# Mokola virus infection: description of recent South African cases and a review of the virus epidemiology

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**ABSTRACT**

Five cases of Mokola virus, a lyssavirus related to rabies, are described. The cases occurred in cats from the East London, Pinetown and Pietermaritzburg areas of South Africa from February 1996 to February 1998. Each of the cats was suspected of being rabid and their brains were submitted for laboratory confirmation. Four of the cases were positive, but with atypical fluorescence, and 1 was negative. Mokola virus infection was identified by anti-lyssavirus nucleocapsid monoclonal antibody typing. As in rabies cases, the predominant clinical signs were of unusual behaviour. Aggression was present, but only during handling. Four of the 5 cats had been vaccinated for rabies, which is consistent with other studies that show that rabies vaccination does not appear to protect against Mokola virus. Since Mokola may be confused with rabies, the incidence of Mokola virus may be more common in Africa than is currently reported. As human infections may be fatal, the emergence of this virus is a potential threat to public health.

**Key words**: case reports, lyssavirus, Mokola virus, South Africa.

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## INTRODUCTION

Mokola virus is a member the *Lyssavirus* genus of the Rhabdoviridae family of viruses that are related genomically, serologically and antigenically to rabies and the bat lyssaviruses, namely Lagos bat virus, Duvenhage virus and the European bat lyssaviruses (EBL1 and EBL2)[3]. Rabies is present throughout most parts of the world and is maintained by various species of the order Carnivora, and, in the Americas, by bat species. Reports of Lagos bat, Duvenhage and Mokola viruses have been confined to Africa. Lagos bat and Duvenhage viruses are thought to be maintained in megachiropterid and microchiropterid bats respectively, while the reservoir host for Mokola virus has not yet been determined. Recently a lyssavirus, possible of a new genotype, has been identified in Australian megachiropterid bats[11].

Mokola virus was originally isolated in 1968 from pooled viscera of 3 insectivorous shrews (*Crocidura* spp.) from the Mokola District of Nigeria[17]. It was subsequently isolated again from shrews from Ibadan, Nigeria, in 1969[12] and Cameroon in 1974[13], and from a rodent (*Lophuromys sikapusi*) from the Central African Republic in 1981[16]. It has been isolated twice from human beings from Nigeria. In the 1st case the virus was obtained from the cerebrospinal fluid of a young girl who presented with fever and convulsions but recovered fully[5]. The 2nd, fatal, case was a 6-year-old girl who presented with drowsiness, paralysis and terminal coma[6]. In neither case was the source of the infection identified.

Mokola virus has been previously isolated from domestic animals showing clinical signs suspicious of rabies. During 1981 and 1982 Mokola virus was isolated from the brains of 6 cats and a vaccinated dog from Bulawayo, Zimbabwe[8,9,10] and in 1989/90 an isolate was made from a cat from Ethiopia[14]. In 1970 a cat from Umhlanga Rocks, near Durban, South Africa, was diagnosed with rabies but, because the virus appeared to be unusual, it was stored and was only some years later identified as Mokola virus[15]. No other isolates were made in South Africa until 1995, when a cat from near East London was diagnosed with the disease[15].

In this paper we discuss 5 further cases of disease in cats caused by Mokola virus in South Africa, its differentiation from rabies and the potential zoonotic aspects.

## CASE REPORTS

### Cat 1

The cat, an adult female aged 10 years, resident in a new housing development adjoining indigenous coastal bush near East London, stopped eating and drinking and was obviously unwell. On 10 February 1996 the cat was taken to a local veterinary clinic, presenting with signs of dehydration, incoordination, some salivation and increased aggression. A tentative diagnosis of meningoencephalitis was made, which led to the animal being euthanased 2 days later on suspicion of rabies. This cat had never been vaccinated against rabies.

### Cat 2

The 2nd cat, also an adult female, originated from a small settlement located in a nature reserve approximately 15 km northeast of Cat 1. On 15 May 1996, after appearing unwell for several days, the cat began vomiting bile-stained fluid and developed diarrhoea. There was also repeated shaking of the head. Veterinary examination suggested gastritis and otitis externa and the animal was treated accordingly. The next day the cat was admitted to hospital, as it had developed signs of shivering, general hypersensitivity and neurological disturbance, thought to be related to the ear treatment. On 17 May 1996 the animal stopped eating and drinking and its general condition had deteriorated. It was therefore euthanased and specimens sent to the Onderstepoort Veterinary Institute (OVI) for virological examination to exclude rabies. Records showed the cat to have been vaccinated against rabies almost 3 years previously.

