurred frequently. Furthermore, 89% 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 the 2010-2011 epidemic. Nevertheless, following high rainfall in December 2019 and January 2020 in certain provinces, 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 *Phenuiviridae* (genus *Phlebovirus*) and causes outbreaks of abortions and deaths of livestock (predominantly sheep, goats and cattle). The disease occurs throughout Africa and Middle East 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: the floodwater *Aedes* species feed at dusk and, to a lesser extent, at dawn; the reason they are not important as a source of virus for humans is because the pans are generally well removed from the farmsteads and kraals and these mosquitoes do not fly far in search of food. The *Culex* species, on the other hand, do fly to kraals and homesteads, hence the need to screen houses because they will feed on humans as well as livestock. The greater the presence of livestock, the lower the interest in humans but some human contact can obviously still occur.

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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 and cattle and also goats to a lesser extent in in East Africa characterised by abortions in ewes and cows and deaths of young animals and sometimes adult animals. Outbreaks occur at irregular intervals of years following heavy rains and significant increases in vector populations. Outbreaks can recur over a succession of unduly wet seasons following an increase in floodwater *Aedes*

populations to ignite outbreaks and a huge increase in the *Culex theileri* population, but may not be seen for decades during drier spells.

Prior to the last major outbreak of RVF in 2010-2011 mentioned above, there was a 35-year interval before the previous large epidemic on the interior plateau of South Africa in 1974-76. However, Pienaar and Thompson's study (2013) showed focal interepidemic outbreaks in livestock in the Free State and other provinces since the 1950s (Table1). 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).

Table 1: summary paper Pienaar, N.J. & Thompson, P.N., 2013, 'Temporal and spatial history of Rift Valley fever in South Africa: 1950 to 2011', *Onderstepoort Journal of Veterinary Research* 80(1), Art. #384, 13 pages. http://dx.doi.org/10.4102/ojvr.v80i1.384

Dates	*Areas*
1976-1977:	small outbreaks in KZN and ECP;
in August, Sept and Oct 1976	FSP; Karoo region
1977-1978:	ECP, Karoo region (WCP+ECP), KZN, FSP
1978-1979:	ECP, Karoo region, KZN, FSP
1979-1980:	KZN
1980-1981:	Highveld (FSP?) but not confirmed
1981-1982:	KZN, ECP, Karoo, FSP
1982-1983:	KZN, FSP
1983-1984:	KZN, NCP (former WCP)
1984-1985:	KZN, FSP, Transvaal (MP?)
1985-1986:	KZN, ECP, Karoo
1988-1989:	good rains but no outbreaks
1990-1991:	KZN
1991-1998:	none
1999:	MP
2000-2007:	none
2008:	MP, LP, GP, NWP
2009:	KZN, ECP, MP, NCP

KwaZulu-Natal (KZN), Eastern Cape (ECP), Free State (FSP), Western Cape (WCP), Mpumalanga (MP), Limpopo (LP), North-West (NWP), Northern Cape (NCP), Gauteng (GP)

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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,
  - inhalation of aerosols produced during the slaughter/necropsy of infected animals.

- 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,
  - 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) with or without 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.

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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's (WHO) RVF 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%.

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 influenza-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 with or without 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%).

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7. How is it diagnosed in the laboratory?

Live virus or viral nucleic acid may be detected in blood during the early phase of illness or in post-mortem tissue by reverse transcription polymerase chain reaction (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 Centre for Emerging Zoonotic and Parasitic Diseases, NICD-NHLS.

8. Procedure following detection of a suspected case

Step 1: Notify the case

- RVF is a notifiable medical condition and should be reported using the Notifiable Medical Conditions (NMC) mobile or web App (http://www.nicd.ac.za/notifiable-medical-conditions/).

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 (±8.5 ml each) taken for viral detection and antibody determination.
- In most cases a second, convalescent blood sample, collected 7-14 days after the acute blood sample is helpful in making a definitive diagnosis.
- 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:

  Centre for Emerging Zoonotic and Parasitic Diseases
  Arbovirus Reference Laboratory
  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 7). These forms can also be emailed to the Centre for Emerging Zoonotic and Parasitic Diseases, NICD-NHLS, at cezd@nicd.ac.za, orienkah@nicd.ac.za, or faxed to +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 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 Centre for Emerging Zoonotic and Parasitic Diseases – Arbovirus Reference Laboratory, NICD-NHLS, at +27-(0)11-386 6391 / +27-(0)11-555 0503 during office hours (07h30-16h00).

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

- No specific approved 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 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.

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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) – search for "Rift Valley Fever".
- 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.

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NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES

RIFT VALLEY FEVER (RVF) SUSPECTED CASE INVESTIGATION FORM, 2020

To be submitted with all requests to NICD-NHLS for human RVF testing. Email to cezd@nicd.ac.za, orienkah@nicd.ac.za or fax to 011 882 3741.

Filled in by: _____ Contact number: (0__) _____

Date: DD / MM / YYYY Information collected from: _____

PATIENT DETAILS

1. Surname, First Name: _____

2. Age/DOB 00 years / DD / MM / YYYY 3. Gender: ☐ Male ☐ Female

4. Contact Number: (0__) _____ (0__) _____ (0__) _____

5. Occupation: _____ 6. Farm Name: _____

7. Town: _____ District: _____ Province: _____

CONSULTATION/ADMISSION DETAILS

8. Name of the Clinician: _____ 9. Cell/Tel Number: (0__) _____ (0__) _____

10. Facility Name: _____

11. Date of First Consultation: DD / MM / YYYY 12. Specimen Collection Date: DD / MM / YYYY

13. Admitted to hospital? ☐ Y ☐ N 14. Required ICU care? ☐ Y ☐ N

If yes, duration of hospital admission? 00 (days) If yes, duration of ICU care? 0 (days)

CLINICAL DETAILS ON FIRST PRESENTATION/ADMISSION

15. PAST MEDICAL HISTORY:

Underlying Illness? ☐ Y ☐ N … If yes, what? _____

Immunosuppression? ☐ Y ☐ N … If yes, give details? _____

Past RVF Infection? ☐ Y ☐ N … If yes, when? _____ (month) 0000 (year)

Unknown ☐

16. Date of onset of illness? DD / MM / YYYY or **Days since onset of illness:** 00

17. 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
☐ None

18. ☐ Haemorrhage (If yes, tick sites that apply):

☐ Epistaxis
☐ Haematemesis
☐ Melaena
☐ Menorrhagia
☐ Bleeding elsewhere? Specify: _____
☐ Petechiae
☐ Bleeding from venepuncture sites

19. EXAMINATION ON PRESENTATION (tick all that apply):

☐ Fever (≥ 38°C)
☐ Shock
☐ Low Blood Pressure
☐ Dehydration
☐ Jaundice
☐ Pallor
☐ Meningism
☐ Confusion
☐ Retinitis
☐ Hepatomegaly
☐ Abdominal tenderness
☐ Rash

20. LIST OTHER CLINICAL FINDINGS?

21. 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

22. OUTCOME: ☐ Alive ☐ Died … If yes, date of death? DD / MM / YYYY

23. EXPOSURE (tick all that apply)

DATE OF EXPOSURE? DD / MM / YYYY

☐ Contact with animals/ tissues
☐ Mosquito bites
☐ Drank unpasteurised milk
☐ Consumed animal meat not sourced from retail outlet

Description of exposure: _____