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Preliminary report on an outbreak of Rift Valley fever, South Africa, February to 3 May 2010

Introduction

Since February 2010, there has been an ongoing outbreak of Rift Valley fever (RVF) in South Africa. This preliminary report summarises the available clinical, epidemiological and laboratory data on human cases for the period of February to 3 May 2010, and will be updated as new data become available.

RVF is a zoonotic, mosquito-borne viral disease of ruminants, most often affecting domestic animals including sheep, goats and cattle, which occurs mainly in sub-Saharan Africa and Madagascar. Large outbreaks of the disease occur at irregular intervals, often many years or decades, when unusually heavy rains favour the breeding of the mosquitoes which transmit the virus. The outbreaks are characterised by deaths, particularly among newborn animals, and abortion in pregnant animals.

The vast majority of human infections are acquired through contact with infected animal tissues/blood. Low concentrations of virus have been found in milk and body fluids (including saliva and nasal discharges) of infected sheep and cattle, and there has been inconclusive evidence of human infection from consumption of raw milk. Transmission from infected mosquito-bites has been described (notably in outbreaks outside of sub-Saharan Africa) and there have been a few cases of tourists acquiring infection from mosquito-bites whilst on safari in East Africa. No instances of human-to-human transmission have been reported, apart from two cases of vertical mother-to-child transmission. Infected humans are often asymptomatic (≥80%). Symptomatic disease is usually manifest by mild to moderate illness (with influenza-like symptoms); severe complications and fatal disease occur in a small proportion of patients.

RVF was first recognized in South Africa in 1950-1951 when an estimated 500 000 ewes aborted and a further 100 000 sheep died. The disease occurred mainly in the panveld areas of the western Free State and adjacent Northern Cape Provinces (where sheep farming predominates), but was also identified in southern Mpumalanga, Gauteng, North West and the Karoo areas of the Western and Eastern Cape Provinces. Smaller outbreaks occurred intermittently over the subsequent years until a major outbreak occurred, again in association with heavy rains, in 1974-1976.

Following good rains in 2008, RVF was reported in game animals and livestock on farms adjacent to the Kruger National Park; subsequent cases were reported elsewhere in Mpumalanga, as well as southern Limpopo, Gauteng and North West Provinces. In 2009 limited outbreaks occurred from February to July in KwaZulu-Natal Province and from October to December in the Northern Cape Province. On 12 February 2010, the first laboratory-confirmed outbreak amongst animals was identified in the Bultfontein area of Free State Province. Progressively, the disease appeared else-where in the province, and has since been confirmed in Northern Cape, Eastern Cape, Gauteng, Mpumalanga, North West and Western Cape Provinces. Domestic animals affected include sheep, cattle and goats, whilst small numbers of wild animals (mostly antelopes and buffalo) have succumbed.

Methodology

RVF in animals

Data on RVF in domestic and wild animals was supplied by the Animal Health Directorate, South African Department of Agriculture, Forestry and Fisheries.

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RVF in humans

Blood specimens were collected from patients meeting the following criteria: any person reporting recent close contact with livestock in or from suspected RVF-affected areas, presenting with:

- Influenza-like illness (which may include fever with: myalgia, arthralgia or headache), OR
- Fever and features of: encephalitis, haemorrhage, hepatitis and/or ocular pathology (retinitis).

Laboratory-confirmation of RVF infection was performed by the Special Pathogens Unit, NICD-NHLS. Testing includes: RVF reverse transcription polymerase chain reaction (RT-PCR), loop-mediated isothermal amplification assay, virus isolation, haemagglutination inhibition assay and IgM-ELISA. Clinical and epidemiological data were obtained from a number of sources, including case and contact interviews, interviews with attending clinicians, and clinical and laboratory records.

Results

Descriptive epidemiology

As of 3 May 2010, approximately one thousand two hundred human specimens have been tested for suspected RVF infection, and we have confirmed a total of 172 human cases and 15 deaths (Table 1, Figure 2). Cases range in age from 1 – 86 years (median 43 years), and the majority (86%, 145/169) are male.

