ODYSSEAN MALARIA OUTBREAK AT A BUSH LODGE IN MADIKWE GAME RESERVE, NORTH WEST PROVINCE, SOUTH AFRICA, OCTOBER-NOVEMBER 2015

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Executive summary

In November 2015, the National Institute for Communicable Diseases (NICD) was notified of malaria cases at a lodge in Madikwe Game Reserve, North West Province – usually a non-transmission area in South Africa. Four laboratory-confirmed malaria cases were investigated. A structured questionnaire was used to gather information on demographic, clinical and exposure history. Interviews were conducted with employees and managers and blood samples were collected. Environmental assessment of the residence and immediate surroundings was conducted. Blood smear microscopy and PCR analysis for the detection of malaria parasites were done. All cases were female, employed, and resided in lodge staff accommodation. None of the cases had travelled to malaria-endemic areas. However, history of travel to possible malaria transmission areas was elicited in eight of the 33 staff members interviewed. Staff residences were within 50-60 m of the parking bay for establishment vehicles, including those returning from malaria-endemic areas. There was no evidence of free-standing water that could enable mosquito breeding. No asymptomatic infections were identified: all laboratory investigations for malaria were negative. The outbreak was most likely caused by the accidental introduction of an infected mosquito by a vehicle returning from a malaria transmission area, namely, odyssean malaria.

Background

In South Africa, malaria is endemic in the KwaZulu-Natal, Limpopo and Mpumalanga provinces, especially in the north-eastern lowveld areas.[1,2] Most cases are due to *Plasmodium falciparum*. The disease is seasonal, occurring during the wetter summer months from October to May and typically peaking in January to April each year. Sporadic transmission of malaria during exceptionally wet seasons has also been reported in areas neighbouring the Molopo and Orange Rivers in the North West and Northern Cape provinces.[3] However, cases have been reported in other non-endemic provinces following acquisition in known transmission areas (imported malaria), or due to the phenomenon known as odyssean malaria. This is defined as malaria acquired locally through the bite of an imported *Anopheles* mosquito, in persons whose recent travel history firmly excludes the possibility of exposure to malaria in an endemic area.[4] Most notified cases of malaria in North West Province are imported but odyssean malaria incidents have also been reported; two such cases near Swartruggens were investigated in March 2017.[5]

On 11 November 2015, the Outbreak Response Unit, Division of Public Health Surveillance and Response of the National Institute of Communicable Diseases (NICD), was notified of a malaria case by the North West Province Department of Health. The case originated from a bush lodge establishment in Madikwe Game Reserve, Bojanala District, an area far outside the recognised malaria transmission zone of South Africa (Figure 1). As a few other people at the same establishment were said to have also presented with fever, headache and 'flu-like symptoms, a preliminary investigation to determine the possible cause of the illness/es was undertaken by the provincial Department of Health. These investigations revealed that four employees of the same establishment had been diagnosed with laboratory-confirmed malaria. None of the four case-patients had travelled to malaria-endemic areas for months. Following the recognition of local malaria cases in a non-malaria endemic area, a collaborative field investigation was conducted on 9 December 2015 by the NICD, the North West Province Department of Health and the Bojanala District Communicable Disease team. The objectives of the follow-up investigation were: 1) to identify undiagnosed malaria cases amongst employees and management at the establishment; 2) to describe the characteristics of laboratory-confirmed malaria cases; and 3) to establish if there were breeding sites for mosquitoes, collect mosquito larvae and, if possible, to collect and identify mosquito vectors of malaria.

