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Contents

Cluster of Fatal Cardiopulmonary Failure among Children Caused by an Emerging Strain of Enterovirus 71, Nakhorn Ratchasima Province, Thailand, 2006

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Introduction

Enterovirus 71 (EV71) infections have been a public health priority in the Asia-Pacific region since 1998 when a major outbreak of hand, foot and mouth disease (HFMD) and herpangina due to EV71 occurred in Taiwan involving 129,106 cases and 78 deaths[1]. In 2006, Malaysia also experienced a large scale EV71 HFMD outbreak, involving at least 13,800 cases and 13 deaths[2]. Fatal cases in both the Taiwan and Malaysia outbreaks had high rates of brain stem infection and cardiopulmonary failure[3].

Many different viruses including Coxsackies A, Coxsackies B, Echovirus and Enterovirus 68-71 can cause HFMD, a clinical syndrome characterized by fever and vesicular lesions on the hands, feet and oral mucosa. EV71 is thought to be an important cause of HFMD though manifestation of EV71 is not restricted to HFMD. EV71 infection is most often asymptomatic or mildly symptomatic, but it may cause acute febrile illness, upper respiratory tract infection, gastroenteritis, limb weakness, myocarditis and/or pericarditis, brain stem infection and other illnesses[4,5].

EV71 was first identified in Thailand in 1998 by positive serology at Sukhothai Province and HFMD was included as a notifiable disease in national surveillance in 2001. Severe HFMD cases, those requiring hospitalization or fatal cases, require investigations that include viral isolation. EV71 was the major cause of HFMD in Thailand between 1998 – 2003 (Table 1), but the yield of EV71 isolation was low (16.7%) compared to other Asian countries[1,6-8].

Table 1. EV71 isolated in cases of hand, foot and mouth disease in Thailand, 1998-2003

Year	Number of Cases	Viral Isolation or Serology* positive for EV71 (%)
1998	27	2 (7.4)
1999	43	3 (7.0)
2000	186	12 (6.5)
2001†	340	93 (27.4)
2002	420	53 (12.6)
2003	125	28 (22.4)
Total	1,141	191 (16.7)

* Serology was tested for EV71 only in paired serum
† HFMD becomes a notifiable disease in Thailand

In July 2006, the Thai Bureau of Epidemiology was notified of a cluster of four pediatric deaths occurring within a three-day period in non-contiguous districts of Nakhorn Ratchasima Province. The children all had clinical presentations compatible with enterovirus infection. We conducted an outbreak investigation to determine the etiology of infection and to identify any additional cases in the community.

Methods

We reviewed both outpatient and inpatient medical records for each of the four fatal cases. The data obtained from the medical records were reviewed by a team of experts including an infectious disease pediatrician, a field epidemiologist, a microbiologist, and a sanitarian. In districts A and B in Nakhorn Ratchasima Province, we conducted active case finding with village health volunteers in the two villages from each district in which cases occurred. We used a structured questionnaire and conducted the interviews before specimen collection.

The definition of a probable EV71 case was a child younger than 15 years old who developed fever (body temperature ≥ 38.0°C) and/or HFMD, or a case of HFMD reported from the district hospital, during 5 Jul to 5 Aug 2006.

A confirmed case was a probable case with laboratory confirmation by at least one of the methods: positive viral isolation by cell culture of EV71, PCR confirmed EV71, fourfold rising of EV71 IgG in acute and convalescent phase serology, and electron microscope evidence of viral-like particle infiltration of the autopsy tissue compatible with enterovirus species and epidemiological linkage with a confirmed case.

The laboratory investigation included viral isolation and PCR from stool specimens, throat swabs and nasopharyngeal swabs. We tested acute and convalescent sera with a microneutralization antibody assay for IgG antibody to EV71. Nucleotide sequencing was performed on EV71 isolates. With electron microscopy, formalin-fixed autopsy specimens of brain, heart and lung tissue were scanned to identify pathogen infiltration.

Results

Through active case finding, we identified an additional eight confirmed and 30 probable cases.

Table 2. Characteristics of patients identified through active case finding, Nakhorn Ratchasima Province, Thailand, 2006 (N=24)

Disease	District A N (%)	District B N (%)
HFMD	12 (50)	0 (0)
Febrile illness	11 (46)	14 (100)

Twelve were diagnosed with HFMD, clinical characteristics of cases found through active case finding in table 2. The epi-curve is presented in figure 1. Most cases occurred in district A.

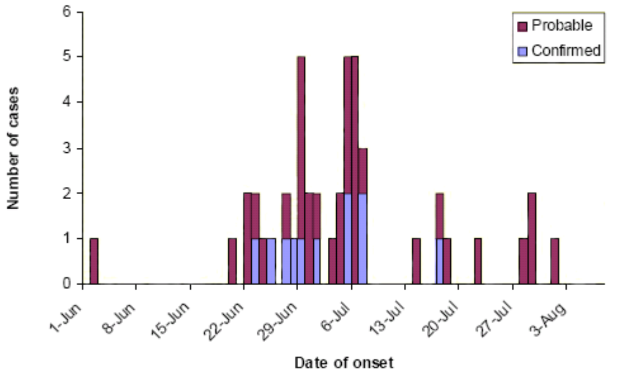

Figure 1. Epidemic curve of probable and confirmed cases of EV71 infection, Nakhorn Ratchasima Province, Thailand, 2006 (N = 42)

Four out of 42 total cases were fatal (case fatality proportion 9.5%). None of the four fatal cases were diagnosed with HFMD. Clinical and demographic details of the fatal cases are presented in table 3.

