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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Table of contents

Disclaimer

These guidelines are intended to be used by healthcare professionals. While the greatest care has been taken in developing this document, the National Department of Health and the National Institute for Communicable Diseases (NICD) of the National Health Laboratory Services (NHLS) are not willing to take responsibility for any errors or omissions. All healthcare professionals should exercise their own professional judgement in interpreting and applying the information set out in these guidelines.

Acknowledgements

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1. Introduction and situation update

Rift Valley Fever (RVF) is an animal and human mosquito-borne zoonotic disease; thus, the risk of occurrence of an outbreak is closely correlated with above-normal rainfall and flooding. Eco-climatic factors modulate the dynamics of RVF. Present cumulative rainfall trends continue to depart from the 2010/2011 season in the Free State and central eastern regions of South Africa, when the most recent RVF outbreak occurred in southern Africa and is well above the long-term cumulative daily mean (See Figure 1).

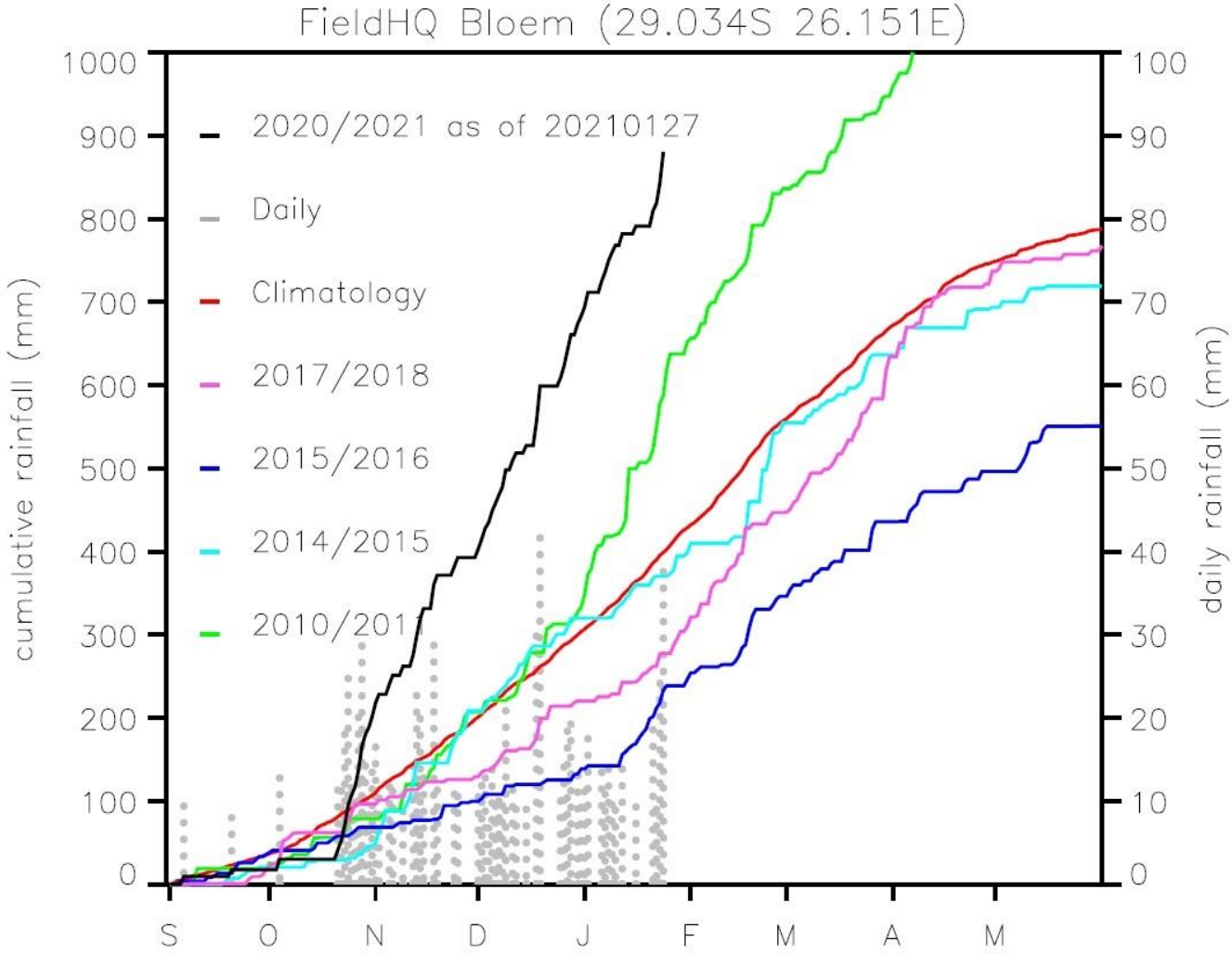

Figure 1. Rainfall trend in Bloemfontein, Free State, South Africa as of 28 January 2021.
(Source: Goddard Earth Sciences Technology and Research (MSU), Code 614, NASA Goddard Space Flight Center Greenbelt, MD 20771, USA.)

RVF outbreaks have historically occurred in central South Africa, but the country as a whole is endemic. Weather forecasts expect more rainfall over South Africa, with possibility of further heavy rain and localized flooding in places over the Free State, KwaZulu-Natal, North West and Mpumalanga provinces.

Although malaria is the most prevalent mosquito-borne disease in South Africa, there are also many mosquito-borne viruses that cause human disease. Chikungunya, West Nile, Sindbis and RVF viruses are the most important viruses in South Africa. The COVID-19 lockdown restrictions on provincial and international travel including border crossings between Mozambique in 2020 resulted in lower malaria numbers compared to 2019. However, as the country slowly reopened and mobility increased, coinciding with the beginning of the 2020/2021 summer and high rainfall season, awareness of the risk of malaria is raised in the country's northeastern provinces and among travelers. There is also an impact of lockdown measures on

