Outbreak, Surveillance and Investigation Reports

OSIR
OUTBREAK SURVEILLANCE and INVESTIGATION Report

Volume 4, Issue 1,
April 2011

Outbreak, Surveillance and Investigation Reports

eISSN: 2286-8933

Outbreak, Surveillance and Investigation Reports
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First Documented Zoonotic Case of Q Fever in Penang, Malaysia

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Abstract

Q fever is a zoonotic disease caused by *Coxiella Burnetti*. In April 2007, Penang hospital notified a case of brucellosis through the syndromic notification which was later confirmed as Q fever. The patient presented with fever for two weeks and a history of handling the abortus of a goat. An epidemiological investigation was initiated to identify source of infection and prevent transmission. Blood samples from farm worker, contacts and animals from affected and neighboring farms were tested for Q fever. The universal precaution practices of the veterinary and laboratory staff were observed and their blood specimens were taken for Q fever serology. The patient was tested positive IgM and IgG for Q fever. Out of the 49 blood samples from farm workers, and veterinary and laboratory staff, 12 were positive for IgM, two were positive for IgG, seven were positive for both IgM and IgG, and 67 (27.2%) of the animal farms were positive for Q fever. There were minimal personal protective equipments used by the veterinary staff when handling the animals. There were goats imported from endemic countries. Prior to this outbreak no screening of imported animals for Q fever from endemic countries was instituted. Overall the farms were kept clean and well managed. All the contacts and animals tested positive for Q fever were treated.

Key words: Q fever, goat farm, livestock, zoonosis, Malaysia

Introduction

Q fever is a rickettsial disease caused by *Coxiella burnetii.* The disease is also known as Query Fever due to its dubious etiology and pathogenesis. Q fever was first identified in Queensland Australia in 1935, since then the disease has been reported worldwide in farm animals[1]. In 1959, there was an outbreak in Queensland, Australia associated with sheep contacts[2] and in 1969, in the Brisbane meat works with a 7.9% incidence[3]. It is highly infectious as clinical illness can be produced by a single inhaled organism. Virulence is low as most patients experience asymptomatic seroconversion[4]. Bush reported the first probable case of human clinical infection in Selangor, Malaysia in 1952[5]. This outbreak was thought to be caused by infection of infected milk. Q fever was also reported in Malaya in 1955[6] during a World Health Organization-assisted survey, but there had not been any references to it in Peninsular Malaysia since. The disease was also not listed as a notifiable disease under the Control of Communicable Act Malaysia 1988[7]. Livestock in Malaysia were subjected to stringent screening measures by the Veterinary Department, but not for Q fever.

Chronology of Events

Dr. P was a General Practitioner in Penang State, who started goat farming in 2006 at Valdor in the District of Province Wellesley South, near the town of Sungai Bakap in mainland Penang. He reared a range of animals, mostly goats, chickens and geese in his farm. There were about 100 goats in his farm, mostly local breed with some Boers and Anglo-Nubians that he had purchased locally. He ran the farm with two other workers; a local and a foreigner who resided on the farm.

The figure 1 showed the chronology of events leading to the diagnosis of Q fever in Dr. P. The Veterinary Department was then notified of the result.

Immediately, the health and veterinary teams carried out the active case detection and investigation in Dr. P's farm and the neighboring farms within the vicinity; farm A and farm B. This paper aimed to describe the epidemiology of Q fever and the investigations carried out during the event.

