INTRODUCED *Plasmodium vivax* Malaria in a Bolivian Community at an Elevation of 2,300 Meters

TINA RUTAR, EDUARDO J. BALDOMAR SALGUEIRO, AND JAMES H. MAGUIRE

*Harvard Medical School, Boston, Massachusetts; Consejo de Salud Rural Andino, La Paz, Bolivia; Brigham and Women's Hospital, Boston, Massachusetts*

**Abstract.** Tuntunani, Bolivia, a community of 199 persons situated at an elevation of 2,300 meters, experienced its first malaria outbreak in 1998. Blood smears from 63 of 183 symptomatic residents were examined, and 52 showed *Plasmodium vivax*. An investigation two years later indicated that the epidemic resulted from introduced transmission, since persons of all ages and both sexes were infected, and there had been no travel to low-lying endemic areas in the five months preceding the epidemic. Treatment became available only two months into the epidemic, at which time 58% of the people had been ill for three weeks or longer. This outbreak demonstrates the vulnerability of highland populations with poor access to health care to introduced malaria.

**INTRODUCTION**

Approximately 30% of the population of the Americas lives in an area of ecologic risk for malaria transmission, and 29% of the roughly one million cases are from Andean countries. In Bolivia, where malaria is common in the tropical lowland departments of Riberalta and Guayamerin, there were a total of 74,571 cases during 1998. That year, villagers from Tuntunani, a small community in the Bolivian Andes, reported a suspected outbreak of malaria to local and regional health authorities.

Most cases of malaria at high elevation are imported by seasonal migrants, who acquire the infection in the lowlands and become ill after returning to their high-elevation homes. Introduced malaria, local transmission by mosquitoes following an imported case(s), is rare at high elevations primarily because of the temperature limitations of the cold-sensitive parasite, and to a lesser extent, of the *Anopheles* vector. At the request of the Consejo de Salud Rural Andino, a nonprofit organization, we carried out a study to determine the source of the 1998 epidemic in the highland community of Tuntunani.

**MATERIALS AND METHODS**

**Study area and population.** The village of Tuntunani, population 199, lies at an elevation of 2,300 meters on the valley floor of Ambaná (15°28'S, 60°0'W), a rugged mountainous area where villages range in elevation from approximately 2,300 to 3,100 meters (Figure 1). Ambaná lies between the arid altiplano (high plateau) near Lake Titicaca and the tropical rain forest on a steep temperature gradient where the isotherm changes from 6°C to 20°C over a distance of 38 km. Annual rainfall is 500–700 mm, and mean annual temperature is 14–16°C, although temperatures vary greatly among villages.

Nearly all Tuntunani residents are indigenous Aymara who work as subsistence farmers. The village has no health clinic, electricity, plumbing, or road access. Health technicians visit Tuntunani once a month, addressing common health problems such as malnutrition, diarrheal diseases, upper respiratory tract infections, and tuberculosis. A physician, nurse, and several technicians used by the Ministry of Health and the Consejo de Salud Rural Andino staff the Ambaná health clinic, which is a five-hour uphill hike from Tuntunani.

**Review of records.** Demographic data were obtained from the year 2000 census carried out by the Consejo de Salud Rural Andino and community leaders. Records of the 1998 epidemic of malaria in Ambaná were reviewed at the Ministry of Health in La Paz. Available information included correspondence between local health authorities and the Ministry of Health, maps, and the results of blood smears. Blood smears were taken during February–June 1998, when teams of local health providers visited villages to identify symptomatic persons. The Department for Vector Control of the Ministry of Health in La Paz subsequently read the smears.

**Survey methods.** In July and August 2000, one of us (TR) conducted individual open-ended interviews with Ambaná health providers and political leaders. Information was gathered on the history of malaria in the area, morbidity and mortality during the epidemic, the management of the epidemic, speculation on its source, population movements, and weather patterns.