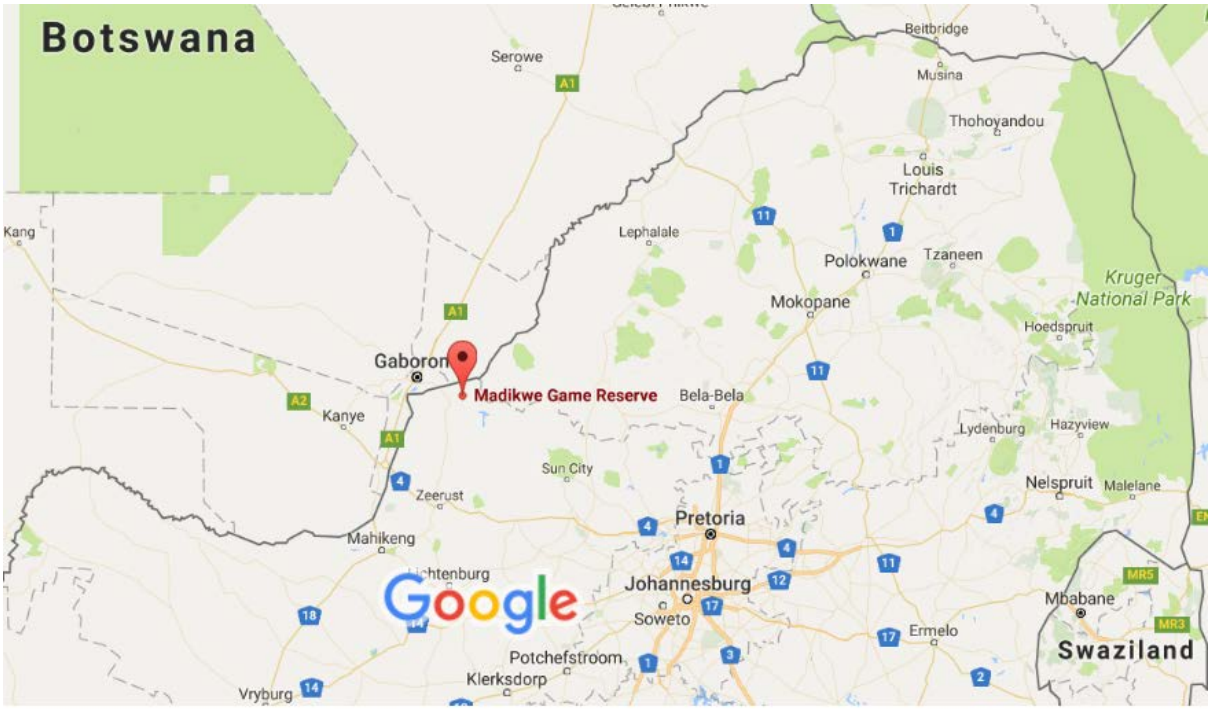

Figure 1. Location of the Madikwe Game Reserve, North West Province, South Africa. The malaria risk areas are adjacent to the north-east and eastern borders of the country (Source: Google Maps)

Methods

The following case definitions were used:

- A suspected case was defined as a person presenting with fever, headache and/or flu-like illness where no obvious cause was evident, during September to November 2015.
- A confirmed case was defined as a suspected case in whose blood smear malaria parasites were observed and/or whose malaria rapid antigen test was positive.
- An asymptomatic infection was defined as the presence of malaria parasites in the blood (tested positive by PCR, smear microscopy or rapid antigen test) in a person with no malaria symptoms at the time of venesection.

To establish the magnitude and possible source/s of the outbreak, the following activities were carried out during the site visit.

- *Epidemiological investigation*: A structured questionnaire/case investigation form was used to gather information on demographic, clinical and exposure history. Where informed consent was granted, face-to-face interviews were conducted with employees who were present on the day of the investigation. Management team members were also interviewed to gather information about malaria exposure in staff members, and about guests who had visited the area before malaria was diagnosed in the case-patients. A line list of cases was compiled.
- *Laboratory investigation*: To detect possible asymptomatic infection with *P. falciparum* in employees and management, EDTA-anticoagulated blood samples were collected. In addition, blood films were prepared on site. Blood smear microscopy and PCR analysis for the detection of malaria parasites were conducted by the Parasitology Reference Laboratory, Centre for Emerging Zoonotic and Parasitic Diseases at the NICD.
- *Environmental investigation*: To identify possible breeding sites for mosquitoes, an environmental assessment of the residence and immediate surroundings was conducted.
- *Intervention measures* included health education/promotion activities, distribution of information pamphlets about malaria to employees and management at the establishment and education of staff on personal protection against mosquito bites.

Results

Epidemiological and clinical findings

During the period October to November 2015, four laboratory-confirmed *P. falciparum* malaria cases were reported and investigated. In all four case-patients, diagnosis was made during November 2015, although all became ill in October 2015. The first case developed symptoms on 17th October, case 2 on 21st October, and the 3rd and 4th case-patients on 22nd October 2015 (Figure 2). All four case-patients were female, aged 27 to 55 years, and resided at the staff residences in the lodge. Three were housekeepers and one was a chef. Cases 1 and 2 had rooms next to each other, while cases 3 and 4 shared a room. None of these patients had a history of travel to malaria-endemic area/s, and no recent blood transfusions were reported. None had received visitors from outside the province. All four case-patients reported fever, while three reported headaches, dizziness and painful joints. Two patients also had diarrhoea, fatigue, nausea and 'flu-like illness, and one reported vomiting. Two of the patients were admitted to hospital and all four recovered following antimalarial treatment.