Table 3. Demographic, laboratory and clinical characteristics of two fatal confirmed, and two fatal probable cases of EV71, Nakhorn Ratchasima Province, Thailand, 2006

Characteristic	Case 1	Case 2	Case 3	Case 4
Sex	Female	Male	Male	Male
Age (months)	4	24	17	39
Village	X	X	Y	Z
District	A	A	B	B
Onset date	25 Jun	23 Jun	22 Jun	24 Jun
Length of fever (days)	3	34	2	3
Length of illness until died (days)	4	3	3	4
High grade fever (>39°C)	Yes	Yes	Yes	Yes
Acute dyspnea	Yes	Yes	Yes	Yes
URI symptoms	No	No	No	Yes
GI symptoms	Yes	Yes	Yes	Yes
HFMD	No	No	No	No
Chest X-ray	Pulmonary edema	Pulmonary edema	Pulmonary edema	Pulmonary edema
EV71 isolation	No specimen	EV71	No specimen	No specimen
Autopsy & electron microscopy	Enteroviral-like particles in brain tissue	Not done	Not done	Not done
Case classification	confirmed	confirmed	probable	probable

URI = Upper Respiratory Tract; GI = Gastrointestinal; HFMD = Hand, Foot and Mouth Disease

Two of the four fatal cases were laboratory confirmed and were linked epidemiologically; they had a history of close contact, i.e., hugging, kissing and holding each other's milk bottles.

Electron microscopy of autopsy tissue samples from fatal case 1, four-month-old female, conducted at the Department of Microbiology, Faculty of Medicine Siriraj Hospital, Mahidol University revealed spherical, non-enveloped, viral-like particles, with an average diameter of 20 nm. Some of the particles were in membrane-bound vesicles and some were scattered in the cytoplasmic matrix (Figure 2).

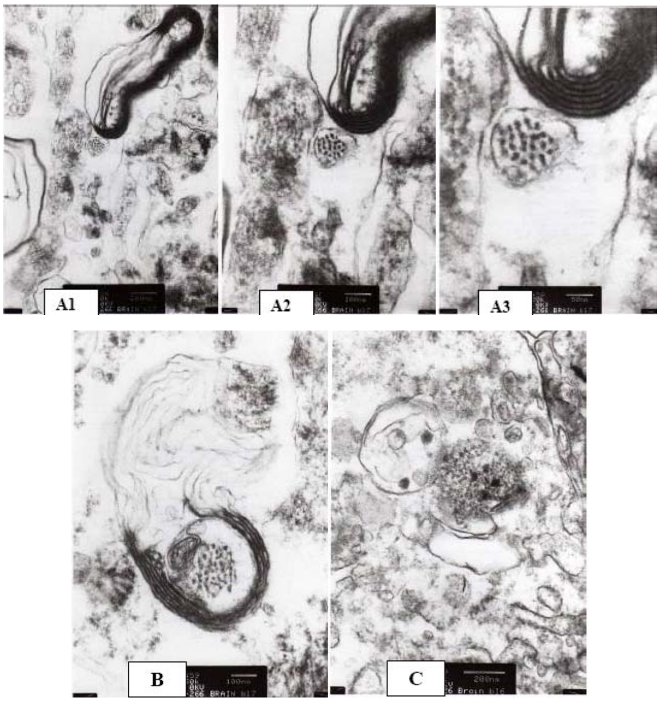

Figure 2. Electron microscopy of brain tissue from a four-month-old case of EV71, Department of Microbiology, Faculty of Medicine and Siriraj Hospital, Mahidol University, Bangkok, Thailand, 2006

No viral particles appeared in the cardiac or lung tissue. Sequencing of EV71 isolated from fatal Case 2, two-year-old boy, was done at the same facility and identified the sample as the sub-genogroup C4:Shenzhen strain (Genbank Locus number: EF203407), a strain first identified in Mainland China[9].

Five of the 32 probable cases (15.6%) had non-EV71 viruses isolated from their samples because they met our probable case definition and kept our case fatality proportion estimate conservative we included them in our analysis.

Discussion

Fatal EV71 infections are not a new occurrence in Asia. However, past fatal infections have occurred within large outbreaks. The case fatality proportions in the 1998 Taiwan outbreak (0.06%) and the 2006 Malaysia outbreak (0.09%) were dramatically lower than the 9.5% observed in our investigation. Another remarkable feature of this outbreak was the absence of HFMD signs and symptoms in the majority of cases. Our investigation was limited in geography (two districts) and in overall scope (42 cases), but if clusters of fatal EV71 cases persist outside the context of large-scale HFMD outbreaks, then a new epidemiological profile may be emerging for EV71 infection. EV71 Subgroup C4 was first isolated in China[9] and has since been isolated in Taiwan[10] and in Japan[11]. The EV71 C4:Shenzhen strain identified in our outbreak has not previously been found in Thailand[9]. The appearance of this strain led us to ask relatives of the fatal cases about travel history.

