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Human Cases of Wesselsbron Disease, South Africa 2010–2011

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Abstract

Wesselsbron disease is a neglected, mosquito-borne zoonotic infection reported from Africa. The disease primarily affects sheep and other ruminants with incidental spillover to humans. As for other arboviral diseases in Africa, little or no active surveillance is conducted, and the public and veterinary health burden of this disease remains unclear. We report on the clinical histories of 2 human cases of Wesselsbron disease that were laboratory confirmed during the 2010–2011 Rift Valley fever outbreak investigation in South Africa. This report describes the first confirmed human cases of Wesselsbron disease since 1996. Molecular sequencing and analysis of the partial NS5 gene of the Wesselsbron genome was used to identify 2 circulating clades of the virus in southern Africa. Clade I included isolates collected from South Africa and Zimbabwe, whereas clade II only included isolates from the KwaZulu Natal Province of South Africa.

Key Words: Wesselsbron virus—Flavivirus—Arbovirus—South Africa.

Introduction

Wesselsbron (WESS) disease is an acute mosquito-borne infection of ruminants in Africa. The disease is caused by infection with a *Flavivirus*, which is an enveloped, positive-sense RNA virus (Thiel et al. 2005). The first outbreak of WESS disease was reported on a sheep farm in Free State Province, South Africa, in 1955. The outbreak was associated with substantial mortality in newborn lambs and abortion in pregnant ewes (Weiss et al. 1956). Several historic investigations point toward a wide distribution of Wesselsbron virus (WESSV) across the African continent (Swanepoel 1989). The virus has been isolated from animals and mosquitoes from South Africa, Zimbabwe, Uganda, Kenya, Nigeria, Central African Republic, Senegal, Cameroon, and Ivory Coast. In addition, serologic evidence of WESSV infection was shown in Mozambique, Botswana, Namibia, Angola, and Madagascar. The only description of the disease outside of Africa was from Thailand in 1966, but these findings were not corroborated in any further investigations (Gould et al. 1967). Presumably, a wide range of vertebrate hosts are also susceptible to WESSV infection. Virus isolation or serologic evidence of infection has been described in several domestic livestock species, including camels, cattle, pigs, donkeys, and horses (Kemp et al. 1973, Blackburn and Swanepoel 1980, Swanepoel 1989). Evidence in wildlife species is more scant (or not well reported), but serological evidence was reported in 24 of 31 wild ruminants in a study in Chad in 1967 (Swanepoel 1989). WESSV is most commonly associated with floodwater-breeding *Aedes* mosquitoes (Muspratt et al. 1957, Kokernot et al. 1958), but an incidental isolation with unknown epidemiological significance was also made from an ixodid tick (Annual Report of the Institute Pasteur, Dakar, 1984, reported in Swanepoel and Coetzer 2004).

Infection with WESSV results in a high mortality rate (up to 27%) in newborn lambs and goat kids and is characterized by a typically short illness (usually about 72 h) including fever, anorexia, listlessness, general weakness, and increased respiratory rate (Coetzer et al. 1978). The disease in adult sheep, goats, and cattle is associated with mild, nonfatal febrile illness or asymptomatic infections. Infection may, however, lead to abortions or congenital disorders in pregnant animals (Swanepoel and Coetzer 2004). Historically, outbreaks of WESS disease coincide with Rift Valley fever (RVF) or Nairobi sheep disease outbreaks (Davies and Terpstra 2004, Swanepoel and Coetzer 2004). RVF and WESS presentations are similar, and consequently they complicate clinical recognition of WESS disease. Outbreaks of WESS disease that are only diagnosed clinically are often ascribed to RVF or the use of the live attenuated RVF vaccine, which causes abortions in

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pregnant animals. Although it is generally accepted from earlier reports that WESS disease is indeed a significant disease of sheep in South Africa, no structured surveillance for this disease exists, so the true burden remains anecdotal.

In humans, WESS disease is associated with sudden onset of a typically mild and short-lived acute phase (typically 1–3 days), including fever, rigors, headache, myalgia, arthralgia, and impaired vision (Swanepoel 1989). To date, no fatal human cases associated with WESSV infection have been reported. One laboratory-confirmed case presented with encephalitis with dementia and temporary loss of hearing (Weinbren 1959). This case involved a laboratory worker who had exposure to WESSV through a splash of virus suspension into the eye. Prior to this study, a total of 29 acute human cases of WESS disease (Table 1) have been laboratory confirmed and described. In addition to these acute cases, retrospective serosurveys conducted prior to 1980 indicated positivity rates of up to 35% in selected populations from Namibia, 30% from southern Mozambique, and 22% from northern Botswana (McIntosh 1980). In limited serosurvey studies, dating from 1955 to 1978, targeting anti-N WESSV antibodies from several different African countries, a total of 547 of 2647 (nearly 21%) human specimens tested positively (McIntosh 1980). In South Africa, serologically positive human cases were recorded along the eastern coast, with detection rates of 32% in the subtropical region of KwaZulu Natal Province (Ndumu area) and 0.7% in the southern Cape (McIntosh 1980). It should also be noted that interpretation of flaviviral serological findings should be made with caution due to the considerable cross-reaction of flaviviral antigens (Kuno 2003).

