Epidemiology of human rabies in South Africa, 2008 - 2018

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Background. Human rabies cases continue to be reported annually in South Africa (SA). Previous investigations have shown the association between the occurrence of human rabies cases and dog rabies cases in the country.
Objectives. To describe the epidemiology of laboratory-confirmed human rabies cases in SA for the period 2008 - 2018.
Methods. A retrospective document review of laboratory-confirmed human rabies cases for the period 2008 - 2018 was performed using a case register and related documentation available from the National Institute for Communicable Diseases.
Results. A total of 105 human rabies cases were laboratory confirmed from 2008 to 2018, with cases reported from all the provinces of SA except the Western Cape. Children and adolescents were most affected by the disease during the study period. In almost half of the cases, medical intervention was not sought after exposure. When victims did seek healthcare, deviations from post-exposure prophylaxis protocols were reported in some cases.
Conclusions. The epidemiological trends of human rabies cases reported in SA for the period 2008 - 2018 remained largely the same as in previous reports. Dog-mediated rabies remains the main source of human rabies in SA.

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Rabies is endemic in South Africa (SA) and circulates in domestic dogs as well as in several wildlife reservoirs.[1] The disease has been reported in the country for more than 200 years, but an increase in the number of animal and human cases has occurred since 1930.[1] Although this period corresponds to the time of improved diagnostics and increasing surveillance for rabies, significant population growth and dispersion across the country are likely to have contributed to the spread of dog-associated rabies.[1] Rabies vaccination of domestic dogs and cats by owners has been required by law in SA since 1952, but it is noteworthy that this regulatory requirement did not prevent the establishment and spread of rabies in domestic dogs in KwaZulu-Natal Province and subsequent introductions and reappearances at various locations in SA.[1-7] The history of rabies in SA has been marked by a more than three-decade epizootic in KwaZulu-Natal and Eastern Cape provinces, and intermittent successes and failures in control of dog rabies there and in other parts of the country.[8,9]

The disease, a fatal neurological infection of all mammals including humans, is caused by the rabies virus or the rabies-related lyssaviruses. Rabies associated with domestic dogs remains the most important problem from a public health perspective, with an estimated 59 000 human cases reported globally every year.[10] Rabies in domestic dogs is most often reported from developing countries where the systematic vaccination of dogs has not been adequately applied to eliminate the disease in this species,[10] despite the fact that vaccination of domestic dogs has been established as the mainstay of rabies control and prevention of human cases.[11] The public health burden associated with rabies is substantial owing to loss of life resulting from untreated exposures, and compounded by the high cost of post-exposure prophylaxis (PEP) that is required to prevent rabies infection in potentially exposed individuals.[10] Rabies PEP, which includes thorough wound washing, rabies vaccine and immunoglobulin therapy, albeit costly, is highly effective if used in accordance with internationally recognised regimens.[12,13]

In SA, human rabies is a notifiable medical condition and laboratory investigation of suspected cases is performed at the National Institute for Communicable Diseases (NICD). From 1983 to 2007, a total of 353 human cases of rabies were confirmed by laboratory testing in SA, an average of ~14 cases per annum.[14] It is highly likely that the number of human rabies cases is underestimated owing to misdiagnosis and underdiagnosis of the disease. The latter is assumed for various reasons. These include instances when clinical material is unavailable or unsuitable for laboratory investigation, cases where patients do not present for medical treatment (or choose traditional healing approaches) and die outside the healthcare system, or failure to consider rabies as part of a differential diagnostic investigation for patients with encephalitis who present for medical treatment. Hampson *et al.*[10] estimated the occurrence of human rabies in SA at 40 cases per year, based on available and extrapolated dog rabies and dog bite data.[10] The study also indicated by inference that ~4 000 human lives per year are saved in SA through the use of rabies PEP.[10] From 1983 to 2007, the majority of human rabies cases originated from the dog rabies-afflicted KwaZulu-Natal (*n*=279; 79%). Cases mostly involved children and young adults, with >70% of cases reported in under-20-year-olds. As expected, nearly all cases were linked to dog bite exposure (*n*=296; 84%), and very few were associated with exposure to wildlife species. Only two cases of human rabies associated with infection with a rabies-related lyssavirus, the Duvenhage lyssavirus, spread through bites of specific species of insectivorous bats, were reported, in 1970 and 2006.[15,16]

Objectives

To provide an update on the epidemiological features of laboratory-confirmed human rabies cases in SA for the period 2008 - 2018.