The grandmother of Case 1 traveled to China and Singapore in May 2006, one month prior to the fatal events. She had close contact with Case 1 and it is possible that she was the index C4:Shenzhen strain infection with asymptomatic disease. After this outbreak, EV71 was found in other parts of Thailand. Genogroup C4 was isolated from three children with severe febrile illness, two of whom died (personal communication). The significance of the association between the high case fatality proportion we observed and this strain is unclear at this time.

This investigation was limited by the low proportion of cases with laboratory confirmation, present in only two of the fatal cases. We chose to include probable cases in our analysis because that provided the most conservative case fatality proportion calculation.

Public Health Action and Recommendations

Standard control measures including improvement of personal hygiene, especially hand washing before eating and after going to the bathroom, and encouraging isolation of sick children at home, were implemented in districts A and B. Pediatricians and general practitioners in the community were asked to be aware of possible severe EV71 infection manifesting without skin lesions.

A new national surveillance system was set up for pediatric cases of fever and pulmonary edema or acute respiratory distress syndrome in July 2006[12]. The new system includes a comprehensive review and investigation of every fatal case and aims to: 1) describe the magnitude and trends of epidemic, severe HFMD and non-HFMD fever with pulmonary edema; 2) identify etiological agent(s) especially EV71; 3) identify risk factor(s) of severe case(s); and 4) implement control and prevention measures[12]. Careful monitoring of the new surveillance system's results and ongoing sequencing of EV71 isolates are necessary to better understand the magnitude of the danger of EV71 infection in Thailand.

Acknowledgments

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Suggested Citation

Buathong R, Hanshoaworakul W, Sutdan D, Iamsirithaworn S, Pongsuwanna Y, Puthawathana P, et al. Cluster of fatal cardiopulmonary failure among children caused by an emerging strain of enterovirus 71, Nakhorn Ratchasima Province, Thailand, 2006. OSIR. 2008 Aug;1(1):1-3. <http://www.osirjournal.net/issue.php?id=5>.

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Human *Streptococcus suis* Outbreak in Phayao Province, Thailand, 2007

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Introduction

Streptococcus suis is a gram-positive bacteria found predominantly in porcine species. The epizootiology of *S. suis* occurrence among pigs is complex; it usually occurs as normal flora, but may be infectious or even lethal, especially among weaning piglets[1,2]. Human disease from *S. suis* infection can manifest as meningitis, septicemia, endocarditis, toxic shock syndrome, arthritis, acute deafness, or other[3]. Human infections generally occur sporadically; outbreaks are uncommon[2]. When they do occur, outbreaks are typically small to medium in scope[4]. To date, more than 400 human cases have been reported worldwide, mostly in areas of intensive pig production or consumption[3]. It is likely that this underestimates the burden of disease.

The first outbreak of *S. suis* infection in Thailand was reported in 1993[5]. That outbreak occurred in Lamphun; ten cases were identified and ingestion of raw pork and blood was thought to be the primary risk factor[6]. A case-series of forty-one cases of *S. suis* meningitis in northern Thailand was published in May 2008[7].

The largest human *S. suis* outbreak reported involved 215 cases in Sichuan, China in July to August 2005[8]. This outbreak followed a pig die-off. It was characterized by a high (28%) prevalence of Streptococcus Toxic Shock Syndrome (STSS) and a high (18%) case fatality proportion; the major risk factors were slaughtering a sick pig or handling the carcass of a pig that had died from unknown causes. Almost half (48%) of the cases had wounds on their hands at the time of slaughter or when they had contact with the carcass[8]. Since the occurrence of this outbreak, human *S. suis* cases have been increasingly recognized worldwide.

On 1 May 2007, a health officer at Hospital A in Phayao Province reported five human *S. suis* cases, all from a single sub-district. Each case had presented with acute onset of high fever, severe headache, arthalgia, severe muscle pain and altered consciousness. All were admitted to the intensive care unit. At the time of the report, two patients had died, and two required mechanical ventilation. We investigated in order to verify the diagnosis, confirm the outbreak, describe the epidemiological characteristics of the outbreak, and assist in implementing control measures.

Methods

Phayao is an agricultural province located in northern Thailand. Traditional ingestion of raw pork and blood remains a common practice.

We performed a descriptive study by reviewing all cases of meningitis, encephalitis, and cases of septicemia of unknown origin during the previous three years in Phu Sang District. We interviewed eight laboratory-confirmed hospitalized cases and for one deceased case interviewed family members as proxies. We performed active case finding by reviewing medical records of admitted patients and also sought to identify additional cases within the community. Duration of the study period was two weeks before the first case occurred (12 Apr) to one week after the last case (11 May).

We defined a suspected case as a person who lived in village 4, 5 or 9 of Thung Kluai Sub-district, Phu Sang District, Phayao Province who had fever and at least one of signs or symptoms, including severe myalgia, severe headache, nausea/vomiting, diarrhea, arthalgia, ecchymosis, neck stiffness, seizure or alteration of consciousness between 12 Apr and 11 May 2007. A confirmed case was defined as a suspected case with laboratory detection of *S. suis* by hemoculture or cerebrospinal fluid (CSF) culture with streptococcal colony growth positive for alpha-hemolysis and confirmation with the API 20 Strep test (bioMérieux) or ELISA. Around all case-patient houses, we conducted a survey of domesticated pigs, pig farms, pig slaughtering processes and cooking techniques. We took blood samples from ten of the pigs at Slaughterhouse C. We did a trace back of sources of pork meat served during the funeral day.