Animal and human RVF cases were reported in South Africa from 2008 to 2011, with the intensification of the outbreak occurring during the summer of 2010 (Archer et al., in press). A total of 302 human RVF cases from South Africa were laboratory confirmed during this period. During this time 2 isolations of WESSV were made from specimens submitted for suspected RVF cases. We report on the clinical case histories of these 2 recent laboratory-confirmed human cases of WESS disease and limited molecular characterization of the virus strains involved. These cases represent the first reported human cases of WESS disease since 1996. Although the majority of previously reported human WESS disease cases were associated with laboratory or field research, both of these cases involved exposures in livestock farmers. Genetic

Table 1. Summary of Documented Human WESS Disease Cases Prior to this Study

Location	*Case history*	*Reference*
Wesselsbron, Free State, South Africa	Five laboratory workers from veterinary laboratory with exposure to 1955 WESS outbreak isolates reported illness. Single isolation and 4 seroconversions were noted.	Weiss et al. (1956)
Lake Simbu, Tongaland (now Kosi Bay, KwaZulu Natal Province, South Africa)	A 35-year-old male mosquito catcher during field expedition in 1955. Virus isolated (strain H177) from blood.	Smithburn et al. (1957)
Lake Simbu, Tongaland (now Kosi Bay, KwaZulu Natal Province, South Africa)	Field worker (no details provided) in 1955. No virus isolated, but seroconversion indicated.	Smithburn et al. (1957)
Middelburg, Northern Cape Province, South Africa	Two field workers in 1957. Both were bitten by mosquitoes, but 1 also performed necropsies on sheep. Virus isolated from 1 patient and only seroconversion in the other.	Heymann et al. (1958)
Entebbe, Uganda	Laboratory-acquired infection in 1959. Infected through splash in the eye.	Weinbren (1959)
Dakar, Senegal	Laboratory-acquired infection in 1965.	Swanepoel (1989)
Ndumu, KwaZulu Natal, South Africa	Field worker with exposure to mosquitoes in 1966.	Swanepoel (1989)
New Haven, United States of America	Laboratory-acquired infection in 1969. Possible aerosol transmission noted. Live virus isolated from throat swab.	Justines and Shope (1969)
Ibadan, Nigeria	Laboratory-acquired infection in 1972. Patient was exposed to mosquito suspensions prepared for virus isolation and challenge virus used for neutralization assays.	Tomori et al. (1981)
Pienaars River, Limpopo, South Africa	Laboratory field worker exposed to mosquitoes in 1972.	McIntosh (1980)
Bloemfontein, Free State, South Africa	Circumstances of infection not clear in 1974.	McIntosh (1980)
Bangui, Central African Republic	Laboratory acquired infection in 1974.	Swanepoel (1989)
Johannesburg, Gauteng, South Africa	Circumstances of infection not clear in 1976.	McIntosh (1980)
Bangui, Central African Republic	Nine cases including 1 laboratory-acquired infection from 1981 to 1983.	Swanepoel (1989)
Dakar, Senegal	Circumstances of infection not clear in 1983.	Swanepoel (1989)
Bultfontein, Free State, South Africa	Field scientist infected while collecting mosquitoes in April 1996.	Jupp and Kemp (1998)

WESS disease, Wesselbron disease.

characterization of nearly a kilobase-pair region at the 3′ terminus of the NS5 gene was used to identify the 2 isolates. In addition, genetic sequencing of this region was performed for a collection of WESSV isolates collected in South Africa and Zimbabwe since 1955 and provides an initial description of the molecular epidemiology of this largely undescribed disease.