outbreaks of mosquito-borne viral diseases. In South Africa, outbreaks of RVF have not been recorded this summer, but preparedness needs to be increased based on the weather and favourable conditions. In 2018, the last record of an outbreak of RVF was at one farm in the Free State, causing abortions and sheep deaths and infection in eight farm workers participating in carcass disposal and meat processing. A widespread RVF epidemic occurred in South Africa in 2010-2011 with more than 14 000 animal cases reported in eight provinces. The NICD reported 278 human laboratory-confirmed infections, leading to 25 deaths. Contact with infected animals, blood and fluids, tissues, particularly aborted animals and placentas, is the main route of transmission to humans. As a result, 83% of the human cases worked within occupations where contact with animals frequently occurred in this most recent epidemic. In addition, 89% of cases reported a history of direct contact with infected animals, prior to illness. Human infections from mosquito bites, unpasteurized raw uncooked milk are also possible.

There is a need for public health awareness of signs of RVF outbreak, monitoring and prevention of human cross-over, according to current weather conditions and summer season; farmers' awareness of vaccination since vaccination will prevent RVF virus epizootics in animals and, as a result, minimize exposure to livestock workers and meat processors. In addition, there is a need for awareness to use personal protective equipment (PPE) amongst animal-related occupational groups. In addition, education on milk pasteurisation and the handling and consumption of freshly slaughtered undercooked meat for the general public needs to be available. Health Care workers should be aware of the signs and symptoms of RVF and refer patients that meet the case definition and epidemiologic exposure criteria for diagnostic testing to the NICD and notify probable cases to the 'Notifiable Medical Conditions (NMC)' surveillance system of the Department of Health – NICD.

RVF

2. What is RVF?

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 belongs to 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 the Middle East, when exceptionally heavy rains favour the breeding of the mosquito vectors. In RVF outbreaks in east or southern Africa, humans become infected primarily by contact with infected tissues of livestock or wild (game) animals, and less frequently by 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 on herbivore animals nearby pans, seasonally flooded shallow depressions. The reason they are not important to humans as a source of virus is that these pans are generally well removed from farmsteads and kraals and these mosquitoes do not fly far in search of food (blood meal). The *Culex* species, on the other hand, fly to kraals and homesteads, hence the need to screen houses because they feed on both humans and livestock. The greater the presence of livestock, the lower the interest by these mosquitoes in feeding on humans but obviously some human contact can still occur.