We conducted a case-control study to determine risk factors for human *S. suis* infection. The first nine cases (31%) with positive hemocultures of the 29 confirmed cases were included in the study. All nine had attended a funeral ceremony. We defined controls as people who had attended the funeral ceremony in village 5 on 25 Apr 2007, had no symptoms during the past two weeks, and had no positive laboratory results. From a list of 2,300 residents registered for care in the local health centers, we used simple random sampling to select 76 potential controls from the three villages. Of these, we identified 36 (47%) people who met the definition for control. We calculated crude and adjusted odds ratios (ORs) to quantify associations between disease and exposure.

Results

Figure 1 shows an increase in the number of unspecified etiology meningitis and encephalitis cases in Phu Sang District in April 2007 compared to the same month in previous years. We identified 50 *S. suis* cases (29 laboratory confirmed, 21 suspected cases); the epidemic curve is shown in figure 2.

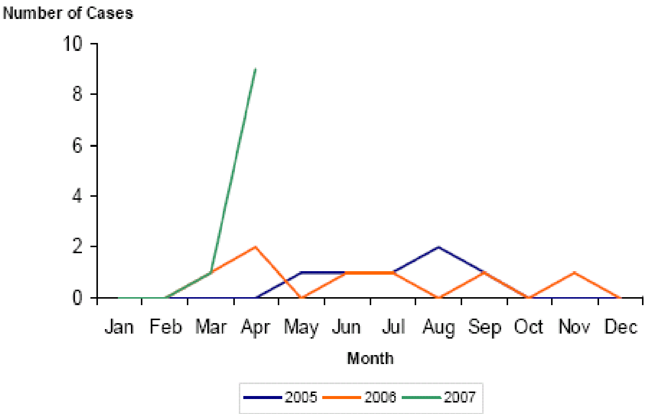
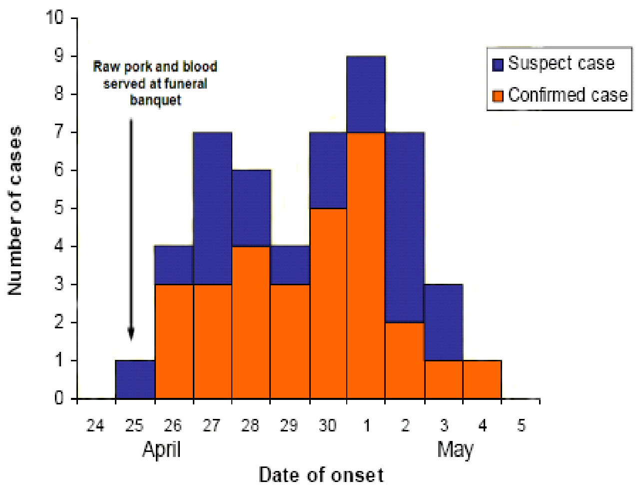


Figure 1. Reported cases of meningitis and encephalitis by month in Phu Sang District, Phayao Province, Thailand, 2005 – 2007



** Date of onset for one case was unavailable*

Figure 2. Cases of *S. Suis* infection (N=49*) in Phu Sang District, Phayao Province, Thailand, April to May 2007

The male-to-female ratio was 1.3:1, and the median age was 49 years old (range 10-77). Of the cases, 48 (96%) were hospitalized, seven in the intensive care unit; one (2%) patient developed STSS, shown in figure 3. Three (6%) patients died. Clinical manifestations are summarized in figure 4; case outcomes are shown in table 1.

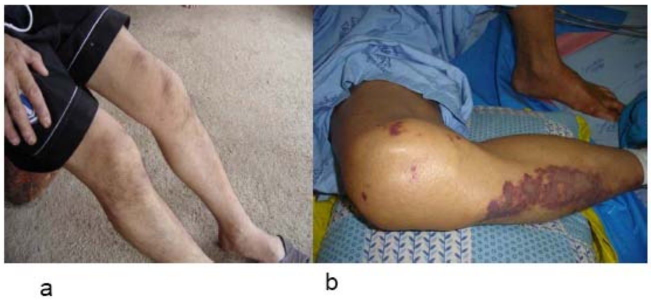


Figure 3. Streptococcal Toxic Shock Syndrome (STSS) (a) septic arthritis; (b) ecchymosis

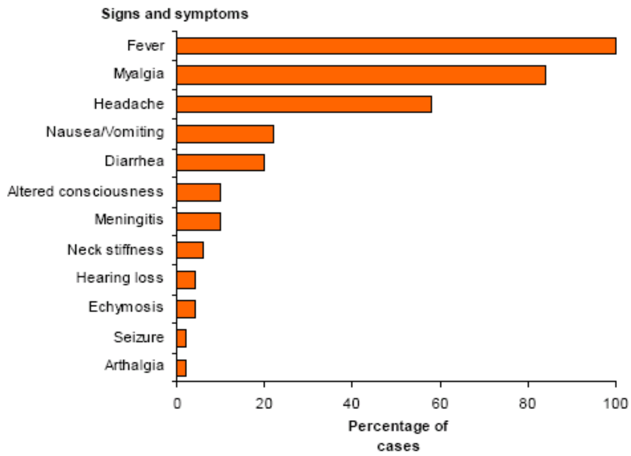


Figure 4. Signs and symptom frequency of *S. Suis* infection in Phu Sang District, Phayao Province, Thailand, April to May 2007 (N=50)

Most cases lived in village 5, in Thung Kluai Sub-district. The index case developed symptoms hours after attending a funeral banquet on 25 Apr 2007 in village 5; the menu for this banquet included fresh pig blood and raw pork. The results from the interviews with the nine patients/proxies are presented in table 2.