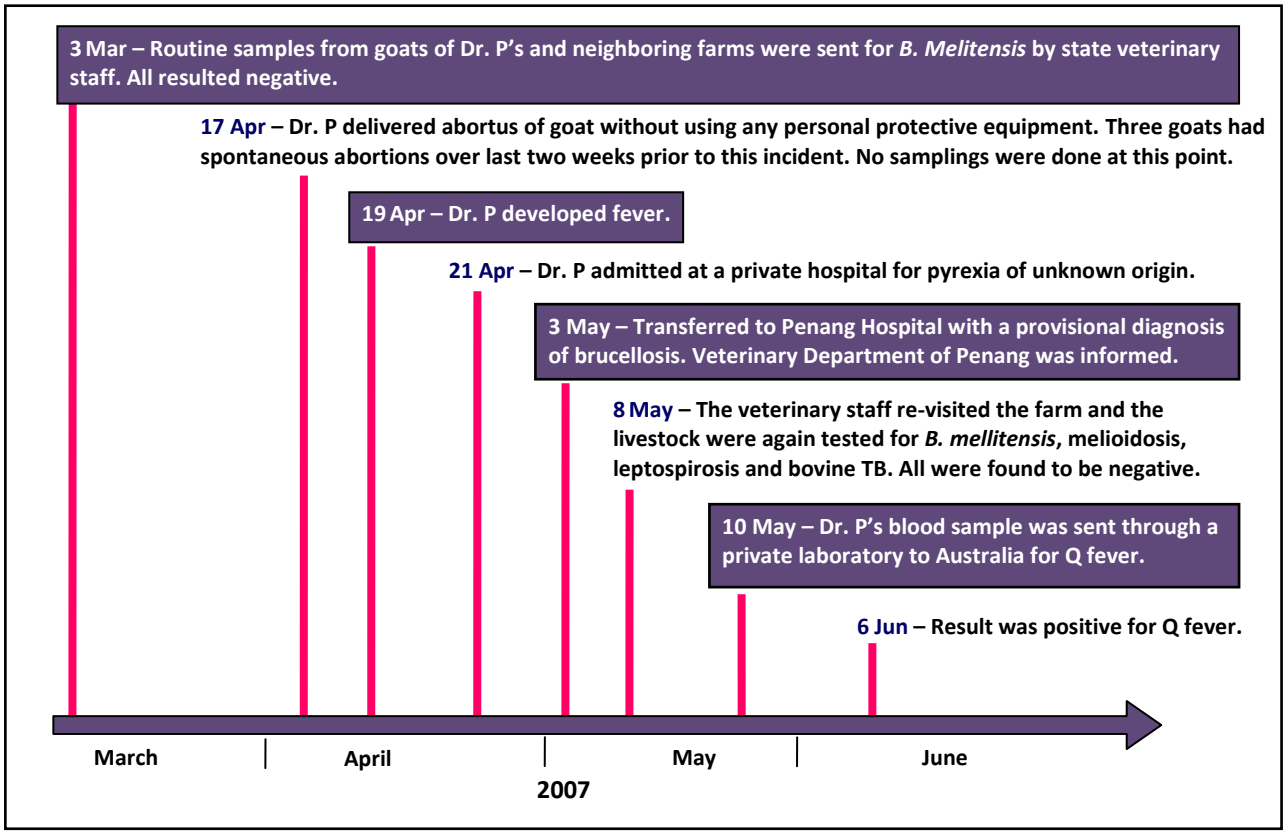

Figure 1. Chronology of Events leading to diagnosis of Q fever in Dr. P, 2007

Methods

This was a descriptive study. A probable case was defined as any farm worker from Dr. P's farm, farm A, farm B or veterinary staff presenting with fever from 1 Mar to 31 May 2007. A confirmed case was defined as a farm worker or veterinary staff with IgG and or IgM positive of Q fever.

The cases were interviewed using a standard questionnaire which included their daily habits and exposure at the farm. Active case detection was carried among the farm workers and amongst Dr. P's family members. Environmental assessment was carried out in all the farms, observing the general conditions and sanitation.

A review on the use of Personal Protective Equipment (PPE) and infection control procedures used by the veterinary staff while they were carrying out their routine activities at the farms were conducted. All those who came in contact with the animals were traced and screened at Bukit Mertajam Hospital and examined by physicians. Their blood samples for IgG and IgM Q fever serology were sent to the Institute of Medical Research in Kuala Lumpur.

The livestock at Dr. P's farm, farm A and farm B were sampled for Q fever and sent to Veterinary Department.

Results

Dr. P's farm was adjacent to the two farms and was located in Valdor, Sungai Bakap. Farm A shared a common fence with Dr. P's farm whilst farm B was located across a narrow dirt road from his farm (Figure 3).