Materials and Methods

Testing of clinical specimens and history of human cases

Serum or blood specimens were submitted to the National Institute for Communicable Diseases of the National Health Laboratory Service (NICD-NHLS) for routine diagnostics during the RVF outbreak in South Africa. The samples were screened for evidence of antibodies against RVF, Sindbis, West Nile, and chikungunya viruses using a hemagglutination inhibition assay (Shope and Sather 1979). Samples were also inoculated into 2- to 3-day-old suckling mice (NMRI strain) for isolation of live virus (Shope and Sather 1979) according to a protocol approved by the National Health Laboratory Service Animal Ethics Committee (reference number, 107/06). The identity of the virus isolates was confirmed with reverse transcription PCR of a segment at the partial NS5 gene and 3′-untranslated region (UTR) and nucleotide sequencing of the amplicons (procedure detailed below). Clinical case histories were investigated by contacting the physicians of patients by telephone with positive test results. The latter was conducted in accordance with an ethics protocol approved by the Human Research Ethics Committee

Table 2. Virus Isolates Used in This Study

Laboratory reference number	*Source*	*Geographical location and collection date*	*Isolate passage number*	*GenBank accession number*	*Reference*
Van Tonder	*Ovis aries* (8-day-old lamb)	Farm Magdalena, Wesselsbron, Free State Province, South Africa. March 1955.	P34	JX423772	Weiss et al. (1956)
H177	Human	Lake Simbu, Tongaland (now Kosi Bay, KwaZulu Natal, South Africa), April 25, 1955.	P14	JX423785	Smithburn et al. (1957)
TAR100	*Aedes circumluteolus*	Lake Tete, Tongaland (now Kosi Bay, KwaZulu Natal, South Africa), May 4, 1955.	P7	JX423788	Smithburn et al. (1957)
AR748	*Aedes* spp.	Middelburg, Eastern Cape, South Africa, April 6, 1957.	P8	JX423773	Kokernot et al. (1960)
AR750	*Aedes juppi/caballus*	Middelburg, Eastern Cape, South Africa, April 9, 1957.	P6	JX423774	Kokernot et al. (1960)
AR778	*Aedes juppi/caballus*	Middelburg, Eastern Cape, South Africa, April 25, 1957.	P2	JX423775	Kokernot et al. (1960)
AR814	*Mansonia uniformis*	Ndumu, KwaZulu Natal, South Africa, May 8, 1957.	P7	JX423776	McIntosh (1980)
AN2351	*Ovis aries* (ewe)	Middelburg, Eastern Cape, South Africa, April 2, 1957.	P6	JX423789	Heymann et al. (1958)
AR2114	*Aedes circumluteolus*	Ndumu, KwaZulu Natal, South Africa, April 21, 1959.	P3	JX423778	McIntosh (1980)
AR2209	*Aedes circumluteolus*	Ndumu, KwaZulu Natal, South Africa, May 2, 1959.	P4	JX423777	McIntosh (1980)
AR3132	*Aedes circumluteolus*	Ndumu, KwaZulu Natal, South Africa, April 20, 1960.	P3	JX423779	McIntosh (1980)
H1028	Human	Ndumu, KwaZulu Natal, South Africa, March 3, 1966.	P3	JX423786	McIntosh (1980)
AR9512	*Aedes circumluteolus*	Ndumu, KwaZulu Natal, South Africa, November 22, 1967.	P4	JX423791	McIntosh (1980)
AN16210	*Desmodillus auricularis* (Cape short-eared gerbil)	Graaf Reinet, Eastern Cape, South Africa, November 4, 1968.	P7	JX423783	Kokernot et al. (1960), McIntosh (1980)
AR11173	*Aedes mcintoshi*	Pearson, near Harare Zimbabwe, May 25, 1969.	P4	JX423780	McIntosh (1972)
AR11189	*Aedes mcintoshi*	Pearson, near Harare Zimbabwe, May 24, 1971.	P3	JX423781	McIntosh (1972)
AR11190	*Aedes mcintoshi*	Pearson, near Harare Zimbabwe, May 24 ,1972.	P2	JX423782	McIntosh (1972)
AV259	Human	Bultfontein, Free State South Africa, April, 1996.	P7	JX423784	Jupp and Kemp (1998)
SA999/10	Human	Schweizer-Reneke, North West, South Africa, April, 2010.	P2	JX423787	This study
SPU195/11	Human	Colesberg, Northern Cape, South Africa, February, 2011.	P2	JX423790	This study

of the University of the Witwatersrand (reference number: M060449).

Viruses

Suckling mice–derived virus isolates were obtained from patient specimens submitted during the RVF outbreak as stated above. Lyophilized WESSV isolates ($n = 18$) archived at the NICD-NHLS were also included in the study (Table 2).