Table 1. Outcomes of *S. suis* cases of in Phu Sang District, Phayao Province, Thailand, April to May 2007 (N=50)

Outcome	Number of Cases (%)
Hospitalized	48 (96)
Intensive care unit	7 (14)
STSS*	1 (2)
Death	3 (6)

** Streptococcus toxic shock syndrome*

Table 2. Demographic and raw pork/blood consumption data for nine confirmed cases of *S. Suis*, Phu Sang District, Phayao Province, Thailand on 25 Apr 2007

Case	Sex	Age	Ate Meal:		
			Breakfast	Lunch	Dinner
1	Male	56	No	Yes	No
2	Male	50	Yes	Yes	No
3	Male	43	Yes	Yes	No
4	Male	51	No	Yes	No
5	Male	41	Yes	Yes	No
6	Male	49	No	Yes	No
7	Male	50	Yes	Yes	No
8	Male	62	Yes	Yes	No
9	Male	71	No	Yes	No

Raw meat and blood served at the funeral banquet came from three sources: four pigs from farm A, seven pigs from farm B and one pig supplied and slaughtered by the family of the deceased. Slaughterhouse C provided 10 kg of raw meat and 200 kg of grilled meat to the funeral and others in the sub-district area. We did not find any cases related to other pork provided by slaughterhouse C.

Farms A and B were located outside the village, and no crowding of animals was observed. No sick pigs or piglets were found. These farms supplied pigs to slaughterhouse C. Slaughterhouse C's pig sties were very crowded and a small number of sick-appearing pigs were present (exact number unknown). Serum specimens taken from three of ten pigs housed in slaughterhouse C were positive for Streptococcus species. The pig supplied from the family of the deceased was slaughtered and butchered beside a pigsty; its heart was punctured by a shape knife and blood was collected for a special breakfast dish served the morning of 25 Apr 2007.

We identified 148 people in the community with connections to the cases; 56 (38%) were willing to submit samples for hemoculture. Ten (18%) of these specimens were positive for *S. suis* type 2. Four of 11 CSF cultures were positive. A total of 1,432 people requested *S. suis* screening at local health facilities; laboratory results are shown in figure 5.

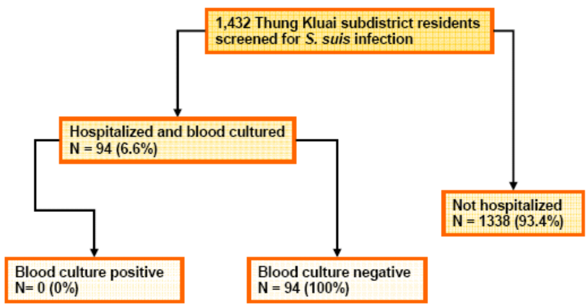


Figure 5. Screening for *S. Suis* infection following outbreak in Phu Sang District, Phayao Province, Thailand, April – May 2007

All nine cases had a history of ingesting raw pig blood or meat on the funeral day. Crude ORs of eating blood, intestines and other internal organs were 48.0, 17.5 and 10.1, respectively (Table 3). In multivariate analysis, the sole factor that remained statistically significant was eating blood, with an adjusted OR of 24.8 (95% confidence interval: 1.46 – 423.53) (Table 4).

Table 3. Univariate analysis of pork-product consumption in *S. suis* outbreak, Phu Sang District, Phayao Province, Thailand on 25 Apr 2007

Type of Pork	Case (N=9)		Control (N=36)		Crude OR	95% CI
	Exposed (N)	Un-exposed (N)	Exposed (N)	Un-exposed (N)		
Any	9	0	35	1	NA	NA
Nose or mouth	0	9	1	34	NA	NA
Neck	1	8	0	35	NA	NA
Pork	9	0	33	2	NA	NA
Blood	8	1	5	30	48.0	4.9-471.3
Intestine	8	1	11	24	17.5	1.9-157.2
Internal organ	7	2	9	26	10.1	1.8-57.9

Table 4. Multivariate analysis of pork-product consumption in *S. suis* outbreak, Phu Sang District, Phayao Province, Thailand on 25 Apr 2007.

Exposure	Crude Odds Ratio	95% Confidence Interval	Adjusted Odds Ratio*	95% Confidence Interval
Blood	48.0	4.9-471.3	24.8	1.5-423.5
Intestine	17.5	1.9-157.2	1.7	0.1-44.8
Internal organ	10.1	1.8-57.9	2.0	0.2-24.5

* *Model included three all three exposure terms*

Discussion

This is the largest *S. suis* outbreak reported in Thailand. This outbreak differs from the 2005 Sichuan, China outbreak in several ways including concomitant porcine disease, risk factors and clinical severity. There was no evidence of a widespread pig die-off in Phayao Province. Our environmental survey of slaughterhouse C indicated that a small number of pigs were ill. Three of ten porcine blood cultures were streptococcus positive, but available evidence cannot confirm that slaughterhouse C was the source of contaminated pork in this outbreak. In the Sichuan outbreak, slaughtering pigs was the strongest risk factor for disease. In this outbreak, consumption of raw pork blood was the principal risk factor. Both the frequency of STSS and the case fatality proportion were lower in this outbreak than in Sichuan.