### Cat 3

An adult male cat became ill on 11 May 1997 in the residential area of Pinetown near Durban. It had been vaccinated against rabies in 1996 (exact date unknown), and according to the owner did not stray but on occasion was seen with dead rats and mice. It was docile and only

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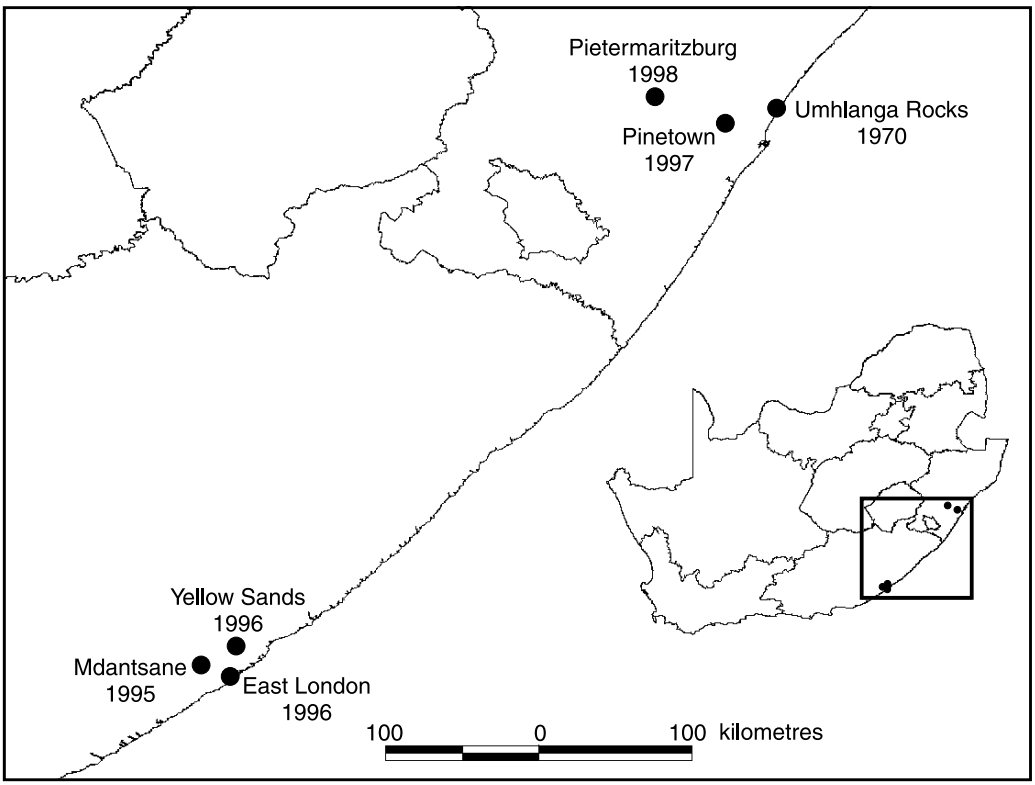


Fig. 1: **Location and year of isolation of Mokola viruses in South Africa. ● = Mokola virus cases.**

when approached by other animals did it appear distressed and aggressive. When attempting to restrain the animal, it became extremely aggressive and attacked one of the veterinary personnel. The cat was admitted to a veterinary clinic where it was observed for 24 hours. Paralysis of the lower jaw and bizarre aggressive behaviour such as biting the cage and sandbox was noted. The animal was euthanased and brain specimens sent for rabies diagnosis.

### Cat 4

About 2 weeks later another domestic cat died within the same general area as Cat 3. An 18-month-old male that had been vaccinated against rabies at about 3 months of age, it had been seen on many occasions to bring home shrews and rodents. Insectivorous bats were seen in the house on occasions but, according to the owner, the cat was never seen with one. On 21 May 1997 the cat started to behave strangely, hissed and evinced distressed vocalisation. After 3 days the animal started to show neurological signs including aggression, circling, incoordination and disorientation. The animal was euthanased and brain samples sent for rabies diagnosis.

### Cat 5

The 1-year-old female cat originated from the residential area of Pietermaritzburg. According to the owner it did not wander far, but was frequently seen with dead rats. It was vaccinated against rabies on 10 June 1997 and about 7½ months after vaccination (24 February 1998) the cat showed a change in behaviour, such as biting a blanket without releasing it and aggression when provoked. Family members were bitten when they tried to stroke their pet. The animal was euthanased and brain material sent for rabies diagnosis.