Nucleic acid extraction and PCR

Total RNA was extracted from 10% (w/v) homogenates of fresh or lyophilized brain material using TRIzol™ (Invitrogen, USA) reagent as described by the manufacturer. RNA pellets were reconstituted in 50 μL of nuclease-free water and stored at −70°C until further use. Attempts to amplify the partial NS5 gene using generic flavivirus primers employed in previous flaviviral phylogenetic studies (Kuno et al. 1998) inconsistently yielded amplicons for some of the WESSV isolates tested. Subsequently, oligonucleotides specific for the same region were redesigned based on the WESSV strain H177 sequence (GenBank accession number: EU707555). The primers, WESSV NS5 F (TACAACATGATGGGGAAACGTG) and WESSV NS5 R (CACTCAGTGATTGGTGTTTTGTC) were used to amplify a 1153-bp product using the Titan One Tube RT-PCR system (Roche Applied Bioscience, Germany) as described by the manufacturer. The reverse transcription (RT) PCR cycle included 30 min at 50°C, initial denaturation for 2 min at 94°C, followed by 35 cycles of 30 s at 94°C; 30 s at 47°C and 1 min at 68°C. An additional elongation step of 7 min at 68°C was included at the end of the last cycle. PCR products were purified using the Wizard® SV Kit Gel and PCR Clean-Up System (Promega, USA) as suggested by the manufacturer. Purified products were stored at −20°C until further use.

Sequencing and phylogenetic analysis

The nucleotide sequence of a 952-bp region of the target was determined using BigDye V3.1 Terminator Cycle Sequencing Ready Reaction Kits (Applied Biosystems, Great Britain) according to the manufacturer's instructions. Sequencing reactions were precipitated using the 60% ethanol protocol, also as recommended by the manufacturer. Sequences were analyzed using the Basic Local Alignment Tool (BLAST, www.ncbi.nlm.nih.gov/), and nucleotide sequence alignments were generated using CLUSTALW Multiple