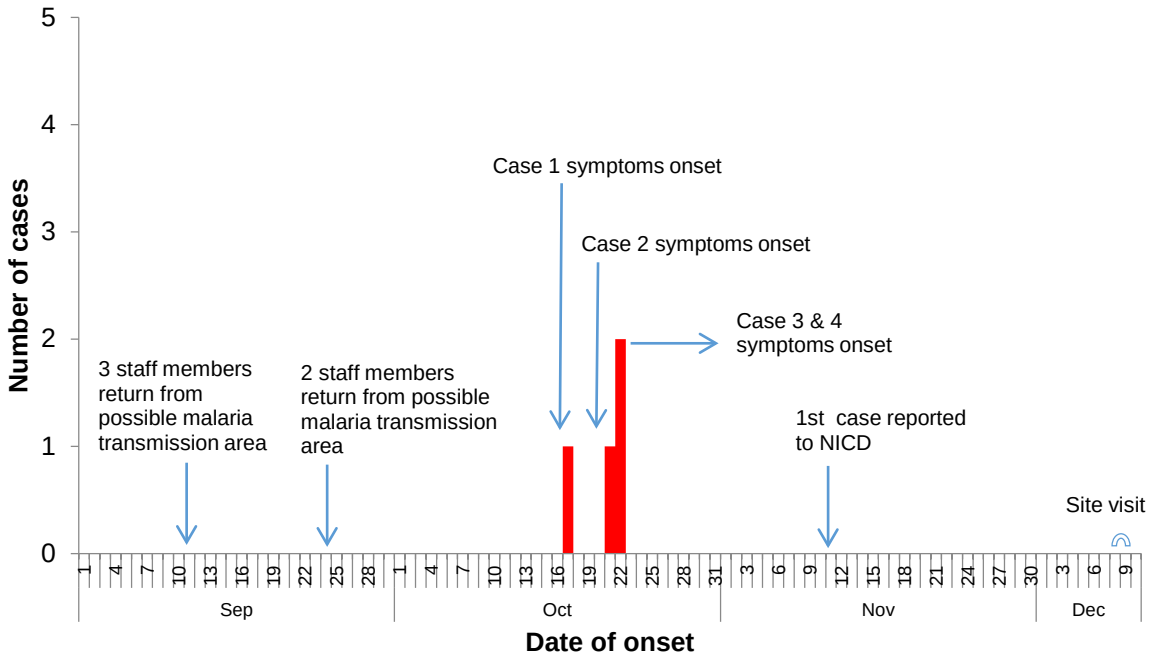

Figure 2. Epidemic curve illustrating number of cases by date of onset of symptoms, affected establishment, North West Province, 1 September to 10 December 2015, with return dates of travel from malaria endemic areas (travellers returning from malaria endemic areas outside likely incubation period not included).

Interviews were conducted with 33 staff members (including three of the confirmed malaria cases). The fourth case-patient was not available as she was on leave. However, information had been obtained during a preliminary investigation while she was hospitalised. Travel to possible malaria endemic areas within the month prior to symptom onset in the case-patients was reported in eight of the 33 staff members: six had travelled to Mpumalanga Province ((Bushbuckridge (n=4) and Kruger National Park (n=2)) and two to Zimbabwe (Table 1). It was established that ten groups of guests visited the lodge during the period August to October 2015. One of these visiting groups was from Zimbabwe, six had no travel history to or from malaria endemic areas, and no information was available for the remaining three. The group from Zimbabwe visited the lodge from 11 to 14 October 2015, too close to onset of disease of the first case to be the source of an infected mosquito.

Table 1. Travel history of staff members to possible malaria transmission areas.