Methods

Cases

Laboratory investigation of suspected human rabies cases in SA is performed at the Centre for Emerging Zoonotic and Parasitic Diseases of the NICD. Clinically suspected human cases are classified as confirmed rabies cases following the detection of rabies virus antigen using a fluorescent antibody test on postmortem-collected brain samples, or detection of rabies virus genomic RNA using reverse transcription polymerase chain reaction on brain, saliva, cerebrospinal fluid or skin biopsy samples, as per World Health Organization recommendations.[17] For all cases investigated, information was extracted from case notes, originating from NICD case investigation forms, from NICD pathologists-on-call notes, and/or from investigation reports from the provincial and district communicable disease directorate that were archived at the NICD. Cases confirmed from 1 January 2008 to 31 December 2018 were included in this study. The cases were classified by the year in which exposure had occurred, i.e. a patient who died in January 2009, but was exposed in November 2008, would be counted as a 2008 case.

Data extraction and analysis

A retrospective document review was performed using the case register and archived patient case histories at the Centre for Emerging Zoonotic and Parasitic Diseases, NICD. Data were extracted by two raters, and each entry in the database was cross-verified. The data were captured in an Excel spreadsheet, 2016 version (Microsoft Corp., USA). Data for the following variables were extracted from the documents: sex, age in years, geographical location, animal involved in the exposure, and details of post-exposure management. Basic descriptive statistics were summarised using Stata 13.0 software (StataCorp, USA). Distribution mapping using approximate global positioning system co-ordinates for geographical location of exposure was performed in ArcGIS 10.2 (Esri, USA). A choropleth layer of districts were created and were shaded according to number of cases normalised by population to indicate which and to what extent districts were affected by human rabies during 2008 - 2018. In addition, we assessed trends by comparing the spatial pattern of human cases across provinces with the previous period, 1997 - 2007. The case data for this period were available from a database described in a previous study.[14]

Ethics requirements

Ethics authorisation for the study was provided through the protocol entitled 'Essential communicable disease surveillance and outbreak investigation activities of the National Institute for Communicable Diseases', approved by the University of Witwatersrand Human Ethics Committee (ref. no. M160667).

Results

Epidemic trends and geographical distribution

A total of 105 human rabies cases were laboratory confirmed from 2008 to 2018. This equates to an average of 10.5 cases per year, with a range of 1 - 17 cases per year reported during this time (Fig. 1). During the reporting period, cases were most frequently reported from locations in Eastern Cape (*n*=34; 32%), KwaZulu-Natal (*n*=31; 30%) and Limpopo (*n*=22; 21%) provinces (Figs 1 and 2). Districts reporting the highest total number of cases in total and per population number were in the Eastern Cape, namely O R Tambo, Alfred Nzo and UThungulu (now renamed as King Cetshwayo), and Limpopo, namely Vhembe district (Fig. 2). Cases were also reported from Mpumalanga (*n*=8; 8%) and Free State (*n*=7; 7%) provinces, with Ehlanzeni and Thabo Mofutsanyane districts, respectively, most affected. A single case each was reported from Gauteng, North West and Northern Cape provinces, with no cases reported from the Western Cape. Data from the report period were compared with data from the preceding years, 1997 - 2007 (Fig. 3). It was found that the number of confirmed human rabies cases in KwaZulu-Natal halved from 64 to 31, while the number of cases reported from the Eastern Cape nearly doubled (34 compared with 19). The number of cases in Free State and Mpumalanga provinces compared with 1997 - 2007 (1 and 2 cases, respectively) increased to 7 and 8, respectively. In the Northern Cape, North West and Limpopo, the rate of cases reported remained the same for the two periods.

For the reporting period, the majority of cases were linked to domestic dog exposures (*n*=79; 75%), but cases of exposure to cats (*n*=5; 5%) and one case related to a mongoose exposure were reported. For 20 cases, no exposure history was apparent or reported. No cases during the study period were reported to be associated with other wildlife exposures. For the cases linked to dog exposure, it was known for 34 dogs that nearly a third were strays (*n*=24; 30% of the total), while the other 10 (13% of the total) were known and owned dogs.