Health records were used to map the residences of the 95 inhabitants of Ambaná who had presented to local health workers in 1998 with symptoms of malaria and had *Plasmodium vivax* on a blood smear. With the assistance of a Spanish/Aymara translator, oral scripted interviews were conducted in the homes of 44 of 52 cases in Tuntunani; five persons had moved to La Paz and were not interviewed, and three persons had died. Family members responded for children younger than 13 years old and for persons who had left the village. Residents provided details of the 1998 epidemic and the course of their illness. They described their usual daily activities and trips outside of Ambaná between 1997 and 2000. Other questions focused on topics related to malaria such as knowledge of the disease, use of prophylaxis, and risk factors for infection.

Oral informed consent was obtained from adult participants and parents of minors. The study was reviewed and approved by the Consejo de Salud Rural Andino, the Municipality of Carabuco, the Department for Vector Control of the Bolivian Ministry of Health, and the International Committee of Harvard Medical School.

**Data analysis.** Epi Info version 6.04 (Centers for Disease Control and Prevention, Atlanta, GA) was used to calculate frequencies, means, and standard deviations and to estimate relative risks (RRs) with 95% confidence limits (CLs).

**RESULTS**

**Description of the epidemic.** Tuntunani residents reported that the malaria epidemic of 1998 was the first in the history...
of the village. According to data collected during the year 2000 census, 185 (93%) of the 199 residents claimed to have had malaria during January−May 1998. Blood samples were taken from 63 of these residents, and 52 smears (83%) showed *P. vivax*. From the rest of the Area of Ambana, 44 smears had been taken, and 43 (98%) showed *P. vivax*. Nearly 90% of the people with malaria lived in the lower-elevation villages of Tuntunani, Huayk’ayapu, Sehuenquera, and Mollebamba, which lie along the Huancotiti River basin at an elevation of approximately 2,300 meters (Figure 1). Only eight cases (8%) were reported from the higher-elevation villages, which lie along the road at an elevation of approximately 3,000 meters. The residences of four persons with malaria were unknown.

**Demographics.** In Tuntunani, malaria affected people of all age categories and both sexes (Table 1). The mean ± SD age was 33 ± 22 years, with a range of 3−83 years. The rate of infection for persons more than 14 years of age was not significantly different from that of younger persons (RR = 1.56, 95% CL = 0.92−2.64). The rate of infection for males was also similar to that for females (RR = 1.23, 95% CL = 0.88−1.71).

**Source of the epidemic.** Local health workers and the mayor recalled that a man from the village of Mollebamba returned from the Yungas lowlands with suspected malaria in December 1997. The subsequent epidemic in Ambaná began in January 1998, peaking first in Mollebamba and then in Sehuenquera and Tuntunani (Figure 2). These villages are located approximately 1 km from each another, and travel between them is common.

None of the persons with confirmed malaria recalled travel to malaria-endemic lowlands during the five months preceding the epidemic, and none had received blood transfusions or previous antimalarial therapy. Travel to the malaria-endemic lowlands was reported by 43% of the interviewed persons during the winter months of June to August, not during the months preceding or during the epidemic. Many men worked in the Yungas region of Bolivia on coffee and fruit plantations from June to August. Forty-three percent of interviewed persons reported never having left the area of Ambaná.

All interviewed persons reported a history of mosquito bites and high numbers of mosquitoes throughout the period of January to June. March was cited most often as the month with high numbers of mosquitoes, which is also when the greatest number of malaria cases occurred. Mosquito biting was most intense during the evenings, and all persons also reported being bitten at night within their homes, which are made of mud bricks and straw or sheet metal roofs. The investigators observed that 73% of the homes had permanently open windows, doorways and cracks, and that no homes had mosquito netting. No Tuntunani resident used a bed net, repellent, or insecticide for malaria prevention.

