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## Chloroquine-Resistant *Plasmodium vivax*, Brazilian Amazon

**To the Editor:** *Plasmodium vivax* is the protozoan that causes the second most common form of malaria. Some resistant strains to chloroquine (CQ) occur in a few places in Asia and the Indo-Pacific Region (1–4). Although resistance of *P. vivax* to CQ has already been described in South America (5–7), there are limited data regarding this issue.

CQ plus primaquine is the standard treatment for vivax malaria worldwide. Presently, this drug regimen exhibits satisfactory efficacy in the Brazilian Amazon. However, in recent years several treatment failures presumably related to CQ resistance, have been reported in the city of Manaus (Amazonas) where vivax malaria predominates (7). This observation warrants local attention despite these cases having no confirmation of CQ blood levels on the basis of the appearance of asexual parasites against CQ plus desethylchloroquine levels exceeding the minimally effective plasma concentration proposed for sensitive parasite strains ( $\geq 10$  ng/mL) (8), according to Pan American Health Organization recommendations (9).

From September 2004 to February 2005, a 28-day in vivo test was conducted at the Foundation for Tropical

Medicine of Amazonas (FMTAM) in Manaus, Brazil, to assess the efficacy of standard supervised CQ therapy. The test involved 166 volunteers with uncomplicated vivax malaria. Each volunteer was administered uncoated, scored, 150-mg CQ tablets (10 + 7.5 + 7.5 mg/kg at 24-hour intervals) (9). Primaquine was withheld until day 28 (dose regimen of 30 mg/day for 7 days). Among the 109 volunteers who completed the in vivo test, 19 had positive blood smears within the 28-day follow-up (1 on day 14, 3 on day 21, and 15 on day 28). All were required to undergo alternative therapy (mefloquine). Adequate CQ absorption was confirmed in these cases on day 2 with a mean  $\pm$  SD CQ plasma concentration of  $785.4 \pm 800.1$  ng/mL (10). Suspected therapeutic failure (*P. vivax* CQ resistance) was confirmed in 11 (10.1%) of 109 persons with a mean isolated chloroquine plasma concentration  $\geq 10$  ng/mL ( $356.6 \pm 296.1$  ng/mL) (9). Desethylchloroquine levels in plasma were not measured.

Previously, a CQ efficacy study demonstrated that 4.4% of those tested had CQ-resistant *P. vivax* (7). In comparison, the proportion of failures (10.1%) in the current study seems to be relevant; even though most of the *P. vivax* infections (98, 89.9%) were successfully evaluated and adequate clinical and parasitologic responses were obtained. Currently, the FMTAM Manaus Outpatient Clinic is detecting patients from different areas of the city who show parasitologic recurrences after correct treatment within 28 days of the routine clinical follow-up. This observation is an indirect indicator of the possible regional spread of *P. vivax* CQ-resistant strains (unpub. data).

We believe our findings are important and merit the attention of local public health authorities. Considering the possibility of emerging underestimated *P. vivax* CQ resistance in Manaus, we feel it is essential to quickly clarify whether such documented resistance can copromote

vivax malaria outbreaks in malaria-endemic areas within the Amazon.

This study was supported by the Brazilian Ministry of Health and the US Agency for International Development as part of the scientific program of the Amazonian Surveillance Network for Antimalarial Drugs Resistance (RAVREDA).

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## Avian Influenza Risk Perceptions, Laos

**To the Editor:** After the 2004 outbreak of highly pathogenic avian influenza (HPAI) in poultry in Lao People's Democratic Republic (PDR), the Ministry of Health implemented extensive virologic surveillance (1,2). Surveillance began in July 2005, and

by early 2006, only sporadic cases were found. In July 2006, an outbreak of HPAI was confirmed on 2 chicken farms in Vientiane, the capital city of Lao PDR (1,3). Most of Laos' ≈20 million chickens are kept on family-owned backyard farms; 3.2 million are on commercial farms (4). This production meets 80% of Lao poultry (chicken, duck, goose, quail) needs; imports from neighboring countries, either through legal trade or cross-border smuggling, account for the rest (3). Common poultry diseases occur frequently during the cold season, and lack of reporting of poultry deaths is of concern (4).

Until February 2007, no human cases of influenza A (H5N1) had been reported in Lao PDR. To learn more about Laotians' knowledge of HPAI and perceptions of their risk, we conducted a cross-sectional survey.

In March–April 2006, participants in 3 settings (Vientiane, urban; Oudomxay, semiurban; Attapeu Province and Hinheub District, both rural) were interviewed in the Lao language by means of a standardized 33-question survey. We recorded information about behavior, poultry handling and keeping practices, and poultry deaths. We used multivariate analysis (Stata, version 8; Stata Corporation, College Station, TX, USA) to analyze the factors associated with behavior changes.

Using a random sampling list of visitors and vendors, we interviewed 461 respondents in 4 Vientiane city markets (Vientiane has 114,793 households and 3,700 registered poultry farms) (5). Semiurban respondents were recruited in Oudomxay (40,987 households, 715 poultry farms), an active trading zone near the Chinese border. Rural respondents were recruited from Hinheup District and in Attapeu (19,050 households, 360 poultry farms), near the Vietnam border. Twenty villages were randomly selected, and 10 participants per village were randomly selected for interview. Approval for the investigation was

obtained from the health and market authorities. Oral consent for interview was obtained from participants.

A total of 842 participants were interviewed (Table). Differences in occupation and literacy were associated with different study areas. Differences in participant sex and age were also noted because, in the rural areas, interviews took place in the home. A total of 583 (69.3%) participants were female: 302 (65.5%), 139 (68.2%), and 150 (79.3%), in urban, semiurban, and rural areas, respectively;  $p = 0.002$ , 95% confidence interval 66–72. Mean ages for participants in these areas were 41 (range 40–43), 34 (range 32–36), and 38 (range 37–41) years, respectively;  $p < 0.001$ . Animal breeding was conducted by 50% of families. Daily close exposure to poultry was common (39.6%). Few families owned a henhouse, and no special handling of poultry was reported. Rates of poultry vaccination against common poultry diseases were higher in urban and semiurban areas; veterinary surveillance was low (10.2%).

Overall, 96.9% of respondents had already heard of HPAI, mainly through television. Urban residents ranked it as the most well-known poultry disease, but rural residents ranked it fifth. Less than half of the respondents had some knowledge of the disease signs and symptoms for humans and poultry; 28.4% could describe 1 symptom. Half of the respondents believed that they were not at risk for human avian influenza or that their poultry were not at risk for it. Respondents in urban and semiurban areas knew more about avian influenza than those in rural areas.

During the cold season, poultry deaths were higher in the north (colder) and south than in Vientiane. The poultry mortality rate during the cold season was similar to that of Cambodia (6). Behavior regarding poultry deaths differed between areas. Despite a high rate of poultry deaths, none of the interviewees had notified authorities. Since hearing about HPAI, 67.1%