Farm A had three workers including one migrant worker. The owner imported goats from Australia and redistributed the stock to other farms nearby. Dr. P bought his imported goats from farm A. Farm B had two workers including one foreigner. All the three workers in farm A and two of the three in farm B were serology positive and were probable cases. There were no more symptomatic cases found in our investigations.

Dr. P was married with two children. They spent a lot of their time in the farm; however, the wife and the children were asymptomatic at the time of the investigation.

The environmental assessment showed that Dr. P's farm was located on the fringe of an oil palm estate. The conditions in all the farms including the workers quarters located within the farm were generally clean and well-maintained, but dusty.

We reviewed the screening procedures by the Veterinary Department staff handling the animals and noted that they had very close contact with the

animals during rounding up and blood-taking procedure. Most of them wore masks and gloves, and some used aprons.

Table 1. Results of sampling of livestock at farms for Q fever by laboratory examination

	Number of sample	Number of sample positive (%)	Treatment
Farm Dr. P	126 goats	32 (25.4)	Oxytetracycline LA
	83 cows	28 (33.7)	
Farm A	14 goats	2 (14.3)	Oxytetracycline LA
	11 cows	1 (9.1)	
Farm B	12 cows	4 (33.3)	Oxytetracycline LA

Forty-nine blood samples taken from farm workers, veterinary staff and laboratory staff were sent for IgM and IgG serology, 21 (42.8%) were laboratory confirmed. Twelve (57%) had IgM positive, seven (33.3%) had both IgM and IgG positive and two cases with IgG positive.

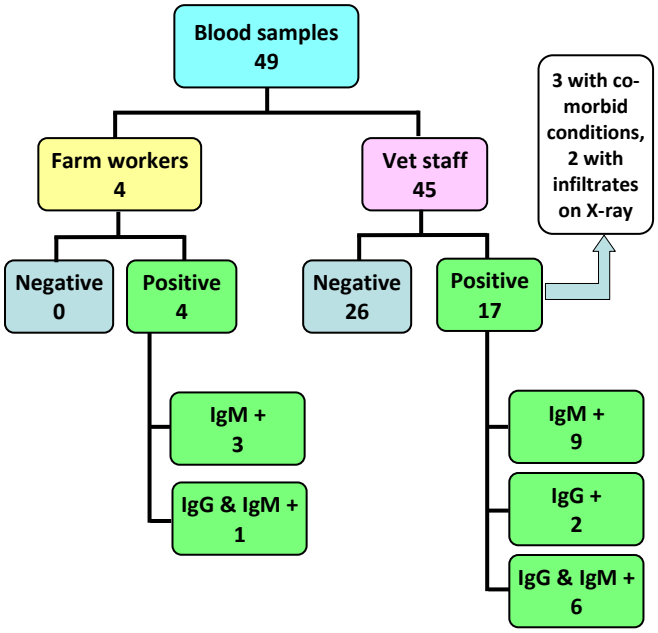

Figure 2. Results of screening for Q fever among the farm workers and Veterinary Department staff from May to July, 2007

Clinical and Preventive Measures

All the serology positive cases were treated with doxycycline for two weeks and their medical status were monitored by a physician from Bukit Mertajam Hospital. The two cases who presented with infiltrates in their chest x-ray were put on long-term follow up. Three farm workers who presented with co-morbid conditions were treated and discharged well.

All the workers in the farms, veterinary staff as well as Dr. P and his family were advised on precautions to be taken when handling animals. The farmers were advised on the proper use of PPE especially when handling the births of animals. They were also advised to maintain cleanliness of the farm and surroundings, to segregate ill stock from the rest and to practice personal hygiene. This included advice on washing hands and changing their clothes after handling animals. Those who did not turn up during the scheduled Q fever screening session were advised to do so at a later date and were advised to seek medical treatment if they developed fever.

