

Rabies in South Africa and the FIFA Soccer World Cup

Travelers' awareness for an endemic but neglected disease

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Rabies is endemic on every continent except Antarctica and is also considered to be a significant health problem in Africa, including South Africa.

With the upcoming FIFA Soccer World Cup to be held in 2010 in cities throughout South Africa, this review depicts the rabies situation in South Africa and discusses what travelers visiting the games should know about rabies and rabies prophylaxis before or after an exposure to a potential rabid animal occurs.

Introduction

From June to July 2010, the Republic of South Africa (RSA) will be the host of the FIFA Soccer World Cup with 32 nations from all over the world participating. Until the finals on July 11, 2010, in Johannesburg, games will be ongoing for a 4-week-period in several cities throughout the country (Fig. 1).¹ Around 250 to 300,000 additional international tourists are expected to visit South Africa,² and while the country and tourism industry are preparing themselves for this event, travelers should be educated about the potential risk of rabies, which is endemic throughout Africa, including South Africa and neighboring Southern African countries.³

Despite the availability of effective human as well as veterinary vaccines against rabies, and other measures for its control, rabies remains a major health problem throughout the World. Rabies is present on every continent except Antarctica. Annually, about 55,000 human deaths occur, mainly in the developing countries of Africa and Asia.^{4,5} In South Africa rabies has been endemic for decades or even centuries with the first confirmed outbreak in 1892 in the Eastern Cape Province after importation of an infected dog from England.⁶ Relative to most other African countries, surveillance for rabies in South Africa is active and comprehensive and the epidemiology of the disease has been well studied. Figure 2 summarizes the geographical occurrence

of animal and human rabies in South Africa. Cases of animal rabies have been reported in all nine provinces. Human deaths have occurred in all provinces except Western Cape. From 2003 to 2008, on average about 15 cases per year have been reported throughout the country, ranging from 7 cases in 2004 to more than 30 cases in 2006. In 2008, 20 people died of rabies in South Africa.⁷ Since the 1970s, the majority of human rabies cases have occurred in the Kwa-Zulu Natal (KZN) Province.⁶ While it is common knowledge that the majority of rabies cases occurs in rural areas rather than big cities, rabid animals have been found in rural as well as urban areas, and exposures to rabid animals have occurred in cities as well.

Dog Rabies in Kwa-Zulu Natal

As reflected by the incidence of human rabies cases, dog rabies in South Africa is most prevalent in the KZN province.⁸ After a major epidemic of dog rabies in the 1960s, rabies had been brought under control in 1968. In the following 8 years, rabies was considered to be under control in KZN. However, in 1976 the disease re-entered northern Natal from Mozambique and since then dog rabies has proved difficult to control in the peri-urban settlements of KZN.⁶ The disease spread from Natal to Lesotho in 1982, and further into regions of Eastern Cape Province in the 1980s and 90s. Much has changed since 1976: AIDS today contributes indirectly to the incidence of rabies. In some villages, the rate of HIV infection is 60–80%, and dogs are often abandoned when their owners die of AIDS.^{9,10} There is widespread poverty and a lack of primary health care for animals. Even owned dogs may wander as packs searching for scraps of food. Sustaining a mass vaccination campaign is an expensive exercise, and financial pressures due to other diseases outbreaks have been a major factor in hampering rabies control in KZN in recent years.⁹ Nevertheless, an ongoing integrated control program for dog rabies in KZN is internationally regarded and supported as a showcase program for rabies eradication in the Southern African region.

