future research. However, given that human infections with a similar toxin type, *C. botulinum* group III, have rarely occurred, this new toxin type might pose little threat to human health.

About the Author

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Plasmodium knowlesi Infection in Traveler Returning to Canada from the Philippines, 2023

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A 55-year-old man sought treatment for an uncomplicated febrile illness after returning to Canada from the Philippines. A suspected diagnosis of *Plasmodium knowlesi* infection was confirmed by PCR, and treatment with atovaquone/proguanil brought successful recovery. We review the evolving epidemiology of *P. knowlesi* malaria in the Philippines, specifically within Palawan Island.

In February 2023, a 55-year-old man sought care at the emergency department of Vancouver General Hospital, Vancouver, British Columbia, Canada, for daily fevers, headache, and abdominal pain 5 days after returning from a 3-week trip to the Philippines. He stayed mostly in Manila but spent 4 days on Palawan Island in the western Philippines 4 days before his return to Canada; he had not taken malaria chemoprophylaxis. Bloodwork was notable for platelet nadir of 48 × 10^9/L (reference range 150–450 × 10^9/L), alanine transaminase of 329 U/L (reference range 10–55 U/L), and alkaline phosphatase of 177 U/L (reference range 30–135 U/L). Results of abdominal computed tomography were unremarkable and of a single-target *Plasmodium falciparum* histidine-rich protein 2 rapid diagnostic test were negative. Peripheral blood thin smear demonstrated variable intraerythrocytic parasite morphology, including band-like forms suggestive of *P. malariae* (<0.1% parasitemia) (Figure, panels A–C). Loop-mediated isothermal amplification testing was

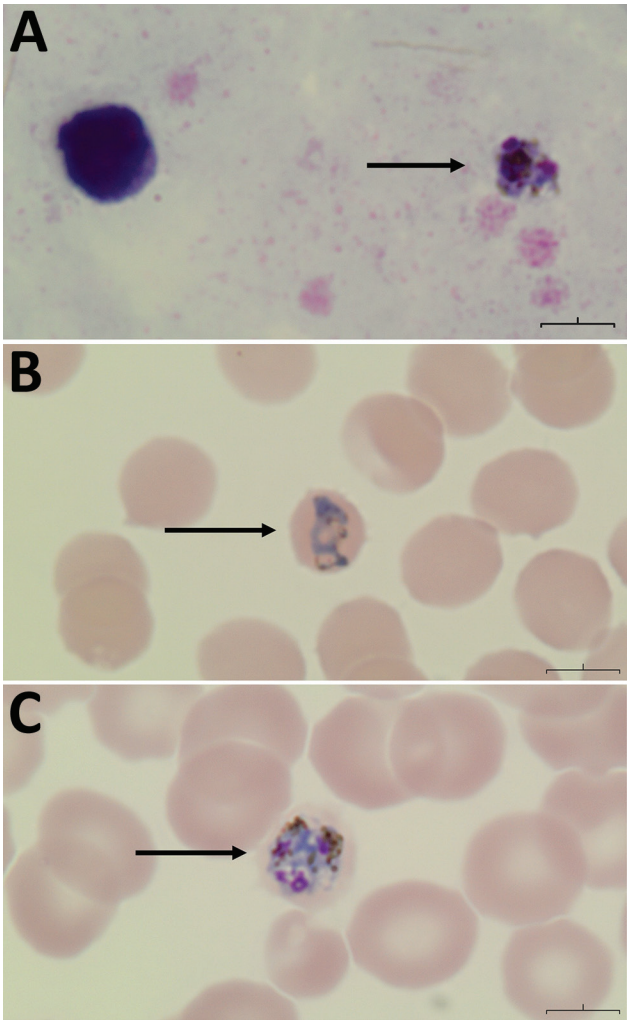

Figure. Peripheral thick and thin blood smears of a man in British Columbia, Canada, with suspected *Plasmodium knowlesi* infection after travel to the Phillippines. A) Thick smear showing *P. knowlesi* gametocyte.. B) Thin smear showing band form within a normal-sized, fimbriated erythrocyte with vacuoles present, similar to *P. malariae*. C) Thin smear showing *P. knowlesi* schizont form with presence of greenish-black pigment and lack of rosette formation. Original magnification x100 for all smears.

positive for *Plasmodium* spp. Given absence of criteria for severe malaria, he was discharged with a 3-day course of atovaquone/proguanil (250 mg/100 mg, 4×/d).

We suspected a diagnosis of *P. knowlesi*, given the patient's travel history and blood smear morphology, and subsequently confirmed the infection via species-specific laboratory-developed PCR. Amplicon sequencing on a 118-bp sequence also confirmed *P. knowlesi* identification. The patient was afebrile at follow-up 4 days after drug therapy, with resolution of thrombocytopenia and symptoms.