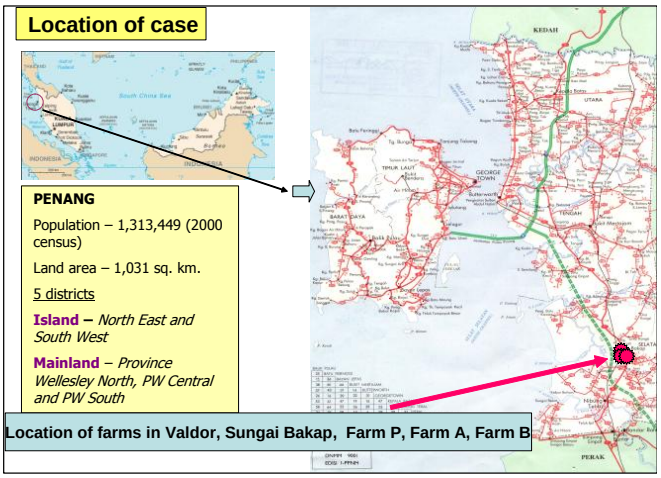

Figure 3. Location of the farms affected with Q fever in Penang

Discussion

Dr. P had Q fever from his infected goat. Since, all the goats in his farms were purchased locally, it showed that Q fever has been in circulation amongst his livestock and the farms in the vicinity. The incubation period of this disease is 18 to 21 days, with a range of four to 40 days, and it was probable that Dr. P was infected even before he handled the abortus of the goat on 17 Apr 2007.

There had been a series of abortions in his farm prior to this day, and he had been in close contact with his animals.

Coxiella burnetii is known to be an important cause of epidemic abortion among farm animals[8]. Veterinary and hospital laboratories in Malaysia do not routinely test for Q fever among animals and human respectively, however, a serological survey in Sarawak, East Malaysia conducted in 1988 detected Q fever among febrile patients in an Iban village[9]. It is possible that the disease is present in West Malaysia too.

Q fever is commonly transmitted through airborne dissemination, raw milk from infected cows and direct contact with infected animals[10]. Laboratory acquired Q fever has also been reported[11] and this could account for some of the cases among the laboratory staff in the veterinary department.

This disease is easily treatable. Tetracyclines[12] and its analogues is the mainstay of therapy amongst animals and livestock.

In conclusion, this was the first documented zoonotic case of Q fever in Penang. The disease was probably present among the farm animals in Penang. Since there was no mandatory screening of imported animals for Q fever, the introduction of the disease from an endemic country was possible. Higher number of serology confirmed cases among laboratory staff of the Veterinary Department staff was probably because of poor handling of infected animals without adequate PPE.

Public Health Actions and Recommendations

Dr. P was initially treated for brucellosis because there was poor awareness of Q fever among medical staff in Penang. In the last three decades, there had been no documented case of Q fever in Penang. On follow-up, Dr. P recovered and was discharged well after 20 days in the hospital. The goat whose abortus he handled had also been treated and had subsequently given birth to a healthy offspring.

However, when Q fever serology was also detected among the veterinary staff, there was panic not only in Penang, but also the rest of the country. This was followed by a high demand for screening. The Institute of Medical Research being the reference laboratory for the country was unable to cope with the sudden surge and the service of a private laboratory in Australia was required.

Following this incident, we traced back previous unaccounted cases of fever among animal farm workers in the Penang. There was a suspected case of brucellosis in farm C, located in Province Wellesley North in March 2007, but serologically negative for brucellosis. Traced back investigation was carried out, and the case was confirmed positive for Q fever. Three out of the four goats in his farm were also positive for Q fever. Four other workers in the farm who were also tested positive for Q fever were treated. All the animals were also treated.

This incident had triggered the Veterinary Department to place Q fever surveillance amongst livestock. Since February 2008, livestock imported from endemic countries were screened for Q fever. The use of proper PPE during all procedures involving animals was emphasized. In addition, routine preventive measures as personal hygiene and hand washing were stressed on as well. The veterinary staff now have to undergo regular screening. Medical officers in Penang were alerted on the possibility of Q fever among farm workers and those dealing with livestock. Two national laboratories now have the capability to test for Q fever.

This incident has resulted in a better collaboration between the State Health Department and Veterinary Department of Penang. Q fever is now a permanent agenda in the State Zoonosis Committee Meeting. Guidelines on the proper use of PPE for veterinary staff and farm workers are now available. Q fever is also a regular topic for presentation during Continuous Medical Education forums in Malaysia.