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, to a lesser extent in goats, in East Africa, characterised by abortions in ewes and cows and the deaths of young animals and sometimes adult animals. Outbreaks occur at irregular intervals of years following heavy rainfall with flooding 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) has shown 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 have been 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 RVF 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)

4. How is RVF 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.

- Human-to-human transmission has not been documented, but cases of prenatal or intrapartum transmission has been reported.

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 is it possible to suspect RVF as a cause of illness? Case definition & criteria for laboratory testing

Case definition
The high risk group for infection with RVF:

a. Recent contact with hoofed livestock or game animals, including commercial or informal slaughtering or butchering activities, handling of freshly slaughtered meat, disposal of carcasses/foetuses/aborted placentas, assistance with animal birthing or any other animal husbandry or veterinary procedures, or necropsy/dissection/autopsy of animals resulting in contact with blood, fluids, tissues, organs in or from RVF affected areas (See Figure 2)
b. History of recent mosquito bites and residing in RVF affected areas (See Figure 2)
c. History of consumption of unpasteurized/uncooked raw milk in or from RVF affected areas (See Figure 2)

A suspected case is a person who meets one or more of the following criteria:

1. Belongs to the category of high-risk and has influenza-like symptoms, including fever, myalgia, arthralgia, or headache.
2. Signs of encephalitis or external or internal bleeding not from trauma/injury/periods or hepatitis or ocular pathology (retinitis) with or without fever and belonging to a high-risk group.
3. Without a clinical diagnosis of what causes symptoms of encephalitis, or hepatitis, or external or internal bleeding not from trauma/injury/periods from RVF affected areas (see Figure 2).

IMPORTANT NOTE: All individuals matching the case description should also be tested for COVID-19 as clinical symptoms and signs overlap with RVF.

NOTE: Malaria, tick bite fever, Crimean-Congo haemorrhagic fever are other differential diagnoses of RVF and must be taken into account according to the appropriate case definitions. Obtaining a comprehensive travel, tick/insect or animal or patient exposure history of the suspected person can assist health care workers in narrowing down the differential diagnosis and will promote timely diagnostic testing, infection prevention and control measures.

The RVF affected areas of 2010 epidemic are shown in Figure 2.