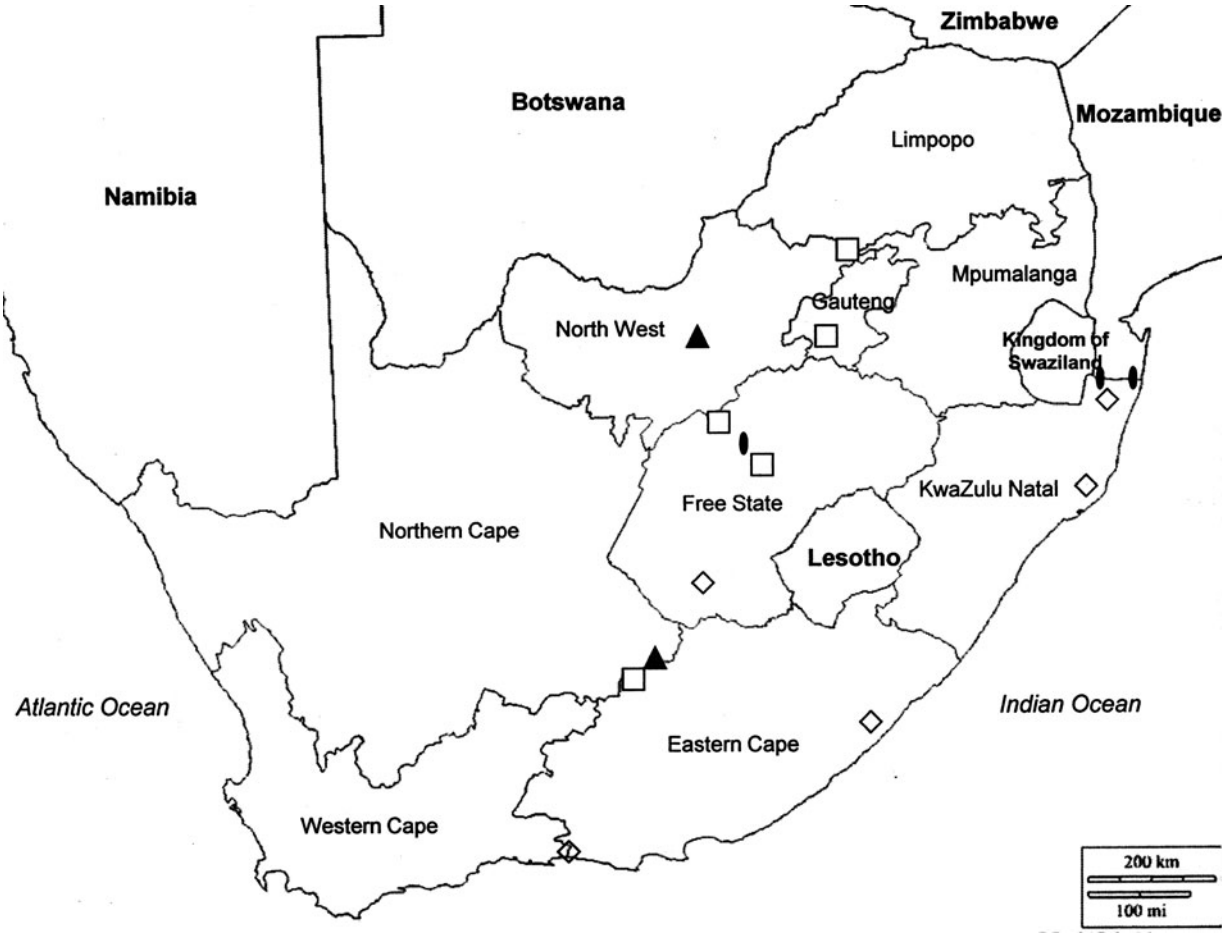

FIG. 1. The map displays the approximate distribution of recorded human cases of Wesselsbron disease (WESS) disease in South Africa. Records of acute cases (⬮, retrospective isolates from human cases available for this study; ▲, isolates from the 2010–2011 human cases described in this study; □, retrospective isolates from human cases not available for this study) and serological evidence of prior infection in humans from serosurveys (◇, previously reported antibody-positive human cases, as described in McIntosh 1980) are indicated.

Alignment analysis software as implemented in BioEdit version 7.0.5.3 (Hall 1999). Unique sequences generated in the study were submitted to GenBank and assigned the accession numbers indicated in Table 2. Preliminary phylogenetic analysis was performed using a neighbor-joining distance method of MEGA version 4 applying a Jukes–Cantor model under 1000 bootstrap iterations (Tamura et al. 2007). Sequence divergence was determined using MEGA version 4 to calculate the average *p*-distances within groups.

Results

Human cases of WESS disease

WESSV was isolated from serum specimens submitted for 2 suspected RVF cases, SA 999/10 and SPU195/11. The WESSV infections were confirmed by RT-PCR and molecular sequencing of the partial NS5 gene of the flavivirus genome and alignment to available sequences on the GenBank database (results not shown).

Upon investigation, the following information was obtained for each case. Case SA999/10 involved a 35-year-old male who fell ill during April, 2010. The patient farmed with goats, sheep, and cattle in Schweizer-Reneke, North West Province, South Africa (Fig. 1). The patient presented to a general practitioner complaining of a 4-day history of fever (up to 40°C), headache, myalgia, and arthralgia. The total blood count was normal, but liver transaminases (ALT 56 units/L and AST 55 units/L) were slightly raised. The patient received only symptomatic treatment and apparently recovered without any sequelae within a couple of days.

The second case, SPU195/11, was a 55-year-old male from the Colesberg area, Northern Cape Province, South Africa who fell ill in February, 2011 (Fig. 1). The patient farmed predominantly with sheep, but also kept cattle. The patient presented to a general practitioner complaining of a few days flu-like illness with fever, headache, myalgia, and arthralgia. No blood tests were performed. Fever persisted in this patient for a week after visiting the general practitioner, but he recovered reportedly without sequelae on only symptomatic treatment.

A summary of the clinical details available for confirmed human WESS disease, including the 2 cases reported here, is provided in Table 3.

Table 3. Summary of Limited, Reported Clinical Signs and Symptoms of WESS Disease Available for 14 Laboratory-Confirmed Human Cases

Clinical presentation	*Number of reported cases (% of total)*
Anorexia	1 (7.1)
Arthralgia	4 (28.6)
Blurred or impaired vision, retro-orbital pain, photosensitivity	3 (21.4)
Fever	8 (57.1)
Gum ulcers	1 (7.1)
Headache	6 (42.9)
Hepatitis	2 (14.2)
Hyperaesthesia	2 (14.2)
Lower-back pain	3 (21.4)
Myalgia (muscle pain)	6 (42.9)
Neurological signs (*i.e.*, impaired speech, auditory dysfunction, memory loss)	1 (7.1)
Prostration	1 (7.1)
Restlessness	1 (7.1)
Rigors	1 (7.1)
Skin rash	3 (21.4)
Splenomegaly	1 (8.3)
Sudden onset	4 (28.6)
Tender liver	2 (14.2)

WESS disease, Wesselbron disease.

Phylogeny of WESSV isolates

Only limited sequence data were available for WESSV at the time of the study for comparison. The 20 sequences grouped into 2 major clades (Fig. 2). Clade 1 was composed of the majority of isolates ($n=15$), including those from Free State, Eastern Cape, KwaZulu Natal, North West and Northern Cape provinces of South Africa, but also Zimbabwe. Clade II included isolates from Kosi Bay and Ndumu located in northern KwaZulu Natal, near the border with Mozambique. This analysis did not further stratify the isolates based on time of collection, host, or geographic origin. Isolates that were obtained from human cases were present in both clades.