Acknowledgements

We would like to record our appreciation for all the kind support from the Penang State Veterinary Department, staff from the Province Wellesley North, South and Central District Offices, Hospital Bukit Mertajam and Hospital Seberang Jaya. We would like to thank the Director General of Health Malaysia for his approval to publish this paper.

Suggested Citation

Bina Rai S, Kamaludin F , Chow TS, Yoon CK. First documented zoonotic case of Q fever in Penang, Malaysia. OSIR. 2011 Apr;4(1):1-5. <http://osirjournal.com/issue.php?id=22>.

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Investigation on Measles Outbreak among University Students in Phrae Province, Thailand: Risk Factors and Seroprevalence of Antibodies to Measles

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Abstract

Medical record review, active case finding and environmental survey were conducted to investigation a suspect measles outbreak notified in Phrae Campus, Maejo University, Rong Kwang District, Phrae Province, Thailand. Specimens were collected for testing Measles IgM, IgG at National Institute of Health, and case-control study was applied among the first year students to identify agent and risk factors of the outbreak. 13.9% (6/43) of symptomatic students were positive to measles IgM. 8.1% (3/37) of asymptomatic students were negative to measles IgG. No virus was isolated from urine and throat swab specimens. Taking care of measles cases (OR=10.9, 95%CI=2.4-50.2) and studying in department of food technology (OR=6.2, 95% CI=1.9-20.6) were identified risk factors. Health education for students about transmission mode of measles and its prevention measures, provision of masks for students having fever during outbreak, strict isolation and vaccination for 77% of all students had been implemented.

Key words: Measles outbreak, Maejo University

Introduction

Measles is an acute, highly communicable viral disease with prodromal fever, conjunctivitis, coryza, cough and small spots with white or bluish white centers on an erythema based on buccal mucosa (Koplik's spots). Its incubation periods normally are 7-14 days.[1] Modes of transmission of measles are by droplet spread and direct contact with nasal or throat secretions of infected persons. Measles vaccination is one of the very effective measures to prevent measles.[2,3] Some researchers found that the efficacy of measles vaccine is 92-98%.[4,5] In Thailand, the first dose of measles vaccination was incorporated into the national immunization program for children aged nine months in 1984, the second dose of measles vaccine was added in 1996 for first grade students aged seven years. The coverage of measles vaccine increased from 49% to over 96% in 2003.[6] In a nationwide cross-sectional survey in Thailand in 2008, Measles, Mumps and Rubella (MMR) vaccine coverage among the first grade students in 360 was reported to be 91.2%.[7] However, Thailand has still reported some measles outbreaks in children, high school students and young adults (Figure 1).[8,9,10] In a hospital-based report on a measles outbreak in children in Suphan Buri Province in 1998, it was concluded that 50% of the cases had not been previously given measles vaccine. Of these, 9-15 years age group (28.9 out of 50%) was the most vulnerable.[8]

Phrae Province is in the north of Thailand, with population of 467,653, covers 6,538.59 km^2. From 2004 to 2007, the number of measles cases ranged from 11 to 30 cases; the highest number of measles cases was recorded in 2006 at 30 (morbidity rate was 6.4 per 100,000). In the first five months of 2008, there was only one measles case reported in March.

In Rong Kwang District, the number of measles cases recorded was few in recent years from 2004 to 2007, and there were one to two cases per year. In the same period in 2008, no measles case was recorded [Annual report of Measles incidence of Rong Kwang District Health Office, Phrae Province, Thailand, unpublished].

