

Toad Poisoning in Laos

Sommay Keomany, Mayfong Mayxay, Phouthalavanh Souvannasing, Chanthala Vilayhong, Bryan L. Stuart, Leila Srour, and Paul N. Newton*

Wellcome Trust–Mahosot Hospital–Oxford Tropical Medicine Research Collaboration, Mahosot Hospital, Vientiane, Lao PDR; Salavan Provincial Hospital, Salavan, Lao PDR; Department of Post Graduate and Research, Faculty of Medical Science, National University of Laos, Lao PDR; The Field Museum, Department of Zoology, Division of Amphibians and Reptiles, Chicago, Illinois; Health Frontiers, Muang Sing, Luang Nam Tha and Vientiane, Lao PDR; Centre for Tropical Medicine, Nuffield Department of Clinical Medicine, Churchill Hospital, University of Oxford, Oxford, United Kingdom

Abstract. We describe two patients who developed severe illness after eating the skin and eggs of a toad, probably *Bufo melanostictus* Schneider, in southeastern Laos. One boy died, and one developed a digoxin toxicity–like syndrome with bradycardia and heart failure but survived. A telephone survey of 16 Lao provincial hospitals suggested that toad poisoning occurs in at least six provinces. That 93% of villagers in three villages in southeastern Laos were aware that toads are poisonous but that 51% had encountered patients with toad toxicity suggests that the potential gravity is not appreciated. These data indicate that toad poisoning may be underestimated and that education on the seriousness of toad toxins could be a useful public health measure.

INTRODUCTION

Toads have a long history of use in medicine and magic.^{1,2} Secretions from toad parotoid glands and skin contain digitalis-like compounds and a diversity of alkaloid toxins, amines, bufogenins, proteins, mucins, and peptides²—“a spectacular laboratory of bioorganic chemistry.”³ There have been reports of toad venom poisoning in America and Asia, especially from aphrodisiac pills and traditional Chinese medicines such as *ch’an su*, made of dried *Bufo melanostictus* Schneider or *B. gargarizans* Cantor toad poisons. The toxins are present in the toad skin, especially the parotoid glands and eggs and include bufagenins (bufagins and bufadienolides) and bufotoxins, which resemble cardiac glycosides, and epinephrine (adrenaline), norepinephrine (noradrenaline), serotonin, and bufotenin hallucigens.^{3–8} Signs and symptoms of toad poisoning in humans resemble digoxin toxicity and include profuse salivation, perioral numbness, nausea, vomiting, dysrhythmias (such as ventricular fibrillation, bradycardia, and heart block), hypotension, hypertension, and seizures. Some relatively non-specific digoxin assays, through a cross-reaction with toad digoxin-like immunoreactive substances, give a positive “digoxin” result.^{4,6–10} Toad mouthing, entire toad ingestion, toad licking, toad soup, and toad egg eating have been reported to cause severe and frequently fatal toxicity.^{9–14}

In the Lao PDR (Laos), toads (*khan khak*) are consumed, especially in rural parts of the country where food may be scarce. We report toad poisoning in rural Laos and briefly describe the local villagers’ knowledge of the dangers of toad consumption.

MATERIALS AND METHODS

We describe the medical consequences of eating toads within a community in Savannakhet Province, southern Laos. We subsequently telephoned the doctors in charge of emergency or intensive care units in the 17 provincial hospitals of Laos (up to five times) to ask about toad poisoning. To obtain

more information about toad consumption and poisoning, an investigator (PS) also interviewed all available and consenting inhabitants of the index village and two adjacent villages (Nalom and Huayla-ar, also in Savannakhet Province) on one visit to these villages in March 2007. They were asked whether they knew that toads were poisonous, which part(s) were poisonous, and whether they knew people who had had toad poisoning. Their names and addresses were not recorded. The study was performed according to the World Medical Association Declaration of Helsinki (52nd General Assembly 2000).