Demographic features

Of the 105 cases, 79 (75%) were in males and 25 (24%) in females (in one case sex was not reported). The age distribution was skewed towards the younger age groups, with 50% of cases reported in children aged ≤9 years (*n*=53) (Fig. 4). A further 21% of cases were reported in children and adolescents between the ages of 10 and 19 years (*n*=22). The remainder of the cases involved adults (*n*=28; 27%). Age was not reported for 2 cases during the study period.

Post-exposure management

Most exposures involved a bite or multiple bites (*n*=65; 62%), but exposures related to scratches (*n*=10; 10%) and licks on broken skin (*n*=1; 1%) were also reported. In 29 cases, no exposure was apparent or reported.

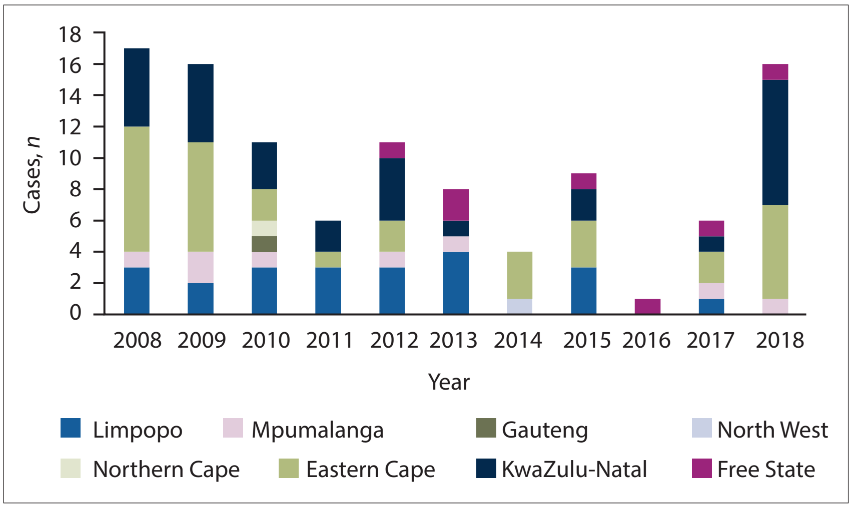

Fig. 1. Number of laboratory-confirmed human rabies cases per province per year in South Africa, 2008 - 2018.