Table 1: Number of laboratory confirmed RVF cases and deaths by province, 3 May 2010

Province (place exposed)	Cases	Deaths
Eastern Cape	10	0
Free State	105	8
Gauteng	0	0
KwaZulu-Natal	0	0
Limpopo	0	0
Mpumalanga	0	0
Northern Cape	53	6
North West	2	0
Western Cape	1	1
Unknown	1	0
South Africa Total	**172**	**15**

Exposures and occupation

Of the 172 confirmed cases, data on occupation is available for 139 cases (81%). Of these cases, the majority (81%, 113/139) work within occupations where direct contact with animals frequently occurs (Table 2). Further history regarding exposure has been obtained for 74% (128/172) of the total cases to date, among whom 97% (124/128) report a history of direct contact with RVF infected ruminants prior to onset of symptoms. Of the remaining four cases investigated, three report exposure to mosquitoes in the absence of direct animal exposure, and one reports drinking unpasteurised milk but no direct contact with infected animals (all are from Free State Province).

Table 2: Number of laboratory confirmed RVF cases by occupation, South Africa, 3 May 2010

Occupation	No. (%)
Farmer or farm worker	81 (58)
Animal health worker†	12 (9)
Abattoir worker, meat inspector or hunter	20 (14)
Farm resident (non-worker)	2 (1)
Non-animal related occupation	24 (17)
Total with known occupation	**139 (100)**

†Includes veterinarians, veterinary assistants/nurses, animal health technicians.

Patients hospitalised with severe illness

Of 30 cases known to be hospitalised with severe illness, sufficient clinical details are available for 14 to date. Clinical manifestations are listed in Table 3. Hepatitis was characterised by markedly elevated alanine aminotransferase (ALT) and aspartate transaminase (AST) levels ± accompanying mild to moderately elevated alkaline phosphatase (ALP) and γ-glutamyl transpeptidase (γ-GT) levels. Of interest, retinitis was not noted in any of the cases.

Table 3: Manifestations of severe RVF disease in hospitalised patients who recovered (n = 14)

Complication	n/N	%
Thrombocytopenia	5/14	36
Active bleeding diathesis	4/5	80
Associated hepatitis	4/5	80
Hepatitis	4/14	29
Encephalitis	1/14	7
Renal failure	1/14	7

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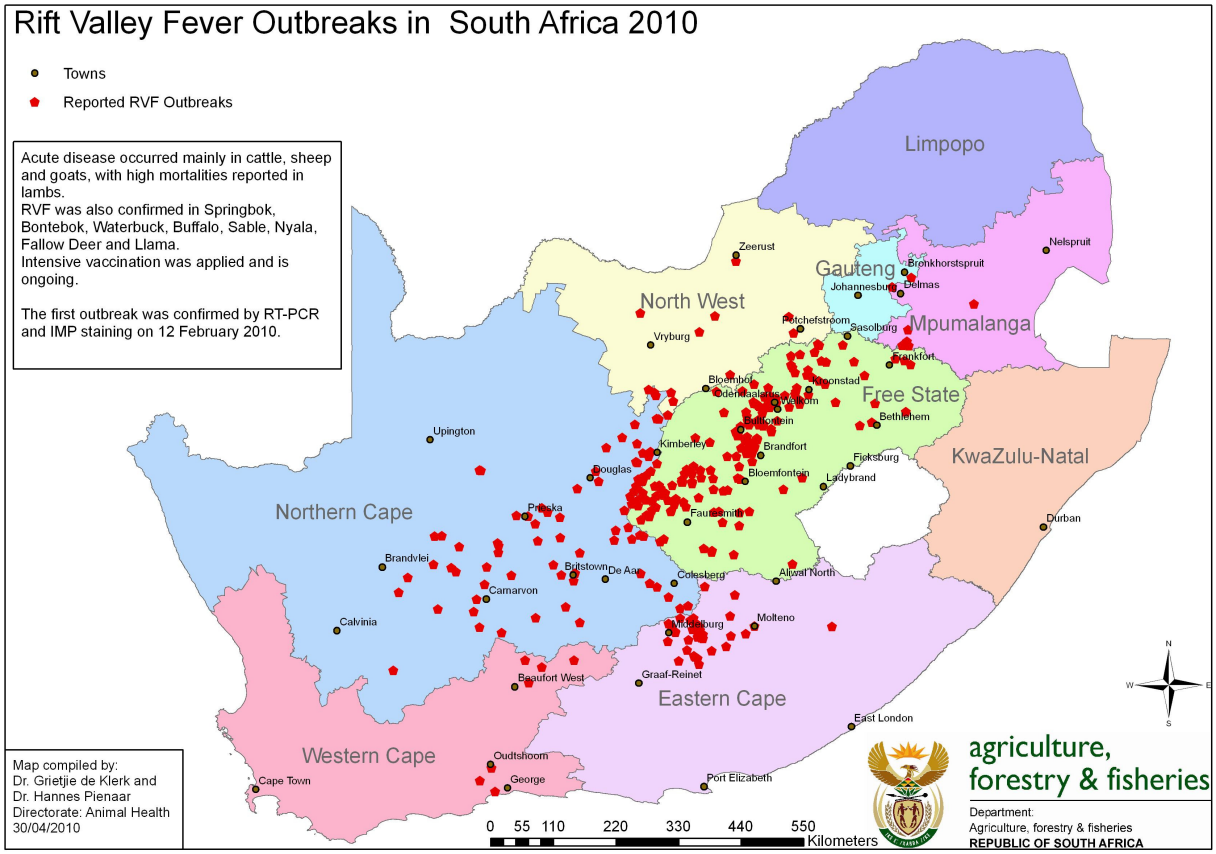