Pairwise nucleotide comparison calculated an average of 4% nucleotide diversity (and maximum of 8.4%) was calculated across the group of 20 sequences (results not shown). Most of the nucleotide changes were synonymous with an average of 0.5% and maximum of 1% amino acid difference between the isolates.

Discussion

It is speculated that the emergence of several arboviruses, particularly flaviviruses, around the world has been ascribed to factors such as increased global travel, which may facilitate the spread of such vectors over vast distances, and global climate changes, which affect mosquito ecology (for review, see Weissenböck et al. 2010). Examples include the introduction of West Nile virus to North America and the emergence of Usutu virus in Central Europe. Spread of these diseases, especially in naïve populations, has been associated with substantial economic, ecological, and public health effects. More thorough surveillance of neglected arboviral diseases, such as WESS disease, is important in this regard. Historic studies have indicated that WESSV is widespread, at least in southern Africa. These studies, however limited in scope, did point toward considerable prevalence of WESS infection in certain human and animal populations. More recent investigations on the prevalence and incidence of WESS disease are not available.

Previously recorded acute human cases of WESSV have been limited to occupational exposures in laboratory and field workers, indicating a bias in the detection of cases. Only 29 acute human cases of WESS disease have been laboratory confirmed and described from 1955 to 1996. More than half of the cases ($n=18$) were associated with laboratory exposures ($n=11$) but also field workers (involved in mosquito collecting or sheep necropsies) ($n=7$). A further 11 cases were reported from Central African Republic and Senegal without clear indication of the source of infection. During investigations of suspected RVF cases in South Africa in 2010–2011, WESSV was isolated from 2 patients' blood specimens. Both patients were sheep farmers, although other livestock was also kept on

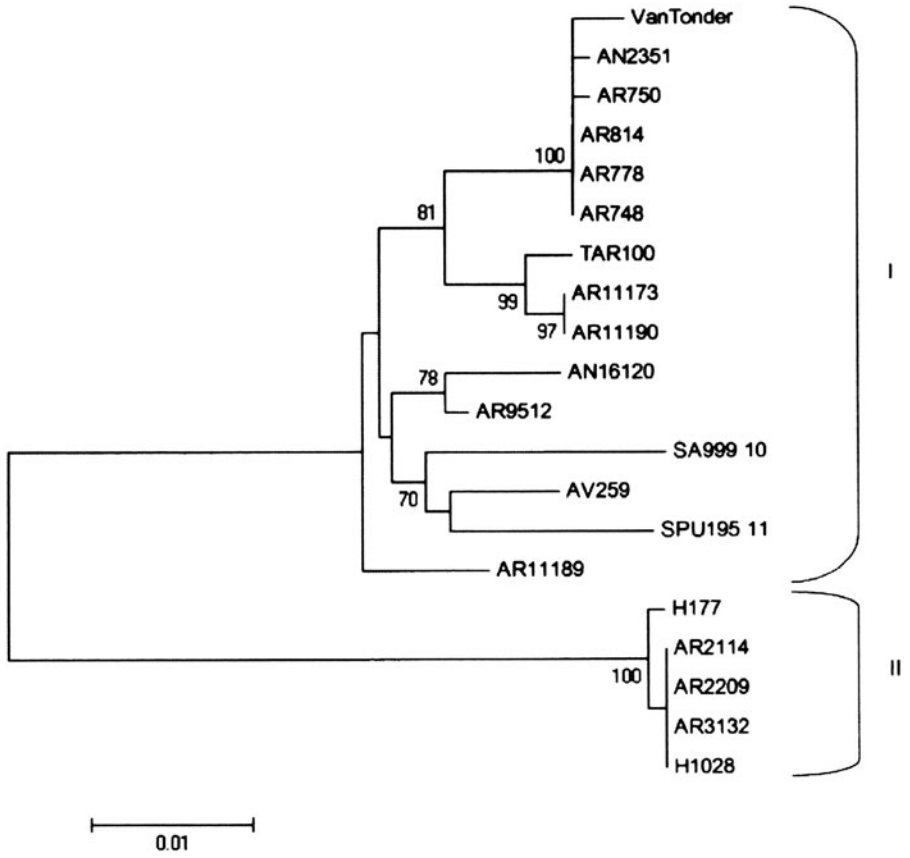

FIG. 2. An unrooted phylogenetic tree of a 982-bp region of the NS5 gene of Wesselsbron disease virus (WESSV) isolates inferred by the neighbor-joining method. The percentage of replicate trees in which the associated taxa clustered together in the bootstrap test (1000 replicates) are shown next to the branches; only bootstrap values of greater than 70% are shown.

their farms. As described before, both patients developed a febrile disease with arthralgia and sudden onset. From the limited documentation of acute WESS disease cases, it would appear that WESSV infection is associated with mild, self-resolving infection most commonly associated with fever, headache, myalgia, and arthralgia. A single report of encephalitis associated with WESS disease may have been associated with the unusual route of inoculation of the virus. This case involved exposure to laboratory-amplified material through the ocular mucosa. Likewise, no sequelae have been recorded in the 2 recent patients with follow-up more than a year after the initial diagnosis in at least 1 of the cases.