The Limpopo Outbreak

In a rabies endemic continent, the spread of rabies virus into regions with appropriate vector populations can lead to epidemic

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Figure 1. Locations of the FIFA World Cup. Soccer matches will be held in Johannesburg (1 and 2; Ellis Park stadium and Soccer City stadium), Tshwane/Pretoria (3), Rustenburg (4), Polokwane (5), Nelspruit (6), Mangaung/Bloemfontein (7), Durban (8), Nelson Mandela Bay/Port Elizabeth (9) and Cape Town (10).

outbreaks of the disease. An example of this occurred in dogs in the Limpopo Province, the northernmost province of RSA. In this province, sharing international borders with Zimbabwe, Botswana and Mozambique, rabies was only occurring in single cases until 2005, when an outbreak occurred.¹¹ From five laboratory confirmed animal cases in 2004 (dogs) the number increased to more than 100 cases in 2006, mainly dogs, as well as black-backed jackal (*C. mesomelas*) and cattle. Subsequently, more than 20 cases were confirmed in humans, with a 100% case fatality rate. Phylogenetic analysis of virus isolates indicated that outbreak virus strains were most closely related to recent canine/jackal strains from Southern Zimbabwe. These analyses as well as temporal and spatial analyses of the occurrence of the cases (the majority of cases emerging in the Vhembe District, which is closest to the northern border) suggested that the outbreak may have extended across the border from Zimbabwe. Control measures, i.e., mainly dog vaccination campaigns in villages, associated with community awareness program related to the hazard of dog bites and the importance of post-exposure prophylaxis, have lead to a decrease of further human cases, although animal cases remain to be reported annually.

Human Rabies Prophylaxis

As described by many authors, there are great underestimates for reported human rabies cases, particularly in Africa.⁴ Contributing factors are failure to seek treatment, in laboratory diagnosis and

in reporting.¹² A recent publication from Malawi identified a substantial percentage of human deaths, which initially were attributed to cerebral malaria, to have been caused by rabies.¹³ Thus, prophylaxis is the best way to avoid any question that might appear in a discussion about a potential rabies case in travelers. Two ways of prophylaxis of rabies are recommended: post-exposure prophylaxis, i.e., vaccination after an exposure to a (potential or suspect) rabid animal has occurred, and pre-exposure prophylaxis.

PEP. WHO recommends administering rabies biologicals as part of post-exposure prophylaxis (PEP) for everybody exposed to an animal, which is suspect or confirmed rabid.⁵ After an exposure has occurred, the wound should be washed thoroughly with soap and water and/or disinfecting agents like alcohol (ethanol 70% v/v) or povidone iodine.⁵ This already reduces the inoculation of the virus and risk of infection. Wounds should only be sutured if medically indicated. Rabies vaccine should

be given without delay according to an approved PEP regimen (Fig. 3A).⁵ The WHO distinguishes different categories of exposure, which are shown in Table 1. For all types of contact and exposures of category II (nibbling of uncovered skin, minor scratches or abrasions without bleeding) and III (incl. single or multiple transdermal bites or scratches, licks on broken skin, as well as contamination of mucous membranes with saliva, i.e., licks, and exposures to bats) immediate administration of vaccine is recommended. In addition, for exposures of category III, also passive immunization with rabies immunoglobulin, infiltrated into and around the wound is indicated.⁵

Although PEP is generally regarded as safe and effective, single cases of PEP failure have been described throughout the world^{14,15} including a case of a farmer bitten by a mongoose in South Africa in 2004 (Blumberg L, personal communication). However, these failure cases are very rare and often associated with incorrect treatment, i.e., delayed administration of vaccine and immunoglobulin, incomplete schedules or rabies immunoglobulin not administered although indicated.

When PEP is necessary to be initiated while visiting South Africa, patients should visit the emergency department of the nearest hospital as soon as possible. Hospitals can be found in every major city. A (not necessarily complete) list of hospitals, sorted by province, can be found in the internet at http://en.wikipedia.org/wiki/List_of_hospitals_in_South_Africa, (accessed February 19, 2010). In addition, the National Institute of Communicable Diseases (NICD) has a 24-hour

rabies hotline for medical professionals with emergency questions, which can be reached at +27 (0) 828839920. If after an exposure the animal (suspected to be rabid) is available for laboratory diagnosis, the diagnostic laboratory at the Onderstepoort Veterinary Institute (OIE reference center) can be contacted for emergency testing, which is available 7 days a week. The telephone service from the laboratory is available for advice and can be reached at +27 (0) 12-5299 420/439 (during the day) and after hours +27 (0) 724282890 or +27 (0) 723220195. If samples for emergency testing are received after 6.00 p.m., advice is generally given (usually advising the patient to seek medical attention depending on the history of the case) and the sample tested the following day.