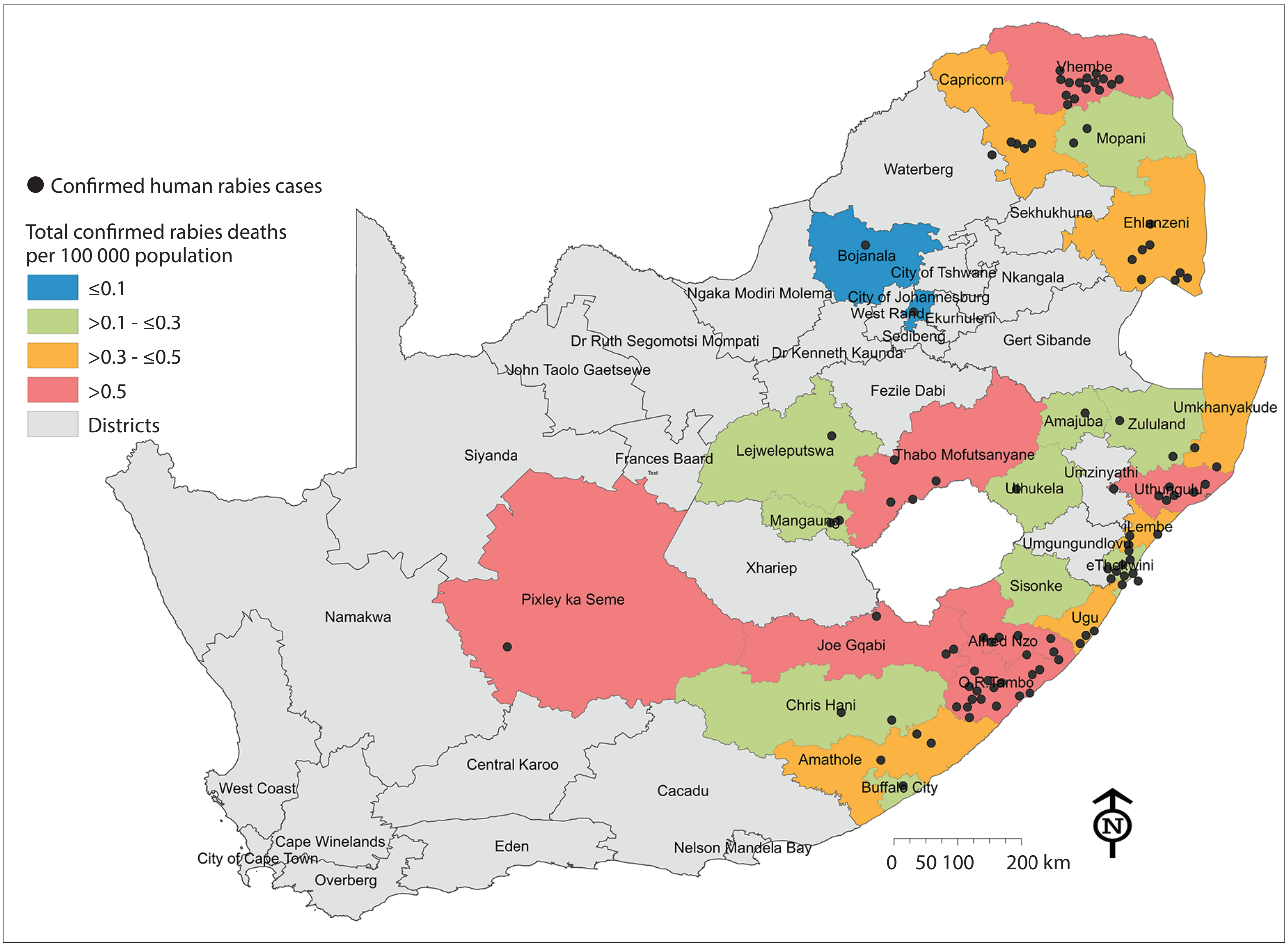

Fig. 2. Geographical distribution of laboratory-confirmed human rabies cases in South Africa, 2008 - 2018.