Figure 1 shows the origin of each of the cases.

## VIROLOGICAL STUDIES

Initial diagnosis by antigen detection using the fluorescent antibody test (FAT) was carried out on brain tissues from Cats 1 and 2 by the Rabies Laboratory at OVI and from Cats 3, 4 and 5 by Allerton Regional Veterinary Laboratory, Pietermaritzburg. Following initial tests, brain material was forwarded by Allerton RVL to OVI for further virological studies. The FAT was carried out by staining acetone-fixed impression smears of selected regions of the brains with a polyclonal fluorescein isothiocyanate-conjugated anti-rabies globulin. Cats 1 to 4 were positive for rabies antigen, although the fluorescence differed from that usually seen with rabies in that the antigen-positive particles stained less intensely. These observations led to suspicion that these infections might be due to a lyssavirus other than classical rabies. Cat 5 was originally negative for rabies, but a lyssavirus infection was suspected when 3-week-old mice died 6 days after intracerebral inoculation of aliquots of its brain suspension. The anti-rabies conjugate used for Cat 5 was of a different batch from that used for the other cats, which may account for its different reactivity.

In order to determine the lyssavirus type, original cat brain or 1st passage mouse brain material was tested by the indirect fluorescent antibody test[18] using a panel of anti-nucleocapsid monoclonal antibodies prepared from various lyssaviruses by the Central Veterinary Laboratory, Weybridge, UK, and the Wistar Institute, Philadelphia, USA. The panel differentiates the lyssavirus types prevalent in Africa and all 5 isolates were confirmed to be Mokola virus.

## DISCUSSION

Although Mokola virus infections have so far not been frequently identified, they may be considerably more common in Africa than is currently reported. Identification of Mokola virus may be dependent upon the spectrum of conjugate activity. When a broad-spectrum conjugate is used, the virus may be identified as rabies, otherwise it may be recorded as negative for rabies unless other tests that

are capable of detecting the virus are carried out. In the former case its differentiation from rabies depends on various typing procedures, as took place with Cats 1 to 4 and other reported cases[9,14,15].

Using mouse models, modern canine rabies vaccines have been shown to protect against most lyssaviruses, but not against Mokola virus[7]. In our study, 4 of the 5 cats had been vaccinated against rabies. A dog diagnosed with Mokola virus infection in Zimbabwe had also been vaccinated 6 months previously[8]. It appears, from these studies, that rabies vaccine does not protect domestic animals against Mokola virus infection. Human rabies vaccines have also failed to protect mice against a lethal challenge of Mokola virus[7] and may therefore not be capable of protecting humans. Nevertheless, in the absence of an effective Mokola virus vaccine, and as there may be a small degree of immunological cross-protection, human contacts should be treated as they would be for rabies. Two cats reported here bit people: these people were advised to undergo rabies treatment and to date they have remained healthy.

The clinical signs demonstrated by the 13 cats in which signs have been described are consistent. Signs in the 6 cats reported from Zimbabwe included changes of temperament, hypersensitivity, aggression, slight salivation, ataxia, paralysis and coma[10]. The only other domestic animal species reported to have been infected with Mokola virus, a dog from Zimbabwe, showed hypersensitivity, vomiting, blindness, head pressing, salivation, mild aggression and ataxia[10]. Aggression was reported in all but 1 of the cases reported here and in the 2 previous cases reported in South Africa[15]. In these cases, aggression was a prominent feature but was only induced when attempting to handle the cats. This picture contrasts with classical rabies infection, where rabid cats typically exhibit extreme unprovoked aggression. As with rabies in all species, unusual behaviour can probably be considered the cardinal sign of Mokola virus infection. Although no specific clinical signs are consistent among all the cases described, it would appear that aggression upon handling, hypersensitivity and ataxia/incoordination are most frequently reported.

The identity of the reservoir species for Mokola virus has yet to be determined. The fact that all cases of Mokola virus infection in South Africa, as well as all but one from domestic animals from other countries in Africa[8,9,10,14] have been confined to cats, strongly suggests that the reservoir is to be found among their prey. Bats are candidates, as all other mammalian lyssaviruses have been found in various bat species. Shrews and rodents are also possible candidates, as the virus has been isolated from them [12,13,16,17]. Shortly after the East London outbreak, a survey of shrews and rodents was undertaken to identify the source of infection for cats in the East London district of the eastern Cape, but without any isolation of the virus (Rabies Laboratory, OVI, unpubl. data). Further detection of this unusual zoonotic virus will lead to better understanding of its epidemiology.

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