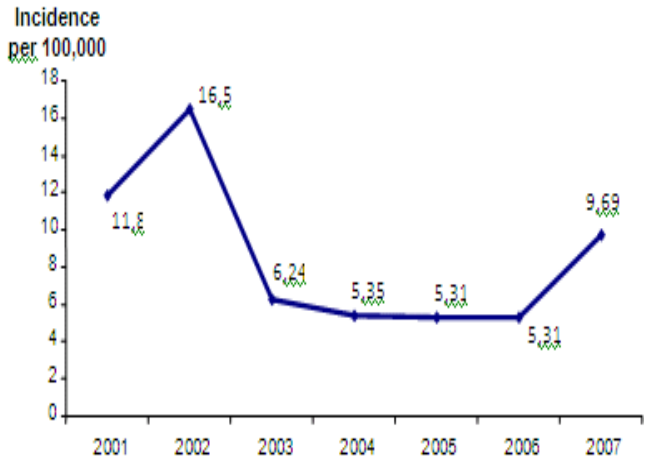

Figure 1. Measles incidence in Thailand from 2001-2007

Mae Jo University is an agricultural university with its main campus located in Chiang Mai Province, having a total number of 8,809 students. The Phrae campus is a branch of Mae Jo University in Rong Kwang District in Phrae Province, with a total student in year 2008 at 1,832. In 2008, all first year students in the Phrae campus participated in orientation in Chiang Mai from 28 May to 8 Jun. During the first week of June 2008, there were reports of some suspected cases of measles in Chiang Mai, before prevention and control measures had been implemented.

On 26 Jun 2008, Bureau of Epidemiology received report from the local public health office in Phrae Province that students reported having fever and rash while some, suspected of manifesting measles symptoms, admitted to the community hospital in Rong Kwang District. Meanwhile, many other students in the Phrae campus developed similar symptoms. Most of them were first year students from different provinces in Thailand, and they had recently returned from the orientation in Chiang Mai Province. As this was an unusual health event in a university campus, Bureau of Epidemiology sent an investigation team to Phrae Province to carry out an outbreak investigation. Participants of team included staff and trainees of Field Epidemiology Training Program (FETP), representatives of Communicable Disease Control and Prevention Office Region 10, the Provincial Health Office in Phrae Province and the Rong Kwang District Health Office. The investigation was conducted from 28 Jun to 2 Jul 2008, and supported for active surveillance which continued until 28 Jul 2008.

The objectives of the study were to investigate and evaluate magnitude of the outbreak, identify risk factors of the outbreak, and recommend preventive and control measures.

Methods

Records of patients visiting the community hospital in Rong Kwang District from 26 May 2008, two days prior to the orientation in Chiang Mai, to 29 Jun 2008, were reviewed to identify suspected cases. There were seven patients suspected of having measles, all of them were students in the Phrae campus. The first case was admitted to the hospital on 16 Jun 2008.

Active case finding was conducted by the investigation team in the Phrae campus from 29 Jun to 3 Jul 2008 through a survey which included interviews and physical examination. Campus announcement was broadcasted to call all students and campus staff to a common building. Students and some staff members in the Phrae campus were asked about whether they had history of fever from 15 May 2008 (date of arrival at the campus by first year students) to 30 Jun 2008 (date of investigation). Students with history of fever during this time were interviewed and physically examined to find out other symptoms related to measles case definition and its complications, bringing the total number of students screened to 1,589 (with a total of 1,832, the screening coverage reached 86.7%).

A suspected case was a student who had fever with rash and any of these symptoms: cough, conjunctivitis, coryza, Koplik's spots from 15 May to 28 Jul 2008. A confirmed case was a suspected case having confirmation by IgM positive or viral isolation from laboratory.

The Provincial Health Office in Phrae Province and the health office in Rong Kwang District additionally carried on a surveillance for all 1,832 students in the university to identify new measles cases for 20 days after the last case identified in the outbreak (28 Jul 2008).

Follow-up measures included creating guidelines on measles such as case definition, preventive and control measures; follow-up on students in the university; reporting all cases that met the case definition, zero report for no case; conducting active surveillance by collecting data from hospital, community, survey; and distributing Information, Education and Communication (IEC) to people about modes of transmission, prevention and control of measles.

A group with five persons in the investigation team was assigned to observe living and studying conditions of students in the campus, dormitories, classrooms, cafeterias and a sporting field. Dormitory rooms of both healthy and sick students were also

observed. Some students were interviewed about their daily life in the campus.

Single serum specimens were collected from students who had fever or rash to be tested for detecting measles IgM antibody by ELISA technique using Enzygnost Anti-Masern-Virus/IgM (Dade Behring, Germany)[11]. Those with both fever and rash had their throat swabs and urine collected for viral isolation using Vero/hSLAM cell. Some students who had no symptoms of measles by case definition had their blood specimens collected and tested for measles IgG to check measles immunity. All the specimens were tested at WHO Measles Regional Reference Laboratory in SEAR, National Institute of Health under Department of Medical Sciences, Ministry of Public Health of Thailand.