Our results raise questions about the magnitude of risk associated with raw blood ingestion compared to the risk associated with raw meat or internal organ ingestion. We did not assess dose response patterns of blood ingestion in our analysis.

Laboratories in Thailand do not routinely test for *S. suis* and may misclassify *S. suis* as *S. viridan* species. In a study in Lumphun Province, of 28 blood cultures reported as *S. viridan*, 19 (67.9%) actually were identified as *S. suis*[9]. Increasing the number of laboratories equipped with appropriate diagnostic capacity to test for *S. suis* – already underway in Thailand – is essential for understanding overall burden of disease and detection of outbreaks.

This investigation was limited by the small fraction of cases included in the analytic study, the small scope of the pig health survey and an inability to trace back the contaminated pork products to a specific source. One major challenge faced by health care workers in this outbreak was social panic. Most hospitalized persons were given intravenous antibiotics for one week while awaiting hemoculture results.

Public Health Action and Recommendations

Soon after confirming the outbreak and verifying the etiology, our team joined with local staff to provide public health education about appropriate cooking of pork and sanitary conditions for pig slaughtering. Due to social panic, many persons requested screening for *S. suis* infection. Team members and local clinical staff provided screening for more than 1,400 people. Provincial Livestock veterinarians conducted a more comprehensive environmental survey and administered antibiotics to domesticated pigs.

Different epizootiological and epidemiological patterns of *S. suis* have been revealed in various outbreak settings. Careful description and analysis of ongoing outbreaks may provide clues as to how to best prevent and control future infections. The degree of risk posed to humans in *S. suis* outbreaks may vary depending upon whether the source of the outbreak is an epizootic with many dying pigs, a single sick pig or asymptomatic pigs colonized by *S. suis*. Gene sequencing of *S. suis* isolates may yield hints about strain-specific virulence that could provide a more complete understanding of the transmission dynamics of *S. suis*. Indiscrimate antibiotic treatment/prophylaxis of pigs in the outbreak area as a means of disease control was an understandable measure given local panic, but at this time there is no evidence that it is effective in decreasing risk of human disease.

In this outbreak, consumption of raw pig blood was identified as a strong risk factor. Changing eating behavior is highly challenging; assessing the baseline risk through behavioral surveillance and also evaluating the effectiveness of health risk communication could better inform long-term disease control programs.

Acknowledgements

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Suggested Citation

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Mushroom Poisoning Surveillance Analysis, Yunnan Province, China, 2001-2006

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Introduction

More than 600 mushroom species can be found in Yunnan Province, of which approximately 450 are edible. In 2002, 17,000 tons of mushrooms, most of which were wild mushrooms, were commercially harvested in Yunnan[1]. Yunnan, with its semitropical climate, provides an ideal environment for the growth of mushrooms. In Yunnan, local cuisine prizes mushroom dishes and collection and ingestion of wild mushrooms is a common practice.

However, it is difficult to visually distinguish poisonous wild mushrooms from edible ones. Food poisoning due to mushroom ingestion has long been noted in this province. From 1985 to 2000, 378 wild mushrooms poisoning events were reported in Yunnan, including 2,330 cases and 326 deaths[2].

Recently disease surveillance reporting methods have changed in China. The "Law of the People's Republic of China on the Prevention and Treatment of Infectious Diseases," first enacted in 1989, was revised in 2004 after SARS[3]. Accordingly, "The regulation on Health Threats emergent response" was issued in 2004, in which the definition of Health Threat and specific criteria for reporting of food poisoning, as a kind of Health Threat, was described: any event involving 30 or more cases or a fatality. Also in 2004, training for reporting of mushroom poisoning events was provided to public health personnel.

We conducted a descriptive study in order to understand the burden of wild mushroom poisonings and evaluate possible risk factors; compare pre-2004 surveillance data with post-2004 data; investigate the role of specific mushroom species in poisonings; and, given our findings, consider implications for control.

Methods

Yunnan Province, located in southwest China, has a population of more than 44 million people residing in 129 largely rural, mountainous counties. We conducted a descriptive study to summarize surveillance data from Yunnan annual epidemiological reports (2001–2006) and mushroom poisoning investigation reports (2004–2006). We collected data on each event including number of cases, deaths, demographic and clinical data of cases and species of suspected mushroom.

We also collected county-level rain fall, temperature and income data from the Yunnan Statistical Yearbook[4], and compared these variables between counties that reported a mushroom poisoning event and counties that did not. In these comparisons, we used the Kruskal-Wallis Test for non-normally distributed variables and t-tests for normally distributed variables.

We created a database and completed our analyses in EpiInfo 3.32. To reduce data error we coded all data collection forms, used double-entry and randomly selected 10% of all forms to double-check our data entry.

Results

From 2001 to 2006, 97 mushroom poisoning events were reported in Yunnan including 662 cases and 148 deaths. The overall case fatality proportion was 22.4% (mean = 30.7%, standard deviation = 15.7). The mortality rates due to mushroom poisoning in 2001–2006 were 0, 0.01, 0.03, 0.07, 0.17, and 0.06 per 100,000 respectively (Figure 1).