Date of Travel	Area travelled to	Number of people
29 August to 11 September 2015	Bushbuckridge	3
13 to 24 September 2015	Kruger National Park	2
27 September to 14 October 2015	Zimbabwe	1
28 September to 16 October	Zimbabwe	1
2 to 15 October 2015	Bushbuckridge	1

Environmental findings: The lodge is immediately adjacent to the Marico River. It was reported that there were mosquitoes inside and outside the residences (both guest and staff residential areas). However, no mosquitoes were observed or collected during the investigation. The staff residences are in close proximity (within 50-60 m) to the parking bay for lodge vehicles, including those used during travel to possible malaria-endemic areas. The lodge managers indicated that they spray a pyrethroid-based insecticide around both the guest and staff residences for nuisance mosquito control. Besides the Marico River and swimming pools in the area, there was no evidence of free-standing water that could enable mosquito breeding.

Laboratory findings: Blood samples were collected from 32 of the 33 staff members available on the day. Laboratory investigations for malaria (microscopy and PCR analysis) were negative on all samples tested.

Discussion and conclusions

We describe a probable odyssean malaria outbreak at a lodge in Madikwe Game Reserve, involving four female case-patients. None of them had a history of travel to any malaria-endemic areas, which led to delays in malaria diagnosis. No additional malaria cases or asymptomatic infections were identified during the follow-up investigation, nor were any reported in the local municipality and district.

Based on the dates of onset of symptoms and usual incubation period for malaria, it is most likely that the four case-patients acquired malaria from the bites of one or more infective *Anopheles* mosquitoes during early to mid-October 2015. The mosquito/es were likely to have been inadvertently translocated from a malaria endemic area in a vehicle (car, bus, taxi) or in an individual's luggage.[6] The parking bay of the lodge is close to the staff residences and feasibly could have been the mosquito release site. In general, malaria vector mosquitoes tend not to disperse more than a few hundred metres, but can fly up to 1.5 km.[7] Adult malaria infective mosquitoes can survive for up to two weeks in a favourable environment, giving them sufficient time to infect several people, even during one night.[8] Therefore, the most likely vehicle to have transported the mosquito/es was the one arriving from the Kruger Park on 24 September 2015. It is likely that the same infected mosquito/es could have infected all case-patients, especially given their close proximity to each other.

We could not conduct a detailed entomological assessment regarding the presence of malaria mosquito vectors in the area, due to non-availability of entomologists. Spraying of interiors of vehicles arriving from, or leaving to, malaria endemic areas using appropriate insecticides would reduce the risk of transporting vector mosquitoes, but would be difficult to apply or enforce. To avoid mosquito bites, staff members were encouraged to use insect repellents and mosquito coils, and to wear long-sleeved clothing and socks in the evenings. Managers at the lodge and healthcare workers in the area were alerted to the cases in order to increase their awareness of malaria as a differential diagnosis in individuals presenting with fever, headache and 'flu-like illness, where no obvious cause is evident and in whom no history of recent travel to a malaria transmission area is forthcoming. It was further advised that potential mosquito breeding sites should be minimised or treated with an appropriate larvicide.

Acknowledgements

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References

1. Blumberg L, Frean J. Malaria control in South Africa – challenges and successes. *S Afr Med J* 2007; 97(11): 1193-1197
2. Moonasar D, Nuthulaganti T, Kruger PS, Mabuza A, Rasiswi ES, Benson FG, Maharaj R. Malaria control in South Africa 2000-2010: beyond MDG6. *Malar J* 2012; 11: 294
3. South African National Department of Health. Guidelines for the Treatment of Malaria in South Africa. Pretoria: NDoH, 2010.
4. Isaäcson M, Frean JA. African malaria vectors in European aircraft [Letter 2: Odyssean malaria]. *Lancet* 2001; 357(9251): 235.
5. Odyssean malaria in Gauteng and North West Provinces. *Communicable Diseases Communique*, March 2017; 16 (3): 3.
6. Frean J, Brooke B, Thomas J, Blumberg L. Odyssean malaria outbreaks in Gauteng Province, 2007-2013. *S Afr Med J* 2014; 104: 335-338.
7. De Meillon B. The Anophelini of the Ethiopian Geographical Region. Johannesburg: South African Institute for Medical Research, 1947: 120-122.
8. Beier JC. Frequent blood-feeding and restrictive sugar-feeding behaviour enhance the malaria vector potential of *Anopheles gambiae s.l.*and *An. funestus* (Diptera: Culicidae) in western Kenya. *J Med Entomol* 1996; 33(4): 613-618