PreEP. In addition to PEP, another way of rabies prevention is pre-exposure prophylaxis (PreEP). WHO recommended vaccination regimens⁵ are shown in **Figure 3B**. PreEP should be offered to people who are at increased risk of exposure to rabies, e.g., laboratory workers or veterinarians. In addition, PreEP also is recommended by WHO, CDC and/or some national or international societies of travel medicine and tropical medicine depending on the risk, i.e., travel destination, duration of stay, and way of traveling.^{5,16,17} Comparing different recommendations, as a common ground PreEP should be offered to international travelers visiting regions of the world where canine rabies is enzootic, and immediate access to the appropriate biological is limited, difficult or impossible to obtain.^{16,17} Benefits of PreEP are that it eliminates the need for rabies immunoglobulin, PEP is reduced from 5 to 2 doses, and protection against rabies is possible in case PEP is delayed.^{5,18} Clearly, in South Africa rabies biologicals including rabies vaccine and rabies immunoglobulin are available in hospitals throughout the country and not every traveler to the World Cup needs rabies PreEP. However, PreEP may be beneficial for travelers to South Africa, for instance if they intend to combine attending the World Cup with additional

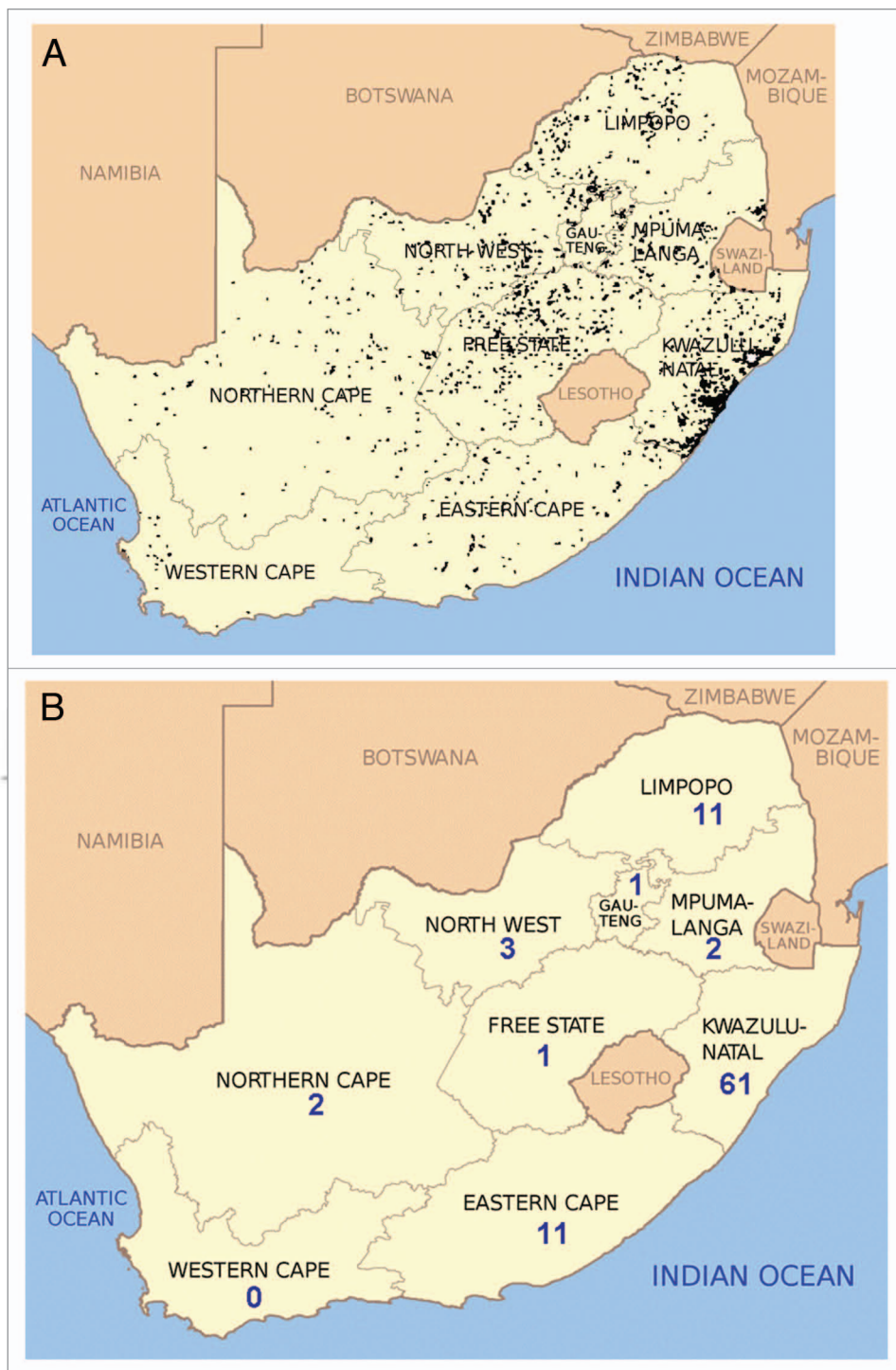


Figure 2. (A) Cases of animal rabies in South Africa from 1995 to 1999. Each dot represents an animal case.¹⁹ Most of these cases were in dogs and mongooses, but the spread of the disease in domestic dogs was followed by the emergence of rabies in jackals, bat-eared foxes and cattle throughout the Southern African regions. (B) Cases of human rabies in South Africa from 1996 to 2006 by province.²⁰

travel throughout the region of Southern Africa, in areas with potential limited supply of biologicals. In addition, PreEP avoids or reduces the psychological stress that a bite victim may experience after an exposure to a potentially rabid animal has occurred.