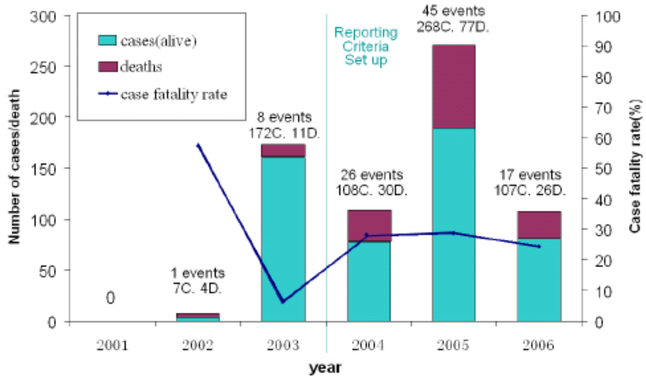

Figure 1. Number of mushroom poisoning event, cases, deaths and case fatality proportion by year, Yunnan, China, 2001-2006

Table 1 compares events, cases, and mortality reported in the three years (2001–2003) prior to adoption of specific event-based reporting requirements with the three years after (2004–2006) adoption of reporting requirements.

Table 1. Comparison of events, cases, and case fatality proportions reported before (2001-2003) and after (2004-2006) adoption of specific event-based reporting requirements, Yunnan, China

	Before (2001-2003)	After (2004-2006)
Number of events	9	88
Number of cases	179	483
Case fatality proportion	8.4%	27.5%

The majority (86.6%) of events occurred from May to August, the rainy season in Yunnan. Table 2 summarizes case demographics from events reported from 2004–2006. Most poisonings occurred in rural settings and were limited to a single household. Table 3 presents environmental and economic variables in counties where a mushroom poisoning event was recorded and counties where no event was reported.

Table 2. Demographic characteristics of mushroom poisoning cases, Yunnan, China, 2001-2006

Age Group	Male		Female		Total	
	Case (n)	Death (n)	Case (n)	Death (n)	Case (n)	Death (n)
0-9	19	12	14	7	33	19
10-19	27	16	12	6	39	22
20-29	22	10	17	9	39	19
30-39	29	16	16	7	45	23
40-49	19	10	8	4	27	14
50-59	13	7	13	8	26	15
60	16	8	9	5	25	13
Total	145	79	89	46	234	125*

*Age and gender were recorded in only 2/3 of total cases. This proportion was much higher in dead cases as there was no standard investigation form for mushroom poisoning and fatal cases usually drew more attention.

Table 3. Comparison of environmental and socio-economic factors among reported counties and non-reported counties, Yunnan, China, 2004-2006

Factors	Reporting Counties	Non-reporting Counties	P value
Median rainfall (range)	917 (483.7-2360.3)	833 (493.9-1864.7)	0.02*
Mean temperature (SD) (°C)	17.4 (2.6)	17.2 (3.0)	0.75**
Median income of peasants in Renminbi (range)	1377 (848-2967)	1728 (697-5333)	0.002*

*Median was tested with Kruskal-Wallis Test

** Mean was tested with t-Test

Source: Yunnan statistical yearbook 2005

In two-thirds (65.9%) of the events, a suspected poisonous mushroom species was documented. Figure 2 shows the mushroom species associated with 42 events where a single species was implicated. Multiple species were implicated in 16 events.

In 85.2% of events, the source of the suspected poisonous mushroom was reported; the majority (94.3%) of events was associated with using fresh mushrooms; most were collected by victims themselves and fried before consumption (Figure 3).

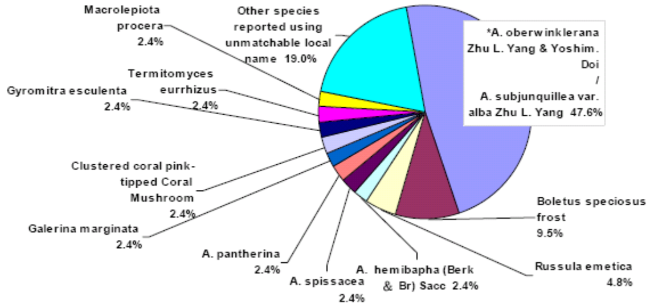

Figure 2. Proportion of single suspected mushroom species in mushroom poisoning events, Yunnan, China, 2004-2006

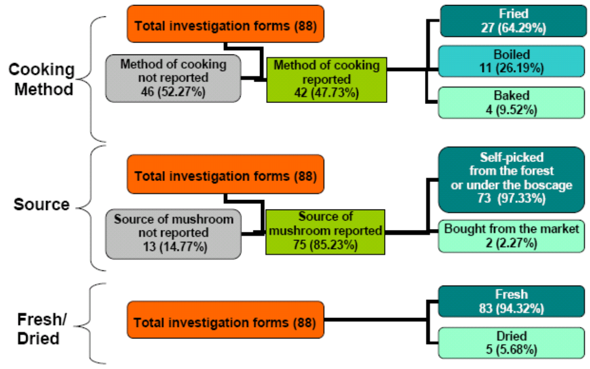

Figure 3. Cooking method, source of mushroom, and type of suspected mushrooms, Yunnan, China, 2004-2006

Figure 4 shows the facilities at which health care was sought by mushroom poisoning victims. The distribution of incubation periods is shown in figure 5 and clinical manifestations are presented in figure 6. Based on our audit of 10% of our data, we estimated an error rate of less than 1.5%.