CASE REPORT

A 6-year-old Lao Loom (*Phoo Thai* ethnicity) boy was admitted from Meuangchane Village to the Xepon Inter-district Hospital (a rural clinic in Savannakhet Province, 665 km southeast of Vientiane, Laos; Figure 1) in September 2006 with repeated vomiting and abdominal pain 8 hours after sharing a grilled toad dish and eating the eggs and meat. At presentation, he was fully alert but drowsy, dehydrated, and weak. He was afebrile with cold extremities, a slow pulse rate (40 beats/min) with extrasystoles, low blood pressure (70/40 mm of Hg), and respiratory distress (42 breaths/min). Rhonchi were heard in both lungs, the abdomen was distended with hepatomegaly, and bowel sounds were decreased. Investigation at admission found that he was anemic (hematocrit, 25%), with mildly elevated peripheral white cell count (13,000/mm³ with neutrophils 50%, lymphocytes 45%, monocytes 2%, and eosinophils 3%). Electrocardiographic recording was not available.

The patient was treated with oxygen, intravenous infusions, oral rehydration solution, and atropine 5 mg intravenously. The following morning, he remained bradycardic (50 beats/min), hypotensive (blood pressure, 80/50 mm of Hg), and in respiratory distress (34 breaths/min), with rhonchi in both lungs, vomiting, abdominal distension, and pain. Dopamine (5 µg/kg/min) and intravenous hydrocortisone 25 mg, every 6 hours, were given. On the second day, the patient had improved, with normal vital signs (heart rate, 80 beats/min; blood pressure, 100/70 mm of Hg; respiratory rate, 32 breaths/min), without respiratory distress and vomiting, but with rhonchi still audible in both lungs. On the third day, lung auscultation was normal, and the patient was discharged well

* Address correspondence to Paul N. Newton, Microbiology Laboratory, Mahosot Hospital, Vientiane, Lao PDR. E-mail paul@tropmedres.ac



FIGURE 1. Map of the Lao PDR showing location of Xepon District and the known distribution of toad consumption (gray with white dots), known toad consumption and poisoning (white with black dots), and no data (gray line) in Lao provinces. Province names follow Sisouphanthong and Taillard.²⁵

on the fourth day. Ten days after discharge, the patient was well with normal vital signs. Subsequent biochemistry showed serum potassium of 2.83 and 5.45 mmol/L on admission and convalescence, respectively. Serum admission and convalescent "digoxin" concentrations, as determined by fluorescence polarization immunoassay (Digoxin II on a TDX Analyser SLX system; Abbott Laboratories, Abbott Park, IL; lower limit of detection = 0.2 ng/mL), were 0.37 and <0.20 ng/mL, respectively. Digoxin was not detected in either sample by a more specific (for digoxin) chemiluminometric assay (Digoxin on a ACS:180 SE automated chemiluminescence system; Bayer, New York, NY; lower limit of detection = 0.1 ng/mL).

An additional seven people from two different families ate the same grilled toad. A 9-year-old boy, who ate a large quantity of the toad meat and eggs, developed severe vomiting an hour after eating the toad and died 12 hours later without being brought to the hospital. His 2-year-old younger brother ate meat and some eggs and developed vomiting and diarrhea 20 hours later but fully recovered at home. His mother (40 years) and sister (18 years) only ate meat and remained well. In the second family, a 7-year-old boy vomited 2 hours after eating meat and some eggs but fully recovered at home. His younger sister (3 years) and brother (2 years) only ate meat and remained well. Toads of the same appearance to that eaten by the patients were collected from the patients' village and were identified as *Bufo melanostictus* (by BLS).

TOAD POISONING IN LAOS

Toad poisoning may be a common occurrence in Laos because toads are used as food, especially in rural areas. We

were able to make contact with doctors in 16 provinces. Of the eight northern provinces contacted (Luangnamtha, Phongsaly, Bokeo, Xayabury, Oudomxay, Huaphanh, Luangphrabang, and Xiengkhuang), only doctors in Luangnamtha reported toad consumption and toad poisoning (Figure 1). Of the eight southern provinces, toad consumption was reported from all except Attapeu and poisoning from Vientiane, Borikhamxay, Savannakhet, Champassack and Sekong but not from Khammouane, Saravane, and Attapeu. These preliminary data therefore suggest that toad poisoning may be more common in the southern parts of Laos where people apparently eat toads more frequently. The incidence of toad poisoning is probably severely underestimated because people tend to seek traditional treatment, and those with severe disease are usually looked after in the village and die at home.