Figure 1: Map illustrating the extent of the RVF epizootic in South Africa, updated 30 April 2010

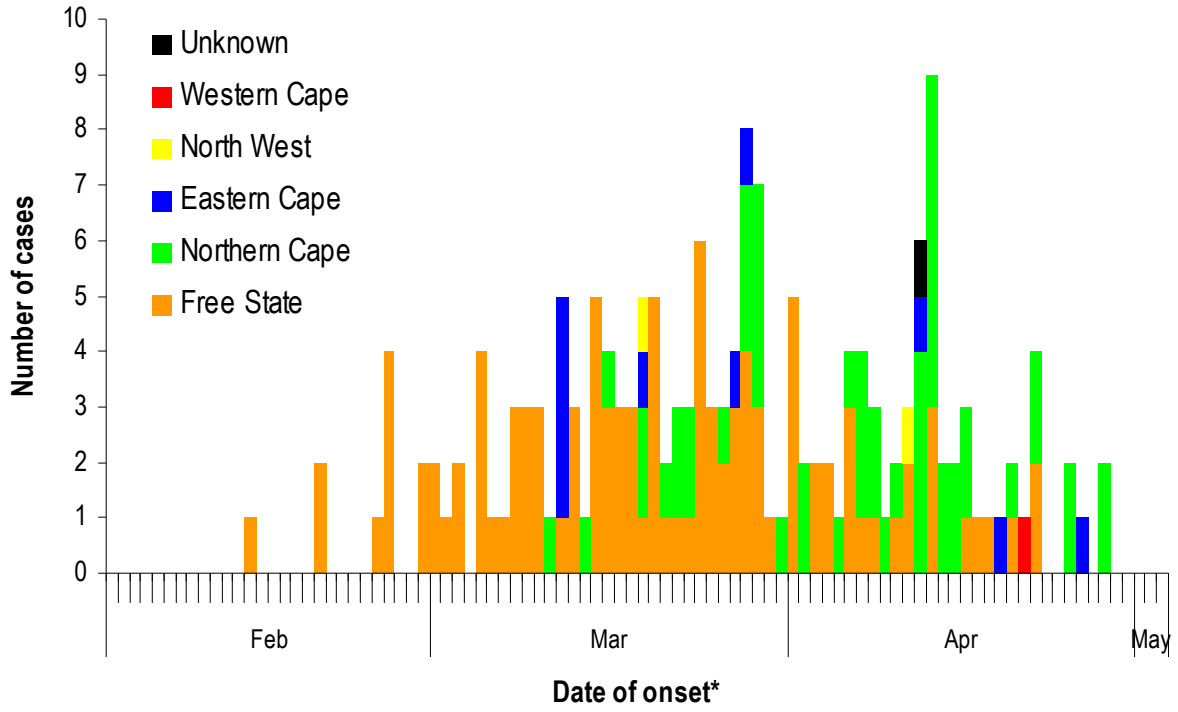

Figure 2: Epidemic curve illustrating the number of laboratory confirmed human RVF cases by date of illness onset and province, South Africa, updated 3 May 2010
*Date of specimen collection utilised as a proxy where date of illness onset was unavailable

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Fatal cases

Of the 15 fatal cases to date, chronic comorbid illness was noted in 4 cases:

- History of alcohol abuse/dependence: n=2
- Type 2 diabetes mellitus and alcohol abuse: n=1
- Pregnant HIV-infected: n=1

Clinical manifestations are listed in Table 4.