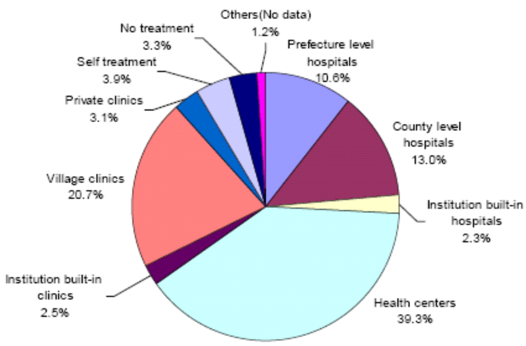

Figure 4. Facilities at which health care was sought by victims of mushroom poisoning, Yunnan, China, 2004-2006

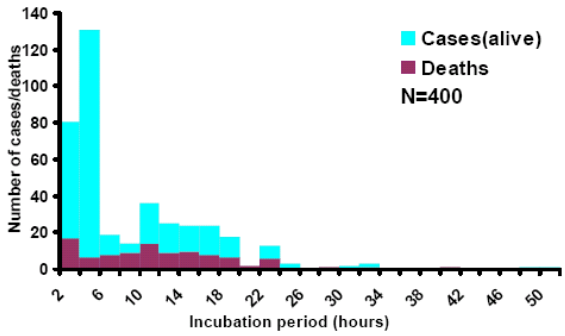

Figure 5. Number of mushroom poisoning cases by incubation period, Yunnan, China, 2004-2006

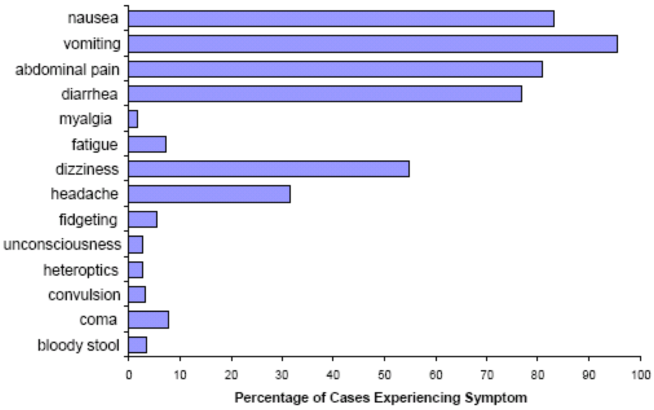

Figure 6. Symptom frequency of mushroom poisoning cases, Yunnan, China, 2004-2006

Discussion

Our results showed that the majority of mushroom poisoning events were associated with ingestion of wild mushrooms picked in rural areas, and limited to single households. Ingestion of commercially cultivated mushrooms appears to have minimal risk. Population-based mortality rates were very low. Mushrooms figure prominently in Yunnan cuisine; population-based rates probably provide a good indicator of overall risk. Despite the low rates, mushroom poisoning is the most common form of lethal food poisoning in Yunnan.

We found that after the adoption of specific reporting criteria in 2004, the number of reported wild mushroom poisonings in Yunnan Province dramatically increased. This likely reflects an increase in identification and reporting of cases rather than an increase in actual poisonings.

The most common poisonous mushrooms in this study were *Amanita spp*. This genus is composed of both edible and poisonous mushrooms which are generally indistinguishable without laboratory tests for the presence of toxin.

Despite the mountainous, remote character of rural Yunnan Province, healthcare is highly accessible to poisoning victims. Primary care such as fluid resuscitation, gastric decontamination by both gastric lavage (with gastric contents submitted immediately for toxicological analysis and spore examination) and multiple doses of activated charcoal (1g/kg initially, 0.5g/kg subsequently) can reduce toxin absorption, decreasing morbidity and mortality[5].

Public Health Action and Recommendations

The adoption of specific reporting criteria and public health training specific for mushroom poisoning appears to have successfully increased surveillance system sensitivity for mushroom poisoning. However, this system is not designed to be 100% sensitive. Event-based reporting has inherent sensitivity limitations and its results usually overestimate case fatality proportion. The utility of event-based surveillance should continue to be assessed over time.

Our results show no clear geographic clustering, and few epidemiological targets for focused prevention programs. Although the poisonings occur seasonally, peak occurrence is not confined to a few weeks or a month; although rural persons are predominantly afflicted, the province itself is largely rural. Little information exists to differentiate poisoning victims from the numerous people who enjoy wild mushroom dishes with no ill effects.

Eating purportedly edible mushrooms appeared to be associated with two poisoning events though possible misclassification makes this uncertain. It is not possible to compare the rate of poisoning due to ingestion of cultivated vs. wild mushrooms given the lack of denominators, but cultivated mushrooms are probably much less likely to be poisonous than wild mushrooms. Cultivated mushrooms were not found to be associated with any mushroom poisonings.

Public health professionals trying to prevent cases of mushroom poisoning might advise people in rural areas to eat only cultivated mushrooms but altering eating customs is difficult. Thorough cooking of certain species of toxic mushrooms reduces the risk of poisoning, but many fungal toxins, including those in poisonous *Amanita spp.*, are heat stable; cooking does not make them less dangerous[6]. Cooking of wild mushrooms should certainly be encouraged though that will likely not eliminate poisonings.

Collaboration with botanical experts and GIS analysis of the site of origin of poisonous mushrooms may provide future clues that will allow more specific targeting of prevention efforts.

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