The combined population of the three villages was 607 (311 women and 296 men), and 293 (48%) were available and consented to being interviewed (146 men and 147 women). Three hundred fourteen (52%) could not be interviewed because they were either too young to answer (38%), were living in their distant rice fields (59.5%), or did not consent (2.5%).

The 293 respondents' median age was 25 years (range, 4–80 years), 2% were ≤ 5 years of age, and 42% were illiterate. Two hundred seventy-two (93%) knew that toads could be poisonous. The percentage who did not know this was higher in Huayla-ar (13/58, 22%) than in Nalom (4/85, 5%) and the village of the index patients (4/158, 2.5%). The villagers usually grilled the toads, boiled them in soup, or fermented them whole in Lao rice alcohol (*lao lao*). When asked which parts of the toad were poisonous, 78% knew that the skin and eggs were toxic, 11% knew that eggs but not the skin were toxic, 2% thought that only the skin or skin secretions were toxic, and 9% did not know which parts were toxic. The percentage of villagers of different ages who knew that toads were poisonous were 50% (1/2) 3–4 years of age, 85% (52/61) 5–10 years of age, 91% (32/35) 11–15 years of age, 100% (17/17) 16–20 years of age, and 96% (170/178) ≥ 21 years of age. However, 150/293 (51%) had encountered toad poisoning in their communities. Vomiting, drowsiness, thirst, difficult breathing, abdominal pain and distension, diarrhea, rash and cold extremities, salivation, nausea, and vertigo were reported as the main symptoms. Some respondents stated that patients consumed jackfruit (*Artocarpus heterophyllus*) peel or rubber (*Hevea brasiliensis*) as therapy.

DISCUSSION

There have been scant reports of poisoning after consumption of toads—mostly from Taiwan^{9,10,14–16} and the People's Republic of China.¹⁷ Jan and others¹⁷ described a 15-month-old boy and a 20-month-old girl who were fed cooked *B. melanostictus* soup; the boy died from ventricular fibrillation and the girl developed A-V block with congestive heart failure but survived. A 5-year-old boy developed profuse salivation and seizures after putting a *B. alvarius* in his mouth.¹²

Consistent with the evidence that clinically significant concentrations of toxins are only found in skin and eggs, the Lao villagers who ate these parts were the only ones to become seriously ill. Hyperkalemia is a poor prognostic factor,¹⁴ and

consistent with this observation, the patient who survived had hypokalemia.

Bufo melanostictus has a wide geographic distribution across South and Southeast Asia.¹⁸ The species thrives in anthropogenically modified environments, including cities and agricultural lands, and is frequently encountered by people. Two additional species of bufonid toads, *B. macrotis* Boulenger and *B. galeatus* Günther, are also known from Laos.¹⁹ Experiments in mammals (guinea pigs and cats) showed that skin extracts of *B. melanostictus* gave dose-dependent negative and positive inotropic and negative chronotropic effects and caused pre-synaptic neurotoxicity. High doses produced asystole.²⁰ *B. melanostictus* is used in Vietnamese medicine as a treatment of toothache, sinusitis, gum hemorrhage, and cancer and as “*Lue Than Hoan*,” as an antipyretic and antiepileptic. Bufadienolides and sterols have been isolated from their venom.²¹

The data from Lao provinces suggest that toad poisoning may be more common there than is currently appreciated. Although Lao people, apparently especially in the south, eat toads as food, *B. melanostictus* occurs throughout Laos. Toads may also be put in fermented rice alcohol with uncertain clinical consequences. Recently, *B. melanostictus* consumption has been described in Sekong Province, southern Laos, among the Katu people who observe a taboo against eating this toad on the first day of rice sowing out of fear that consumption would cause them to work very slowly.²²

Although 93% of respondents knew that toads could be poisonous, 51% knew of cases of toad poisoning in their community, suggesting that the information on the dangers of toad consumption is not necessarily acted on, perhaps because of food scarcity and because toads are abundant and easy to catch. Because 85% of those 5–10 years of age were aware of the toxic properties of toads, this important information is mostly acquired, at least in these southeast Lao communities, in childhood. Limitations of this study include the brevity of information by telephone interview, the restricted geographical area in which we inquired about toad poisoning, and the very small sample size in children < 5 years of age. However, the information suggests that further research would be useful in more fully defining the extent of the problem. Toad poisoning may not come to the attention of public health authorities because patients are often in remote rural areas, and patients may often be treated with traditional medicines and not transported to government health facilities.

