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SHORT COMMUNICATION

Plant poisoning outbreak in the western area of Cambodia, 2005

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Disease outbreak;
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Summary An outbreak investigation was conducted during February–March 2005 to determine the cause of several sudden deaths occurring in Pailin Province, Cambodia. Sixty-seven patients presented with non-febrile poisoning-like symptoms and 15 died of coma, including 53% children under 10 years old. Symptoms included sore throat (92%), sore lips (73%), swollen tongue (54%) and gastrointestinal signs (41%). A plant locally called *prik* was the source of poisoning (97.0 vs. 28.7%, odds ratio 74.3, $P < 0.001$). Patients may have confused the edible *Melientha suavis* Pierre with *Urobotrya siamensis* Hiepko, both from the Opiliaceae family. This was the first report of *Urobotrya* poisoning and its clinical manifestations.

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1. Introduction

On February 16, 2005 several sudden deaths preceded by sore throat, vomiting and coma were reported in Pailin Province, Cambodia. An outbreak investigation was launched to identify the cause of death and generate recommendations for prevention and control.

2. Methods

Pailin is a remote province in western Cambodia covered with dense tropical forests (population 54 600 scattered over Pailin town and 60 villages). After years of civil strife and isolation, the province has been recently opened to attract many farmers in search of new lands. Since 2000, Médecins Sans Frontières has run a malaria control programme using a village malaria volunteers (VMV) network throughout the province. In each of the 60 villages, volunteers were taught to use malaria immunochromatographic diagnostic tests and give appropriate treatment.

For active case-finding we defined a 'probable' case as a patient presenting with altered consciousness and sore

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Table 1 Risk factors for disease outbreak, Pailin, Cambodia, 2005

| Exposure | Cases n/N (%) | Control cases n/N (%) | Odds ratio (95% CI) | P-value |
|---|---------------|-----------------------|---------------------|---------|
| Used to eating <i>prik</i> | 31/33 (93.9) | 57/101 (56.4) | 12.0 (2.4–58.3) | <0.001 |
| Ate <i>prik</i> in the previous 2 weeks | 30/31 (97) | 23/80 (28.7) | 74.3 (5.5–1003) | <0.001 |
| Knowledge about <i>prik</i> toxicity | 9/19 (47.4) | 34/47 (72.3) | 0.34 (0.11–1.08) | 0.054 |
| Knowledge about how to recognize <i>prik</i> leaves | 7/20 (35) | 44/85 (52.3) | 0.5 (0.18–1.4) | 0.17 |
| Used pesticides in the previous 2 weeks | 1/33 (0.03) | 7/100 (7) | 0.4 (0.05–3.4) | 0.388 |
| Ate dead animals in the previous 2 weeks | 1/34 (2.9) | 4/100 (4) | 0.7 (0.1–6.8) | 0.778 |
| Ate dry fish (<i>prohoc</i>) in the previous 2 weeks ^a | 33/35 (94) | 86/100 (86) | 2.7(0.6–12.6) | 0.192 |
| Source of drinking water: well | 10/26 (38.5) | 44/91 (48.4) | 0.7 (0.3–1.6) | 0.372 |
| Source of drinking water: river | 16/26 (61.5) | 47/91 (51.6) | 1.5 (0.6–3.7) | 0.372 |

^a Traditional Khmer homemade fermented fish.

throat and/or history of painful mouth and/or vomiting, and a 'possible' case as a patient presenting with sore throat and/or painful mouth and/or vomiting, with disease occurrence since 1 February 2005. The case definition was disseminated by radio to the VMV and health centres. Two investigation teams led by an experienced physician each visited case-reporting villages for case ascertainment.

We collected information about patients' demographics, symptoms and various exposures within the previous 2 weeks (i.e. water sources, types of food intake, contact with any dead animals, use of any chemical products and contact with forest fire or smoke). Because of frequent references to the consumption of a plant called *prik*, botanic-related variables were added into the standardized questionnaire. Data were entered into a case–control study. Each patient was matched to two to three controls by age and village residence. A control was defined as a healthy individual living in the same household as a patient. When possible, we also collected whole blood samples, which were kept at 4 °C and transported to the Institut Pasteur, Cambodia for analysis.