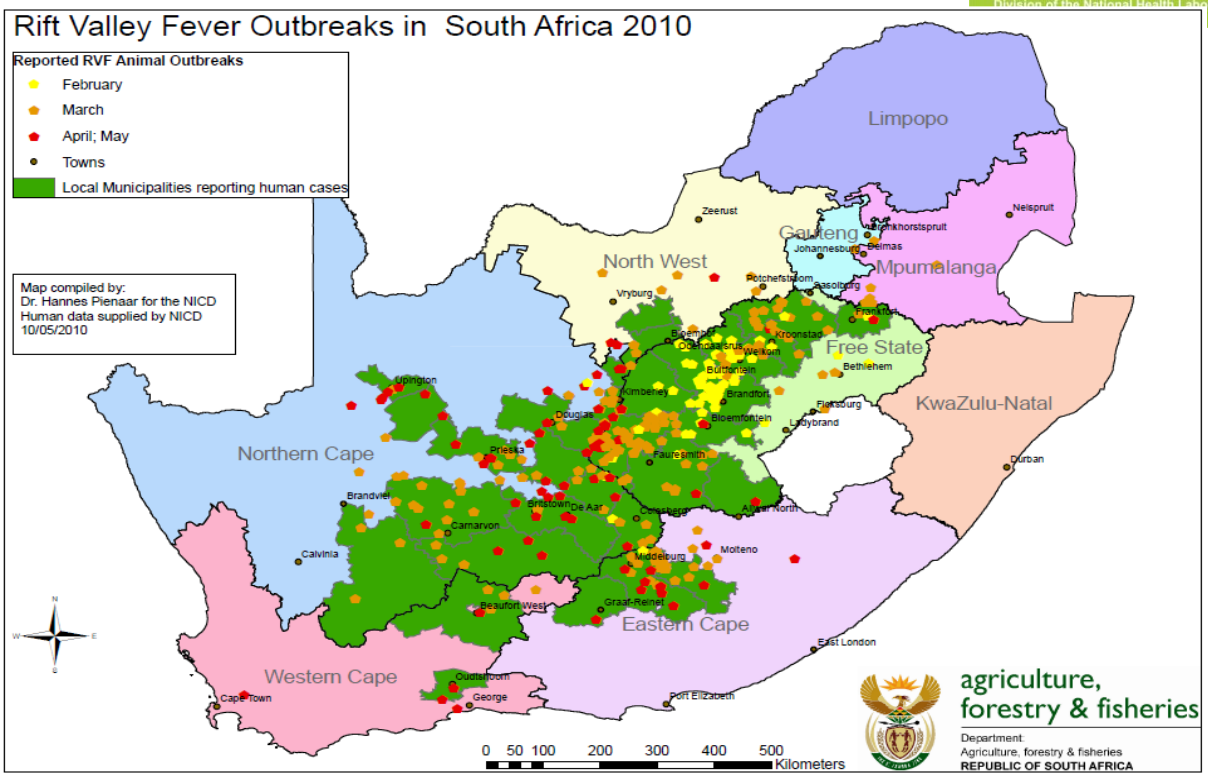

Figure 2. Geographic overlap of RVF cases in animals (red, yellow and brown circles) and humans (green area) in February-May 2010, South Africa (From Department of Agriculture, Land Reform and Rural Development.

6. What are the clinical features in humans?

Typically, RVF disease is asymptomatic or mild in the vast majority of infected individuals, with a small proportion of them experiencing severe illness. The true overall mortality rate from RVF infection is difficult to estimate, given that the case definitions and laboratory testing methods used in the various documented outbreaks differed significantly. Although the World Health Organization's (WHO) RVF fact sheet shows an overall mortality rate of <1%, the reported mortality rates for 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, with a case fatality rate of 14%.

Mild illness

- The incubation period (interval from infection to onset of symptoms) for RVF varies from two to six days.
- Clinically, RVF 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 by 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 experiencing 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 (heavy or prolonged vaginal bleeding with menstrual cycle), 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%).

7. How is RVF 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 appendix and available on NICD website (http://www.nicd.ac.za/diseases-a-z-index/riftvalley-fever/). These forms can also be emailed to the Centre for Emerging Zoonotic and Parasitic Diseases, NICD-NHLS, at Jessicac@nicd.ac.za; Orienkah@nicd.ac.za.
- Samples should be kept cold during transport (cold packs are sufficient).

The NICD-NHLS Hotline (0 800 212 552) 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 a different NICD-NHLS Hotline (0 800 02 9 999) 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)11-386 6424/6382 during office hours (07h30-16h00).

9. How is RVF 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, but cases of prenatal or intrapartum transmission have been reported
- 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 theoretical 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" defines the work practices that are required to ensure a basic level of infection control and is recommended for 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), whether or not 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 of mitigating the spread of RVF involve control of the vector and protection against arthropods 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. However, during periods of flooding, 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 (http://www.nicd.ac.za/notifiable-medical-conditions/) – search for "RVF".
- Questions from the general public can be directed to the NICD-NHLS hotline:
  - (0 800 02 9 999)
- Additional information on RVF is available on the following website references:
  - World Health Organization. RVF. https://www.who.int/health-topics/rift-valley-fever#tab=tab_1/.
  - Centers for Disease Control and Prevention. https://www.cdc.gov/vhf/rvf/index.html.

NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES
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RVF (RVF) SUSPECTED CASE INVESTIGATION FORM, 2021

To be submitted with all requests to NICD-NHLS for human RVF testing. Email to jessicac@nicd.ac.za, orienkah@nicd.ac.za.

Filled in by: _____ Contact number: (000) 000 0000

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: (000) 000 0000 (000) 000 0000 (000) 000 0000

5. OCCUPATION: _____ 6. FARM NAME: _____

7. TOWN: _____ DISTRICT: _____ PROVINCE: _____

CONSULTATION/ADMISSION DETAILS

8. NAME CLINICIAN: _____ 9. CELL/TEL NUMBER: (000) 0000000 (000) 0000000

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? 00 (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 RVFV INFECTION? ☐ Y ☐ N … If yes, WHEN? 00 (month) 0000 (year)

16. DATE OF ONSET OF ILLNESS? DD / MM / YYYY

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

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 (↓BP)
☐ 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: _____