**Morbidity and mortality.** Fourteen percent of the individuals with documented malaria presented to a health clinic;
health workers, who first visited Tuntunani in March 1998, identified the remaining 86%. They presumptively treated symptomatic persons with a three-day course of chloroquine and a 14-day course of primaquine, giving preference to children and those appearing acutely ill. According to health records, the mean ± SD time between fever onset and receipt of medication was 17 ± 16 days. Fifty-eight percent of the people reported being unable to leave home for work or school for three weeks or longer. Common symptoms included fever (100%), anorexia (100%), fatigue (98%), rigors (95%), headache (93%), nausea (77%), sweating (74%), vomiting (70%), and diarrhea (56%). Symptoms resolved within one week of initiating treatment in 93% of the people who received treatment. Twenty-one percent of the people reported completing only partial treatment because they shared medication with family members. Four persons experienced a second episode of smear-proven \textit{P. vivax} malaria approximately two months after their first episode. According to the Tuntunani mayor and health workers, at least five persons died during the epidemic, all of whom were elderly and had symptoms consistent with malaria. Two had blood smears positive for \textit{P. vivax}; there are no records for the others. There have been no documented cases of malaria in Ambaná since 1998.

**DISCUSSION**

The available data suggest that the Tuntunani outbreak of malaria during January to May 1998 was introduced following an imported case or cases from lowland malarious areas. The demographic data, based on health records and the census, are consistent with local malaria transmission. Rates of infection were similar in males and females, and individuals of all age categories were affected. Had all cases been imported, a disproportionate number of working-age males (migrant workers) would likely have been affected.

Resident migration histories, though subject to recall bias, corroborate the presence of local malaria transmission. No resident of Tuntunani reported travel to a malaria-endemic area during the five months preceding the epidemic, a period of time far exceeding the typical two-week incubation period of tropical strains of \textit{P. vivax}.\textsuperscript{5} In fact, 43% of the people with confirmed malaria reported never having traveled outside Ambaná.

Although we can only speculate, an ill traveler returning to Mollebamba during December 1997 or an unrecognized gametocyte carrier may have triggered the epidemic. A less likely source of the epidemic would have been relapse or recrudescence of \textit{P. vivax}, since residents reported no prior history of malaria, and those who had traveled to the malaria-endemic Yungas region did so during winter months, when low temperatures limit malaria transmission. There are no health records to verify the oral reports of the Mollebamba traveler; however, health records do show that the epidemic peaked first in Mollebamba and two months later in the neighboring villages of Tuntunani and Sehuencuera.

The epidemic in Tuntunani peaked during March 1998, which is near the end of the rainy season in this otherwise arid region. When questioned about mosquito abundance, residents reported high numbers of mosquitoes from January to May, and most indicated that mosquito numbers were typically highest in March. Because their recollection of mosquito abundance is subjective and likely to be biased, a formal entomologic study is needed to characterize the vector and its population dynamics. The most likely vector is \textit{Anopheles pseudopunctatopennis}, which is found throughout the Americas from the south-central United States to Argentina.\textsuperscript{6} It is often the sole mosquito vector present in mountainous locations, and in Bolivia, it exists at elevations of up to 2,500–3,000 meters.\textsuperscript{3,6,7}

The consequences of this first-known malaria epidemic in Tuntunani were severe. While 26% of the population had documented malaria, blood smears were taken only from persons who could be treated with the limited supply of antimalarial drugs, and nearly all inhabitants reported malaria-like illness. The high rate of self-reported malaria may reflect the psychological toll of the epidemic: most persons believed they had malaria whether they actually did. Fifty-eight percent of the persons with confirmed infection reported illness lasting three weeks or longer. Of the five persons who died during the epidemic, two had \textit{P. vivax}-positive smears; however, \textit{P. vivax} malaria rarely causes death.\textsuperscript{8} No autopsies or other health records exist for these individuals to provide additional insight into their causes of death. Since births and deaths were not formally recorded in this community prior to the 2000 census, it is not known whether this number of deaths was unusual.

Both a lack of acquired immunity to malaria, which is typical of highland populations, and late detection by health authorities contributed to the severity of the epidemic.\textsuperscript{9,10} Medical personnel first visited Tuntunani two months after the onset of the epidemic, in part because they did not believe that malaria could occur at such high altitude. It was necessary for an ill village leader to travel to La Paz and have his blood smear examined to convince health authorities that malaria was occurring in his village. In Tuntunani, poor access to health care was due largely to the more than 5 km distance over difficult terrain to the nearest health clinic, which was accessible only by foot. Only 14% of the affected persons presented to a health clinic; health workers who hiked into the village identified the remainder. Moreover, health workers rationed antimalarial drugs, and 21% or more of persons who received the medications did not complete therapy.