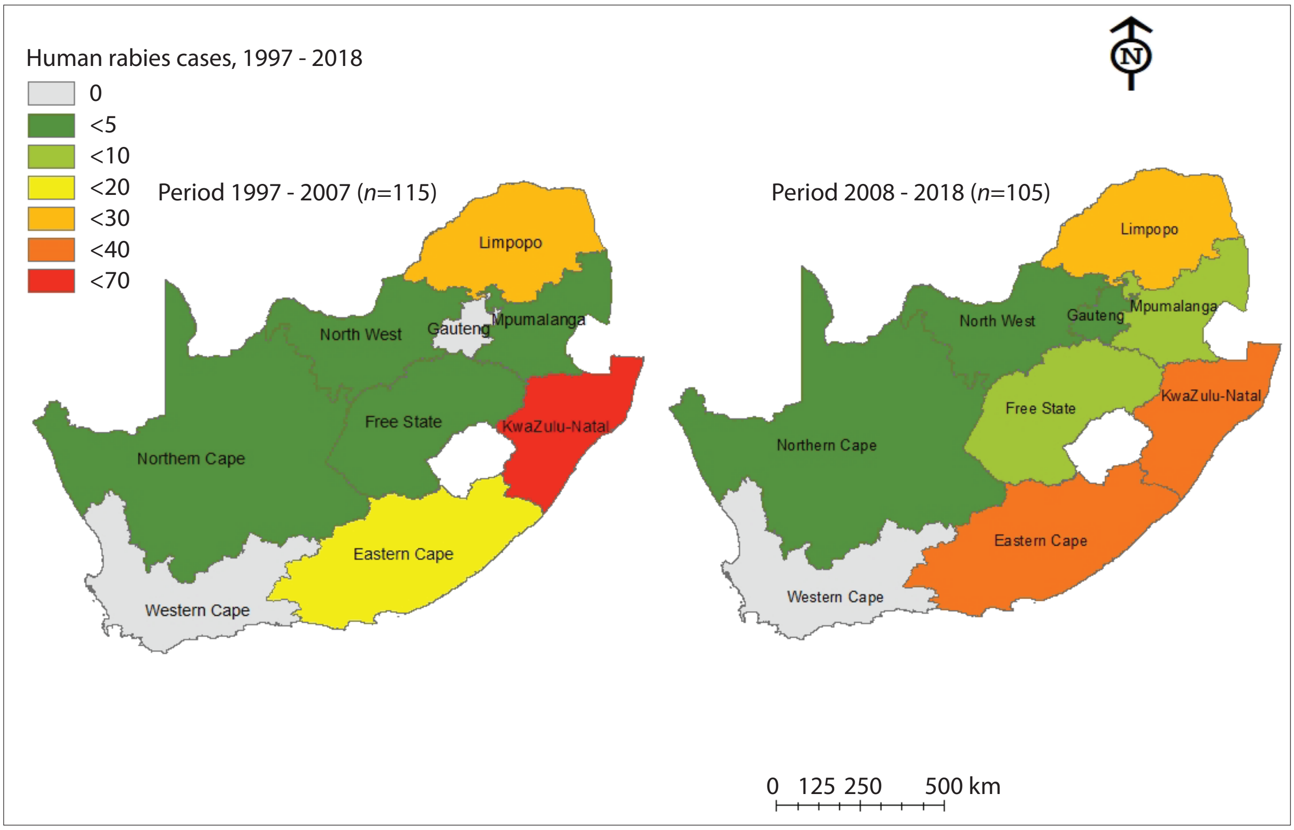

Fig. 3. Geographical pattern of laboratory-confirmed human rabies cases in South Africa, comparison between 2008 - 2018 and 1997 - 2007.

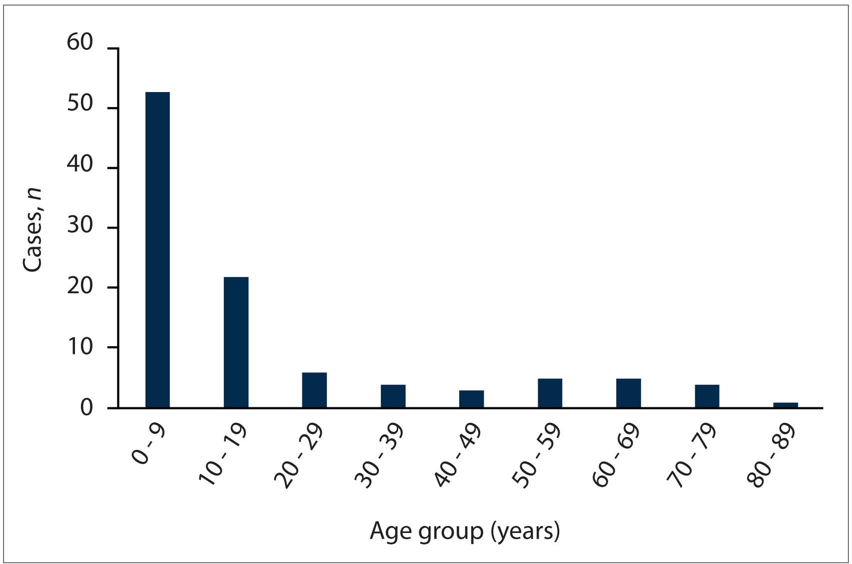

Fig. 4. Age distribution of laboratory-confirmed human rabies cases for the period 2008 - 2018.

Nearly a third of the individuals who were exposed reportedly did not seek medical intervention after the event (*n*=32; 30%). Although 31 did visit a healthcare facility after exposure, several failures contributed to ineffective prevention of rabies virus infection. Nearly a third (*n*=9; 29%) of the individuals who sought medical intervention after exposure only received wound treatment at the facility, while of those for whom rabies vaccination was prescribed, 7 (23%) defaulted vaccination before completion of the full schedule (i.e. four doses, on days 0, 3, 7 and 14). One patient, who had severe injuries to the head and neck, reportedly developed signs and symptoms of rabies disease before completing the full vaccination schedule. In addition, a total of 12 individuals (39%) did not receive rabies immunoglobulin treatment although it was indicated. For a total of 42 cases, no post-exposure management information was recorded or available for this study.

Discussion

The epidemiology of human rabies in SA from 2008 to 2018 remained largely the same compared with the preceding time period, 1997 - 2007. It was noteworthy that a shift in the number of cases was reported from KwaZulu-Natal and the Eastern Cape. While cases decreased in the long-affected KwaZulu-Natal, cases in the Eastern Cape nearly doubled during the study period. The drop in human rabies cases in KwaZulu-Natal relates to the efforts in dog rabies control in the province from 2009 to 2015, again reiterating the link between dog rabies and the occurrence of human cases.[9] It should, however, be noted that nearly a quarter of the cases (*n*=8) in KwaZulu-Natal occurred in 2018 alone, and were linked to the collapse in dog rabies control efforts in the province.[9] The latter is attributed to many factors, including diminished resources for dog rabies control in the province.[9] Apart from the increase of cases in the Eastern Cape, increases were also noted in Mpumalanga and the Free State during the study period. Numbers of cases increased nearly seven- and four-fold for the Free State (from 1 case to 7 cases) and Mpumalanga (from 2 cases to 8), respectively. The increase in cases in the Free State and Mpumalanga coincides with the emergence of dog rabies in parts of these provinces during this time period.[2,7]