Atropine, temporary pacemaker insertion,^{10,15} gastric lavage, and charcoal (cardioactive steroids and bufadienolides are absorbed by charcoal)²³ have been recommended as therapy. Dog poisoning by cane toads (*B. marinus*) in Australia has been treated with diazepam, atropine, propranolol, lignocaine, and verapamil, but there have been few controlled studies.²⁴ Digoxin-specific antibody fragments have been reported to be useful in the treatment of toad poisoning^{6,10} but are not available in Laos and are very expensive elsewhere (e.g., in the United Kingdom, the equivalent of \$US1,900 for the dose/patient used in reference 6). Temporary cardiac pacemakers, which may be indicated,^{6,10} are also not available in Laos. If the finding that the majority of children and adults are insufficiently aware of the dangers of toad poisoning is applicable elsewhere in Laos, prevention through edu-

cation, emphasizing the great danger of eating skin and eggs, may be useful.

We suggest that the incidence of toad poisoning may be underestimated in the available literature and that, if these observations are confirmed, radio and school campaigns to emphasize the dangers of toads may save lives in rural Asia.

Received May 26, 2007. Accepted for publication August 4, 2007.

Acknowledgments: We thank Stuart Blacksell, Jutta Krahn, Arlyne Johnson, and Michael Hedemark. Phannala Baysi kindly helped with interviewing. The digoxin assays were performed by RAI and Ramathibodi Hospital, Bangkok, laboratories.

Financial support: This work was supported by the Wellcome Trust of Great Britain. PNN and MM are supported by the Wellcome Trust.

Authors' addresses: Sommay Keomany, Wellcome Trust- Mahosot Hospital-Oxford Tropical Medicine Research Collaboration, Mahosot Hospital, Vientiane, Lao PDR, Telephone and Fax: 856-21-242168 and Salavan Provincial Hospital, Salavan Province, Lao PDR. Mayfong Mayxay and Phouthalavanh Souvannasing, Wellcome Trust Mahosot Hospital-Oxford Tropical Medicine Research Collaboration, Mahosot Hospital, Vientiane, Lao PDR, Telephone and Fax: 856-21-242168 and Department of Post Graduates and Research, Faculty of Medical Science, National University of Laos, Lao PDR. Chanthala Vilayhong, Wellcome Trust- Mahosot Hospital-Oxford Tropical Medicine Research Collaboration, Mahosot Hospital, Vientiane, Lao PDR, Telephone and Fax: 856-21-242168. Bryan L. Stuart, The Field Museum, Department of Zoology, Division of Amphibians & Reptiles, Chicago, IL, 60605-2496. Leila Srour, Health Frontiers, Muang Sing, Luang Nam Tha, and Vientiane, Lao PDR. Paul N. Newton, Wellcome Trust Mahosot Hospital-Oxford Tropical Medicine Research Collaboration, Mahosot Hospital, Vientiane, Lao PDR, Telephone and Fax: 856-21-242168 and Centre for Tropical Medicine, University of Oxford, Churchill Hospital, Oxford OX3 7LJ, UK.