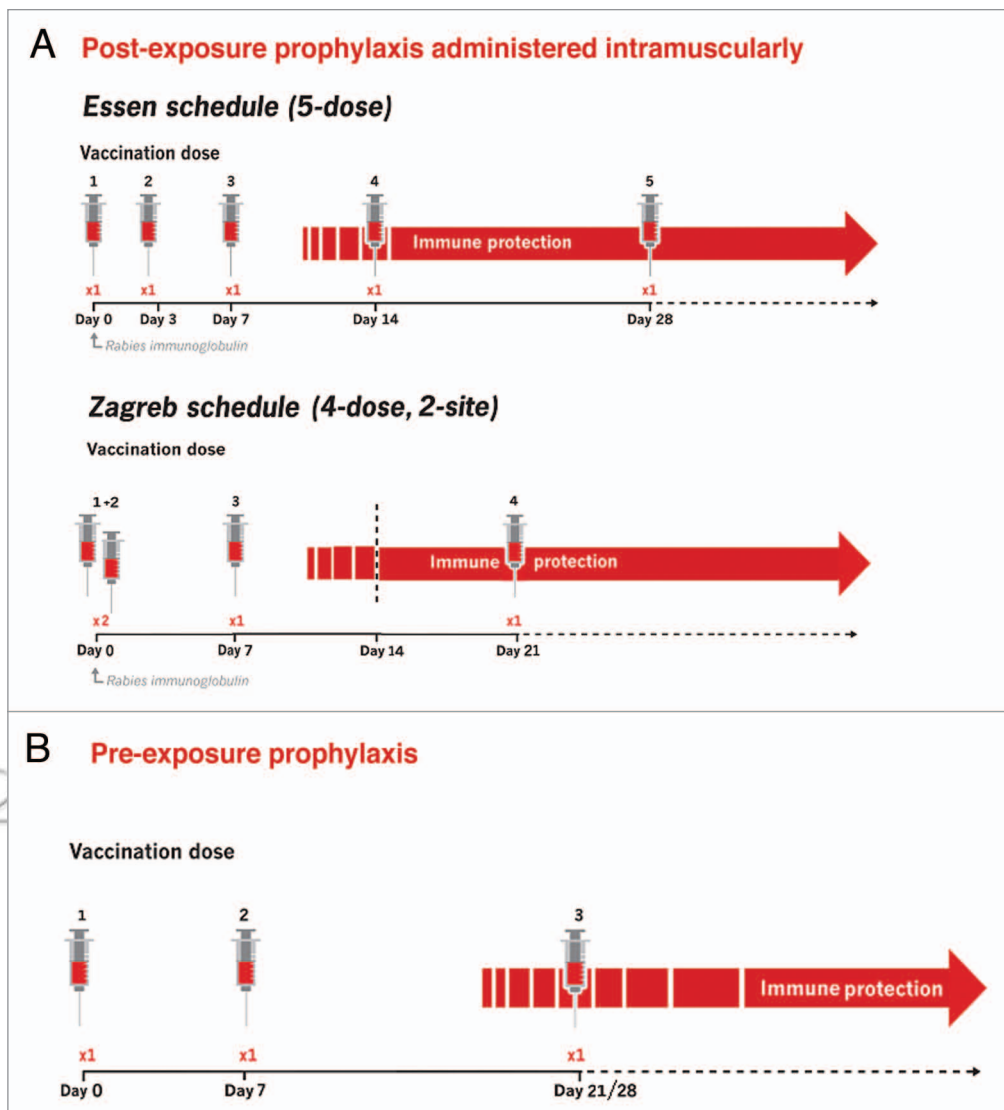


Figure 3. WHO recommended post- (A) and pre-exposure (B) regimens, using cell culture rabies vaccine. (A) Post-exposure prophylaxis, (B) Pre-exposure prophylaxis.

Conclusion

Travelers visiting the FIFA World Cup should be aware of rabies and potentially rabid animals and seek medical advice before traveling to rabies endemic areas but latest—and as soon as possible—in case they get exposed to a suspect rabid animal.

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Conflict of interest

C. Malerczyk and D. Gniel are full time employees of Novartis Vaccines and Diagnostics, manufacturer of human rabies vaccine. L. Blumberg has received travel grants from pharmaceutical industry for attending rabies conferences.

Table 1. Type of contact, exposure and recommended post-exposure prophylaxis

Category	Type of contact with a suspect or confirmed rabid domestic or wild ^a animal, or animal unavailable for testing	Type of exposure	Recommended post-exposure prophylaxis
I	Touching or feeding of animals Licks on intact skin	None	None, if reliable case history is available
II	Nibbling of uncovered skin Minor scratches or abrasions without bleeding	Minor	Administer vaccine immediately ^b Stop treatment if animal remains healthy throughout an observation period of 10 days ^c or if animal is proven to be negative for rabies by a reliable laboratory using appropriate diagnostic techniques
III	Single or multiple transdermal bites or scratches, licks on broken skin Contamination of mucous membrane with saliva (i.e., licks) Exposures to bats ^d	Severe	Administer rabies immunoglobulin and vaccine immediately. Stop treatment if animal remains healthy throughout an observation period of 10 days or if animal is found to be negative for rabies by a reliable laboratory using appropriate diagnostic techniques

^aExposure to rodents, rabbits and hares seldom, if ever, requires specific anti-rabies post-exposure prophylaxis. ^bIf an apparently healthy dog or cat in or from a low-risk area is placed under observation, the situation may warrant delaying initiation of treatment. This observation period applies only to dogs and cats. Except in the case of threatened or endangered species, other domestic and wild animals suspected as rabid should be humanely killed and their tissues examined for the presence of rabies antigen using appropriate laboratory techniques. ^cPost-exposure prophylaxis should be considered when contact between a human and a bat has occurred unless the exposed person can rule out a bite or scratch, or exposure to a mucous membrane.

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