Another noteworthy finding was the report of a human rabies case in Gauteng Province in 2010. It was significant, as this case represented the first human case of rabies acquired following exposure that occurred within the borders of the province.[3] This case was associated with the emergence of dog rabies in south-western Johannesburg following an introduction of the disease from KwaZulu-Natal.[3] This outbreak demonstrated the vulnerability of many similar communities in SA where the level of rabies vaccination in dogs may be low, probably because of low commitment to rabies control and vaccination in areas that have not been affected by the disease, or have not been affected for an extended period of time. Owing to low vaccination coverage and consequent low herd immunity in such dog populations, introduction of the disease may be followed by a sustained outbreak. The occurrence of dog rabies in areas either previously known to be rabies free, or where dog rabies was under control, provides many challenges. These include potential delays in recognition of the disease in both animals and humans, low community participation in dog rabies vaccination programmes, and low awareness and knowledge of appropriate post-exposure responses, both in the affected communities and among healthcare workers.[3]

The source and demographics of human rabies cases from 2008 to 2018 remained unchanged from previous reports. Domestic dogs as the vector of rabies virus to the human population in SA was also reaffirmed through analysis of exposure histories. Only a single case was related to exposure to wildlife (a mongoose) during the study period. These findings again reiterate the importance of dog rabies control in SA as the critical strategic approach to prevent human rabies deaths. The age distribution of human rabies cases in SA has remained the same in over three decades.[12] Children and adolescents are most affected, accounting for more than 70% of cases. This observation is in line with what is observed in other places where dog-mediated human rabies is still reported, and rabies is often referred to as 'a disease of children'.[10,17] This information is important, as it points to the critical target group for rabies health awareness and education campaigns in dog rabies-affected areas. During the study period, males were also three times more likely to contract rabies than females. This finding has previously been observed in SA.[12]

Health awareness and education are crucial in rabies prevention strategies. Their lack may have played an important role in nearly a third of the confirmed human cases reported here, in which no medical intervention was sought following exposure. It is important to raise awareness of rabies and the risks associated with dog bites in communities affected by dog rabies. Rabies virus is transmitted not only through serious wounds, for which a victim would be likely to seek medical treatment, but even through small wounds such as scratches, or contamination of broken skin or mucosa with the saliva of a rabid dog. The latter accounted for ~10% of the confirmed cases reported here. Education in rabies PEP and its importance as a life-saving treatment for victims potentially exposed to the virus should also be improved in healthcare workers serving communities where dog rabies is reported. A total of 16 confirmed human rabies cases involved victims who presented to a healthcare facility after exposure, but received only wound care because there was no appreciation of the risk of rabies. In addition, in several cases the risk of rabies was acknowledged, but rabies

PEP was not delivered in accordance with national and international guidelines. The major factor contributing to post-exposure failure in these cases was the omission of rabies immunoglobulin from post-exposure schedules. In a total of 12 cases no rabies immunoglobulin was received, and in one of these cases it was documented that there was none available at the health facility. In 7 cases the risk of rabies was anticipated and rabies PEP was initiated, but the patients defaulted the complete vaccination schedule. This observation reiterates the importance of instituting measures to ensure that patients are aware of the repeat vaccinations required, and realise the importance of completion of the prescribed schedule.

Conclusions

Although the overall epidemiological trends in human rabies in SA during the study period remained similar to findings reported previously, it is important to note that increases and decreases in numbers of cases were reported at district and provincial levels. While cases dropped in KwaZulu-Natal, the province that has produced the greatest number of human rabies cases since 1983, an increase in cases was reported from four provinces. The increase in human cases in these locations coincides with the emergence or re-emergence of dog rabies. The known interlinked epidemiology of dog rabies and human rabies was further supported by the finding that the majority of human rabies cases were associated with dog exposure. This information reiterates the importance of dog rabies control in SA as the approach for primary prevention of human rabies cases.

Declaration. None.

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Conflicts of interest. None.

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