REFERENCES

1. Chen KK, Kovarikova A, 1967. Pharmacology and toxicology of toad venom. *J Pharm Sci* 56: 1535–1541.
2. Lazarus LH, Attila M, 1993. The toad, ugly and venomous, wears yet a precious jewel in his skin. *Prog Neurobiol* 41: 473–507.
3. Erspamer V, 1994. Bioactive secretions of the amphibian integument. Heatwole H, Barthalmus GT, Heatwole AY, eds. *Amphibian Biology. Vol. I. The Integument*. Chipping Norton, Australia: Surrey Beatty & Sons, 178–350.
4. Kwan T, Paiusco AD, Kohl L, 1992. Digitalis toxicity caused by toad venom. *Chest* 102: 949–950.
5. Radford DJ, Gillies AD, Hinds JA, Duffy P, 1986. Naturally occurring cardiac glycosides. *Med J Aust* 144: 540–544.
6. Brubacher JR, Ravikumar PR, Bania T, Heller MB, Hoffman RS, 1996. Treatment of toad venom poisoning with digoxin-specific Fab fragments. *Chest* 110: 1282–1288.
7. Ko RJ, Greenwald MS, Loscutoff SM, Au AM, Appel BR, Kreutzer RA, Haddon WF, Jackson TY, Boo FO, Presicek G, 1996. Lethal ingestion of Chinese herbal tea containing Chan Su. *West J Med* 164: 71–75.
8. Gowda RM, Cohen RA, Khan IA, 2003. Toad venom poisoning: resemblance to digoxin toxicity and therapeutic implications. *Heart* 89: e14.
9. Chern MS, Ray CY, Wu D, 1991. Biologic intoxication due to digitalis-like substance after ingestion of cooked toad soup. *Am J Cardiol* 67: 443–444.
10. Kuo HY, Hsu CW, Chen JH, Wu YL, Shen YS, 2007. Life-threatening episode after ingestion of toad eggs: a case report with literature review. *Emerg Med J* 24: 215–216.
11. Licht LE, 1967. Death following possible ingestion of toad eggs. *Toxicol* 5: 141–142.
12. Hitt M, Ettinger DD, 1986. Toad toxicity. *N Engl J Med* 314: 1517–1518.

13. Horgan J, 1990. Bufo Abuse: a toxic toad gets licked, boiled, teed up and tanned. *Sci Am* 263: 26–27.
14. Chi H-TM, Hung D-Z, Hu W-H, Yang D-Y, 1998. Prognostic implications of hyperkalemia in toad toxin intoxication. *Hum Exp Toxicol* 17: 343–346.
15. Yei CC, Deng JF, 1993. Toad or toad cake intoxication in Taiwan: report of four cases. *J Formos Med Assoc* 92: S135–S139.
16. Cheng CJ, Lin CS, Chang LW, Lin SH, 2006. Perplexing hyperkalemia. *Nephrol Dial Transplant* 21: 3320–3323.
17. Jan S-L, Chen F-L, Hung D-Z, Chi C-S, 1997. Intoxication after ingestion of toad soup: report of two cases. *Acta Paediat Sin* 38: 477–480.
18. Bourret R, 1942. Les batraciens de l'Indochine. *Mém Inst Océanogr l'Indochine* 6: 1–547.
19. Stuart BL, 2005. New frog records from Laos. *Herpetol Rev* 36: 473–479.
20. Das M, Dasgupta SC, Gomes A, 2001. Isolation, purification and partial chemical characterization of a lethal factor from common indian toad (*Bufo melanostictus*, Schneider) skin extract. *Indian J Exp Biol* 39: 781–785.
21. Verpoorte R, Kinh P-Q, Svendsen AB, 1979. Chemical constituents of Vietnamese toad venom collected from *Bufo melanostictus* Schneider. Part I. The sterols. *J Ethnopharmacol* 1: 197–202.
22. Krahn J, 2005. *The Dynamics of Dietary Change of Transitional Food Systems in Tropical Forest Areas of Southeast Asia—The Contemporary and Traditional Food System of the Katu in the Sekong Province, Lao PDR*. PhD dissertation, University of Bonn, Bonn, Germany. Available at: http://hss.ulb.uni-bonn.de/diss_online/landw_fak/2005/krahn_jutta/krahn.htm
23. Mack RB, 1990. Kiss me and the world is mine. Toad toxins. *NC Med J* 51: 375–377.
24. Reeves, 2004. A retrospective report of 90 dogs with suspected cane toad (*Bufo marinus*) toxicity. *Aust Vet J* 82: 608–611.
25. Sisouphanthong B, Taillard C, 2000. *Atlas of Laos*. Chiang Mai, Thailand: NIAS/Silkworm Books.