P. knowlesi malaria cases within the Philippines have been concentrated in Cebu Province and, as in this case, Palawan Island (Appendix Figure, http://wwwnc.cdc.gov/EID/article/29/10/23-0809-App1.pdf) (*1*–*4*). Although *P. knowlesi* is primarily a simian malaria infecting nonhuman primate hosts, there has been clear transmission evidence across Southeast Asia since the large 2004 Malaysian outbreak in Sabah (*5*).

Palawan Island contains a diverse landscape of beaches, karst, and mangrove forests, including its well-known Puerto Princesa Subterranean River National Park. The island provides an ideal feeding and breeding ground for ≈500 long-tailed macaques (*Macaca fascicularis*), the only monkey species naturally found in the Philippines and natural host reservoirs for *P. knowlesi* (*6*). Given the close proximity of the island's diverse habitats to human settlements and recreation areas, constant contact occurs between forest mosquito vectors, macaque hosts, and, potentially, human hosts (*6*). The first 5 confirmed local cases within Palawan were documented in 2005 (*1*); since 2008, only 2 *P. knowlesi* malaria cases have been documented in North America, both in travelers with implicated exposure from Palawan (Table) (*2*,*7*). According to the Philippines Research Institute of Tropical Medicine, >30 *P. knowlesi* cases have been documented, <5 in tourists traveling to Palawan (Philippines Research Institute of Tropical Medicine, pers. comm., email, 2023 Mar 1). However, the true burden is likely underestimated, given the lack of routine molecular testing for species confirmation in the Philippines. Because early ring-form trophozoites of *P. knowlesi* can resemble *P. falciparum* and developing band-like trophozoites can resemble *P. malariae*

Table. Summary of published *Plasmodium knowlesi* cases in North America imported from the Philippines*

Patient age, y	Patient sex	Year	Geographic location presented	Region of Philippines traveled	Diagnosis	Treatment
50	F	2008 (*2*)	New York, NY, USA	Palawan	PCR failed to identify species; confirmed by 1,055-bp PCR product sequencing	Atovaquone/ proguanil and primaquine
NA	NA	2018 (*7*)	NA	NA	PCR	Atovaquone/ proguanil
55	M	2023 (this case)	Vancouver, British Columbia, Canada	Palawan	PCR; confirmed by 118-bp PCR sequencing	Atovaquone/ proguanil

*NA, not available.

(*1*), molecular species confirmation is a highlighted need in areas at risk for *P. knowlesi*.

The 24-hour *P. knowlesi* erythrocytic cycle is shortest among *Plasmodium* spp., which may contribute to rapid development of high parasitemia (*5*), although this case showed ultra-low parasitemia. The World Health Organization (WHO) recommends that uncomplicated *P. knowlesi* malaria infections acquired in *P. vivax* chloroquine-susceptible regions be treated with an oral artemisinin-combination therapy or chloroquine; cases acquired in *P. vivax* chloroquine-resistant regions should be treated with locally available artemisinin-combination therapy (*8*). Despite limited data regarding antimalarial resistance among *P. knowlesi* parasites, this strategy ensures adequate treatment of undiagnosed mixed infections and simplification of uncomplicated malaria treatment. Intravenous artesunate remains first-line treatment for severe *P. knowlesi* malaria. As in this case, atovaquone/proguanil is also considered reasonable empiric treatment.

The Philippines successfully established 0 indigenous cases of malaria across 78 of 81 provinces in 2019; ≈97% of indigenous cases were *P. falciparum* or *P. vivax*. Recent serologic work showed that 1.1% of personsin Palawan tested positive for *P. knowlesi*–specific PkSERA3ag1 antibody (*9*). Current control strategies for human-species malaria (e.g., insecticide-treated nets, indoor spraying) have limited impact on monkey reservoirs and on forest-dwelling *P. knowlesi* vectors, given limited evidence of indoor biting (*9*,*10*). Palawan and Sabah surveillance data identified that most biting by *Anopheles balabacensis* mosquitoes occurred during 6–10 PM, when many rural residents are still outdoors. Although Palawan reports more sporadic cases than does Malaysia, increased encroachment into deforested areas and close proximity (<100 km) to endemic Sabah raises concern of *P. knowlesi* becoming a predominant species in future years. Ongoing investigations into mosquito behavior implicated with cross-species transmission will help inform appropriate control strategies for *P. knowlesi* and other simian species (*9*).

In summary, *P. knowlesi* malaria should be considered in persons with febrile illness who have traveled to the Philippines (especially Cebu Province and Palawan Island). Because of overlapping microscopy features with *P. falciparum* and *P. malariae*, molecular confirmation is required to enable early diagnosis and appropriate treatment. Despite gains in control of *P. falciparum* and *P. vivax* infection in Southeast Asia, the zoonotic nature of *P. knowlesi* and rise in cases highlight the need for tailored prevention and control strategies.

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Dr. Lo is a medical microbiology resident physician at the University of British Columbia. His research interests include tropical infectious diseases, parasitology, and *Clostridioides difficile* infection prevention.