Table 4: Manifestation of RVF disease in fatal cases (n=15)

Complication	n/N	%
Thrombocytopenia	13/15	87
Active bleeding diathesis	13/13	100
Associated hepatitis	11/13	85
Hepatitis	13/15	87
Progression to liver failure	4/13	31
Encephalitis	2/15	13
Renal failure	5/15	33

Hepatitis was characterised by markedly elevated ALT and AST levels ± accompanying mild to moderately elevated ALP and γ-GT levels. Fulminant hepatitis with resultant liver failure was noted in four cases. Of the 13 cases with active haemorrhage, secondary to thrombocytopenia, seven (54%) presented initially with gastrointestinal bleeding; one patient presented with a generalised petechial rash and 2 cases developed disseminated intravascular coagulation (DIC). All patients presenting with renal failure had numerous possible causes for renal dysfunction; all had concomitant severe hepatitis and thrombocytopenia with bleeding diathesis. Retinitis was not noted in any of the fatal cases.

Discussion

This report refers only to laboratory-confirmed RVF cases, all but one of whom was tested as a result of symptomatic illness. It has been estimated that ≥80% of 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 incidence of severe disease or calculate an accurate case fatality rate since we lack a reliable denominator. Serosurveys are currently underway in Free State and Northern Cape Provinces to gain a representative estimate of RVF infection prevalence in the current outbreak.

The overwhelming majority of cases have reported direct contact with animal tissues/blood in areas with proven animal RVF cases. However, mosquito-borne transmission of RVF cannot be excluded in a few cases where investigation revealed no other likely mode of transmission, and it is possible that additional cases were missed since the case definition might have excluded these from being tested.

Although mosquito-borne transmission of RVF to humans was thought to be important in outbreaks that occurred in Egypt, West Africa, the Arabian Peninsula and East Africa, the epidemiologies of these outbreaks were very different from the situation in South Africa, in that they were associated with domestic/peridomestic vectors or vectors that bred out during major flooding events. In contrast, the principal mosquito vectors of RVF on South Africa's inland plateau are restricted to sparsely populated agricultural areas with localised foci occurring near pans, vleis or farm dams. In the early stages of the epidemic, vector species that are responsible for initiating outbreaks, the so-called "floodwater *Aedes*," are restricted to the immediate vicinity of the pans and vleis which form their breeding habitats. As these habitats typically occur well away from human habitation, the floodwater *Aedes* are far more likely to come into contact with livestock than humans. However, where these flooded areas persist for several weeks or months, they allow breeding of large numbers of *Culex theileri* and *Culex zombaensis* mosquitoes. *Culex theileri* in particular, is capable of flying to homesteads and animal shelters (kraals and stables) in order to find blood-meals. This species also breeds in watering troughs in the kraals and finds refuge in farmhouse gardens. It also feeds on a wide range of vertebrate hosts and therefore presents a possible source of infection for humans. However, the risk is still limited to farmsteads and does not extend to larger human settlements.

Health promotion, which is ongoing in RVF-affected areas, needs to be strengthened and focused towards prevention of infection, including:

- The use of personal protective equipment during risky animal husbandry/slaughtering and veterinary procedures;
- Discouraging consumption of unpasteurised milk or informally slaughtered meat; and,
- Encouraging personal and community protection against mosquito bites through the use of insect repellents, insecticide-treated bed nets, and wearing of light-coloured clothing.

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Conclusions

Although neither true prevalence of disease nor accurate mortality rates can be inferred from currently available data, severe and fatal cases of RVF have been observed in the current outbreak. Haemorrhagic complications and hepatitis are the most common manifestations of severe disease and the most frequent complications associated with fatal outcome. Increasing public awareness and enhanced health promotion activities are important measures to reduce risk of transmission of RVF. From past experience it can be surmised that there may be a sharp decline in transmission of the disease when the onset of colder weather with frost at the end of May suppresses mosquito activity.

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