3. Results

Fourteen (estimated population ~8000) of 60 villages reported 67 cases, yielding an attack rate of 838/100 000. The median age was 18 years (2–54) and 49% were male. The median percentage of cases per family was 33% (9–100%) and the median number of cases per village was 6 (1–14).

Among patients for whom medical information was available, 92% (55/60) complained about unusual sore throat, 73% (43/59) presented with painful and unusual sore lips, and 54% (31/57) had swollen tongue with loss of gustatory papillae. Vomiting (42%, 25/60) was reported, followed by nausea (41%, 23/56), dizziness (34%, 19/56) and abdominal pain (32%, 19/59). Of 18 patients with altered consciousness, 15 (22%) evolved into flaccid coma and died within 3–8 days of symptom onset, with convulsions reported in seven comatose patients. Of 15 children <10 years old, 8 (53%) died. The average incubation period between intake of the plant and the first symptoms was 5 days (1–8 days). No patient had fever, shock, neurological localization signs or pupil abnormalities. Because of poor treatment conditions at Pailin Hospital, no patient underwent respiratory assistance, and no computed tomography scan was available to explore the causes of coma.

Thirteen blood samples were collected from mild cases and one from a comatose case who later died. Eight (57%) had neutropenia <2000/mm³ (700–1830); four (29%) had thrombopenia <150 000/mm³ (40 000–123 000); and five (36%) had anaemia <12 g/dl (10–11.2).

For the case–control study, 38 ascertained cases and 100 controls were included; 15 deceased and three patients for whom no controls could be identified were excluded, as were 11 patients presenting with isolated sore throat or sore lips, in order to increase specificity. The only exposure significantly associated with the disease was *prik* consumption within the previous 2 weeks (97.0 vs. 28.7%, matched odds ratio 74.3, $P < 0.001$) (Table 1).

4. Discussion

Our results confirmed a compelling association between disease and *prik*: a well-known wild plant. The extent of the outbreak was probably underestimated, as active case-finding was not exhaustive. Although this plant has been known to have two forms (edible and toxic) in Pailin Province, our botanic investigation identified two different species: the edible plant as *Melientha Suavis* Pierre (Supplementary Figure 1), and the poisonous plant as *Urobotrya siamensis* Hiepko (Supplementary Figure 2), both from the Opiliaceae family. *Melientha* is well known in Southeast Asia, whereas *Urobotrya* was used in traditional Thai medicine and could be poisonous at high doses.¹ *Urobotrya siamensis* Hiepko, first described in 1972,^{2,3} was never reported in Cambodia.

The particular clinical manifestations combined with lengthy incubation period and the observed haematological disorders suggested possible cytotoxic effects. Despite testing *Melientha* for antimutagenic potential effects,⁴ the chemistry and pharmacology of neither of the two plants have been studied.

Our investigation lacks evidence of plausible biological relationship between disease and the toxic plant. Compound identification was performed by gas chromatography–mass spectrometry, followed by HPLC coupled with UV-vis diode array detectors. High-frequency discharge plasma-induced technique was used for metal detection. The results were inconclusive, but this is likely to be explained by the low state of preservation of the plants sent to France. This may have led to the decay of a potential toxic

compound. Nevertheless, case reports ceased within 2 weeks of the prevention measures based on repeated FM-radio messages to the public regarding the toxicity of *prik*. Interestingly, A. Kerr described the same poisoning symptoms and fatal cases associated with *Melientha suavis* Pierre in Thailand, in this journal in 1931, years before *Urobotrya* was discovered.⁵

Authors' contributions: SV designed the study and led the investigation; MT, RS, TKS and BJ conducted the field investigations; SH botanically identified the plant samples; MGG conducted the toxicological analysis; ST was instrumental in implementing the control measures and facilitating collaborations with the provincial authorities and authorized the international shipping of the plant samples; MT and SV analysed and interpreted the data and wrote the manuscript; SV and ST revised the article for intellectual content. All authors reviewed the draft of the manuscript and read and approved the final version. MT and SV are guarantors of the paper.

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Conflicts of interest: None declared.

Ethical approval: Not required.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at [doi:10.1016/j.trstmh.2009.01.022](https://doi.org/10.1016/j.trstmh.2009.01.022).

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