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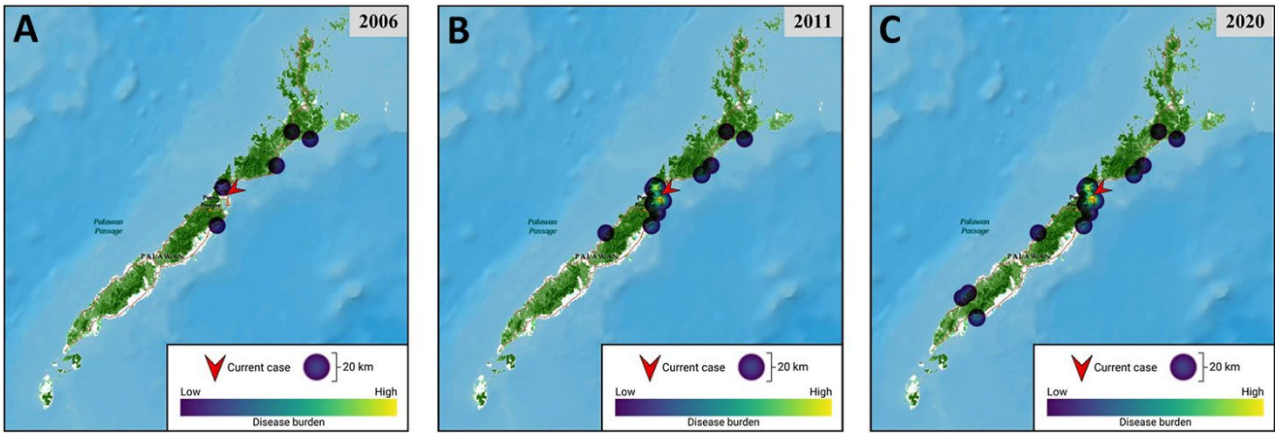
Appendix



Appendix Figure. Heatmap of cumulative reported human cases of *Plasmodium knowlesi* in Palawan, Philippines. Representation based on unpublished data reported to the Research Institute for Tropical Medicine, the Philippines, at 3 timepoints from 2006, 2011, and 2020 (Appendix Table).

Appendix Table. Reported human cases of *Plasmodium knowlesi* in Palawan, Philippines, at 3 timepoints from 2006, 2011, and 2020

Date of Collection	Year	Residence/ Address (Sitio, Brgy, Municipality)	Latitude	Longitude
6-Jul	2006	Bacungan, PPC	9.909596	118.7012
6-Jul	2006	Balogo, San Miguel, Roxas	10.1159	119.2111
6-Jul	2006	Caibulo, Iraan, Roxas	10.4377	119.358
6-Jul	2006	Inagawan, Tagbarungis, PPC	9.5477	118.6453
6-Jul	2006	Taradungan, Roxas	10.3685	119.5313
16-Nov	2007	San Jose, PPC	9.7944	118.749
22-May	2008	Purok Magalang, Sta. Monica, PPC	9.787061	118.7393
21-May	2008	San Manuel, PPC	9.7793	118.7569
5-Sep	2011	(No data on Sitio) Bacungan, PPC	9.909596	118.7012
9-Feb	2011	(No data on Sitio) Bacungan. PPC	9.909596	118.7012
19-Jul	2011	(No data on Sitio) Inagawan, PPC	9.547699	118.6453
21-Jul	2011	(No data on Sitio) Irawan, PPC	9.810579	118.6946
6-Jun	2011	Berong, Quezon	9.477072	118.2127
9-Jun	2011	Bukang Liwayway, Langogan, PPC	10.03032	119.1235
9-Jun	2011	Iwahig Penal Colony, PPC	9.75028	118.6617
6-Jul	2011	Iwahig Penal Colony, PPC	9.75028	118.6617
16-Feb	2011	Kandis III, Bacungan, PPC	9.891391	118.6571
10-Jun	2011	Langogan, PPC	10.03032	119.1235
30-May	2011	Maranat-3, Bacungan, PPC	9.924164	118.6785
7-Sep	2011	Purok Samplaloc, Irawan, PPC	9.801	118.6971

Date of Collection	Year	Residence/ Address (Sitio, Brgy, Municipality)	Latitude	Longitude
3-Mar	2011	Rubber, Luzviminda, PPC	9.6682	118.7043
2-Jun	2011	San Miguel, PPC	9.7793	118.7569
14-Jul	2014	Candawaga, Bacungan, PPC	8.862	117.4893
13-Aug	2014	Ransang, Rizal	8.90806	117.5502
14-Jul	2014	RJL Marangas, Bataraza+C30	8.6729	117.6292
24-Jul	2014	Ilog-Ilog, Campung Ulay , Rizal	8.9602	117.6143
19-May	2010	Sta. Lourdes	9.8317	118.7222
23-Jul	2014	Tigwayan, Marangas	8.6729	117.6292