The 2 recent cases of WESS disease were incidentally confirmed during laboratory investigation of suspected RVF cases. These unlinked cases originated from farms approximately 450 km apart. Schweizer-Reneke is located in the North West Province, which is typically characterized as wooded savannah or bushveld region. Schweizer-Reneke receives an average of 350 mm of rainfall per year, with January being the wettest month. Colesberg in the Northern Cape Province is, however, classified as semidesert and receives only an average of 262 mm of rainfall per year. The highest rainfall is typically recorded in March. Both cases were recorded following the average highest rainfall months, which is not unexpected because higher levels of mosquito activity could be expected at such times. RVF was also recorded from these areas during this time. WESSV is most often isolated from *Aedes (Ochlerotatus) caballus/juppi*, *Ae. mcintoshi*, and *Ae. circumluteolus*, all being anthrophophilic in nature and feeding readily on humans. *Ae. caballus*, *Ae. juppi*, and *Ae. mcintoshi* are typical pan-associated floodwater aedines, which most likely contribute to the virus transmission in humans during high rainfall seasons on the African inland plateau (*i.e.*, outbreak associated). *Ae. circumluteolus*, on the other hand, is typically associated with river systems in the lowveld and subtropics (extending from St. Lucia northward to Mozambique and including the Pafuri area), and therefore WESSV might be more frequently encountered in these regions with higher average rainfall (*i.e.*, interepizootic). This proposed epidemiological cycle of WESSV is supported by the phylogenetic inference performed in this study. The panel analyzed in this study represents isolates collected over a period of 56 years from southern Africa and yielded 2 major groupings of WESSV. Isolates from clades I and II co-circulate in subtropical Kosi Bay and Ndumu, located in the north of KwaZulu Natal. Clade II was exclusive to this area and only associated with *Aedes circumluteolus.* Clade I included 15 of the 20 isolates analyzed and is widely distributed through South Africa. Isolates collected from a single site in Zimbabwe, the Pearson settlement located approximately 15 km north of Harare, was also included in this grouping. Clade I isolates were heterogeneous based on mosquito vector and included isolates from *Aedes juppi/caballus*, *A. mcintoshi*, *A. circumluteolus*, and *Mansonia uniformis*. Isolates from clades I and II co-circulate in Kosi Bay and Ndumu, located in the north of KwaZulu Natal. Clade II was exclusive to this area and only associated with

Aedes circumluteolus. The biological or pathogenic significance of these 2 clades is not apparent based on the inference in this study. The isolate (AV259) associated with a human case of encephalitis clustered with other febrile human cases. The inclusion of sequences of WESSV isolates from elsewhere in Africa and the vaccine strain should be included to further elucidate this phylogenetic inference but was not available for this study.

Conclusion

WESS disease is an important, but neglected, disease of ruminants. Recognition of acute human cases has been incidental in the past. This was also the case with the recently confirmed human cases that were originally submitted for RVF investigations. Nevertheless, serologic studies have suggested a wide distribution and relatively high prevalence of WESS disease in the human population in several locations, but specifically the coast of KwaZulu Natal in South Africa. The spectrum of clinical disease, pathogenicity factors, and epidemiology of the disease are not well described. Hence, the disease is likely underreported in both ruminants and humans. A limited phylogenetic analysis of 20 isolates of WESSV collected from South Africa and Zimbabwe from different mosquito species, sheep, and human cases identified 2 clades of the virus.

Author Disclosure Statement

The authors declare no competing financial interests exist.

References

Archer BN, Thomas J, Weyer J, Cengimbo A, et al. Epidemiological investigations into outbreaks of Rift Valley fever in humans, South Africa 2008–2011, submitted.

Blackburn NK, Swanepoel R. An investigation of flavivirus infections of cattle in Zimbabwe Rhodesia with particular reference to Wesselsbron virus. J Hygiene 1980; 85:1–33.

Coetzer JAW, Theodorodis A, Van Heerden A. Wesselsbron disease. Pathological, haematological and clinical studies in natural cases and experimentally infected new-borne lambs. Onderstepoort J Vet 1978; 45:93–106.

Davies FG, Terpstra C. Nairobi sheep disease. In: Coetzer, JAW, Tustin, RC, eds. *Infectious Diseases of Livestock*, 2nd ed. South Africa: Oxford University Press, 2004:1071–1076.