Highland malaria is defined as malaria that exhibits an epidemic pattern and occurs near its altitudinal limit (generally above an elevation of 1,600 meters).\textsuperscript{11} The only reports of highland malaria in the Americas of which we are aware are from the 1940s in the Bolivian Andes at an elevation of 2,440–2,770 meters, where mosquitoes bred in thermal springs, and from the 1960s in Peru at a elevation of 2,000 meters.\textsuperscript{12,13} Outbreaks of highland malaria are also unusual outside the Americas, with reports primarily from Africa and Papua New Guinea.\textsuperscript{9,14–25} Highland malaria in these areas differs from highland malaria in the Americas due to the predominance of \textit{P. falciparum}, not \textit{P. vivax}, and due to different species of \textit{Anopheles} vectors.

Hills and mountains have long been regarded as a natural shelter from malaria because of their cool temperatures and paucity of mosquito breeding sites.\textsuperscript{22} The mean annual temperature of 14–16°C in Ambaná overlaps the minimum temperature required by \textit{P. vivax} to complete sporogony (15°C).\textsuperscript{5,4} Nearly all of the malaria cases came from the lower-elevation villages, which are sheltered from the wind and
slightly warmer than the higher-elevation villages. Because Ambaná’s climate barely permits malaria transmission, epidemics may take place only during idiosyncratic weather periods. Although there are no records of temperature and rainfall in Tuntunani, residents recalled that 1998 was unusually warm. Regional weather data, which document a severe El Niño/Southern Oscillation event characterized by increased temperature, drought, and crop shortages in the Bolivian highlands during 1997–1998 support residents’ observations.26,27 During the 1982–1983 El Niño, an increase in malaria was documented in a flooded area of the tropical lowlands of Bolivia.28 Elsewhere, the 1997–1998 El Niño was associated with increased malaria in the highlands of Irian Jaya29 and Uganda,30 but decreased malaria in the highlands of Tanzania.31

The upper elevation limit for malaria transmission depends in part on human activities, such as migration and alterations in the local environment. Travel to the malaria-endemic lowlands and changes in land use, such as terracing and the construction of irrigation canals, probably contributed to the introduction of malaria to Tuntunani.

There is debate whether global warming will broaden the distribution of tropical vector-borne diseases into more temperate zones. Investigators in Rwanda found that mean minimum temperature was the best predictor of malaria incidence at high altitudes, and suggested that non-climatic factors were of minimal importance.25 Other authorities consider human activities to be more important.32 The potential impact of global warming on malaria transmission in different locales is a complex subject. In malaria-endemic areas, local weather idiosyncrasies may affect malaria prevalence more than slight changes in global temperature. In areas on the fringe of malaria transmission, however, both local variations and global trends are likely to be important.

Because of continued travel by residents of Ambaná to and from the Yungas lowlands, the region remains at risk for malaria epidemics. This risk could be reduced by implementing surveillance at the local level, increasing the capacity of local and regional health centers to expeditiously diagnose and treat suspected cases of malaria, and providing chemoprophylaxis for travelers to the lowlands when transmission of malaria is intense. The Tuntunani epidemic highlights the vulnerability of nonimmune high-elevation populations, which are not prepared for an expansion of the distribution of malaria.

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Authors’ addresses: Tina Rutar, 5 Stratford Place, Flemington, NJ 08822, Telephone: 617-216-4793, E-mail: tina_rutar.98@alum.dartmouth.org. Eduardo J. Baldomar Salgueiro, Consejo de Salud Rural Andino, Casilla 13387, La Paz, Bolivia, Telephone: 591-2-412-495, E-mails: csra@caoba.entelnet.bo and ebaldoma2@hotmail.com. James H. Maguire, Division of Parasitic Diseases, Centers for Disease Control and Prevention, Mailstop F-22, 4770 Buford Highway NE, Atlanta, GA 30341-3724, Telephone: 770-488-7766; Fax: 770-488-7761, E-mail: jmaguire@cdc.gov.

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