Gould DJ, Gunakasem P, Marshall JT, Nisalak A, et al. Ecology of arboviruses in Thailand. Annual progress report, South East Asia Treaty Organization, Bangkok, Thailand 1967:43–71.

Hall TA. User friendly biological sequence alignment editor and analysis program for Windows 95/98/NT. Nucleic Acids Symposium Series 1999; 14:95–98.

Heymann CS, Kokernot RH, de Meillon B. Wesselsbron virus infections in man. S Afr Med J 1958; 32:543–545.

Jupp PG and Kemp A. Studies on an outbreak of Wesselsbron virus in the Free State Province, South Africa. J Am Mosquito Contr 1998;14:40–45.

Justines GA, Shope RE. Wesselsbron virus infection in a laboratory worker, with virus recovery from throat washing. Health Lab Sci 1969; 6:46–49.

Kemp GE, Causey OR, Moore DL, O'Connor EH. Viral isolates from livestock in northern Nigeria: 1966–1970. Am J Vet Res 1973; 34:707.

Kokernot RH, Paterson HE, De Meillon B. Studies on the transmission of Wesselsbron virus by Aedes (Oclerotatus) caballus (Theo.). S Afr Med J 1958; 32:546–549.

Kokernot RH, Smithburn KC, Paterson HE, de Meillon B. Further isolations of Wesselsbron virus from mosquitos. S Afr Med J 1960; 34:871–874.

Kuno G. Serodiagnosis of flaviviral infections and vaccinations in humans. Adv Virus Res 2003; 61:3–65.

Kuno G, Chang G-J, Tsuchiya R, Karabatsos N, et al. Phylogeny of the genus flaviviruses. J Virol 1998; 72:73–83.

McIntosh BM. Rift Valley fever 1. Vector studies in the field. J S Afr Vet Assoc 1972; 43:391–395.

McIntosh BM. The epidemiology of arthropod-borne viruses in Southern Africa. DSc dissertation, University of Pretoria, Pretoria 1980:144–159.

Muspratt J, Smithburn KC, Pathmanathan R, Kokernot RH. Studies on arthropod-borne viruses of Tongaland. X. The laboratory transmission of Wesselsbron virus by the bite of *Aedes (Banksinella) circumluteolus (Theo.)*. S Afr J Med Sci 1957; 22:121–126.

Shope RE, Sather GE. Arboviruses. In: Lenette EH, Schmidt NJ, eds. *Diagnostic procedures for viral, rickettsial and chlamydial infections*. Washington DC: American Public Health Association, 1979:767–814.

Smithburn KC, Kokernot RH, Weinbren MP, De Meillon B. Studies on arthropod-borne viruses of Tongaland. IX. Isolation of Wesselsbron virus from a naturally infected human being and from *Aedes (Banksinella) circumluteolus* (Theo). S Afr J Med Sci 1957; 22:113–120.

Swanepoel R. Wesselsbron virus disease. In: Monath, TP, ed. *The Arboviruses: Epidemiology and Ecology*. Boca Raton, FL: CRC Press Inc, 1989:32–57.

Swanepoel R, Coetzer JAW. Wesselsbron disease. In: Coetzer, JAW, Tustin, RC, eds. *Infectious Diseases of Livestock*, 2nd ed. South Africa: Oxford University Press, 2004:987–994.

Tamura K, Dudley J, Nei M, Kumar S. *MEGA4*: Molecular Evolutionary Genetics Analysis (MEGA) software version 4.0. Mol Biol Evol 2007; 4:1596–1599.

Thiel H-J, Collett MS, Gould EA, Heinz FX, et al. Flaviviridae. In: Fauquet CM, Mayo MA, Maniloff J, et al., eds. *Virus Taxonomy: Eighth Report of the International Committee on the Taxonomy of Viruses*. Elsevier: Amsterdam, 2005:981–998.

Tomori O, Monath TP, O'Connor EH, Lee EH, et al. Arbovirus infections among laboratory personnel in Ibadan, Nigeria. Am J Trop Med Hyg 1981; 30:855–861.

Weinbren MP. Some clinical observations on a human case of infection with Wesselsbron virus. East African Virus Research Institute Report July 1958– June 1959, 1959:22.

Weiss KE, Haig DA, Alexander RA. Wesselsbron virus—a virus not previously described associated with abortion in domestic animals. Onderstepoort J Vet 1956; 27:183–195.

Weissenböck H, Hubálek Z, Bakonyi T, Nowotny N. Zoonotic mosquito-borne flaviviruses: Worldwide presence of agents with proven pathogenicity and potential candidates of future emerging diseases. Vet Microbiol 2010; 140:271–280.

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