The case-control study was conducted among the first year students in the university. The first year students who met case definition were defined as cases while controls were the first year students who had no symptoms, were without laboratory result tested positive for IgM or IgG and were with no history of getting measles. The case and control ratio was 1: 4.

Therefore, from 537 first year students interviewed, 279 students had neither symptoms nor positive laboratory results, and without history of getting measles. We randomly selected 128 students to be control of the analytic study (case = 32).

The reasons to choose the first year students were because of the highest attack rate among them (5.5%), primary cases among them and convenience in control selection.

However, there were limitations as association of risk factors related to students in the other groups could not be analyzed.

By active case finding, reported measles cases in the first year students was 32 (5.5%), and it was the highest incidence among students in any other years. The 32 cases and the 128 controls among the first year students were interviewed to identify risk factors for getting measles among the first year students in the university.

In data analysis, descriptive statistics, chi-square, odds ratio and 95% confidence interval were employed. Risk factors showing statistical differences were further tested for association with measles by employing multiple logistic regression analysis.

Of the total 1,832 students in the Phrae campus, Mae Jo University, 1,589 (86.7%) were interviewed in a survey in order to detect suspected measles cases. The first case was identified at Mae Jo on 4 Jun 2008, one week after their orientation in Chiang Mai campus, while the last case was identified on 10 Jul 2008. Most of the cases occurred in a period 16-30 Jun 2008. The number of cases dropped sharply after 30 Jun 2008 (Figure 2). In the mean time, measles vaccine mop-up was provided.

Results

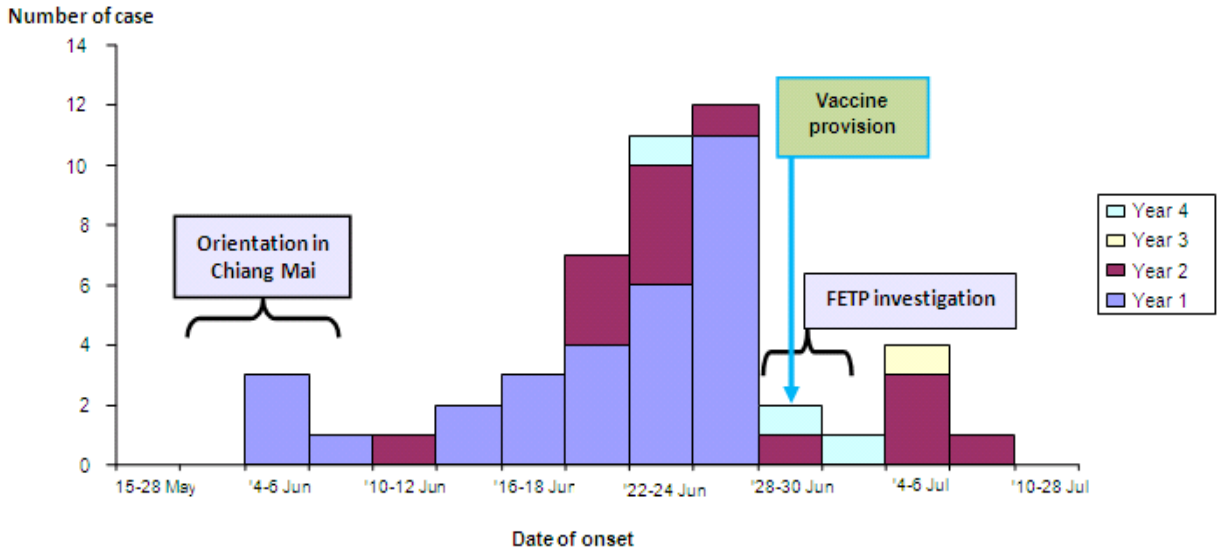

Figure 2. Measles cases by date of onset in Phrae campus, Mae Jo University, 2008 (Three cases have no information on date of onset)

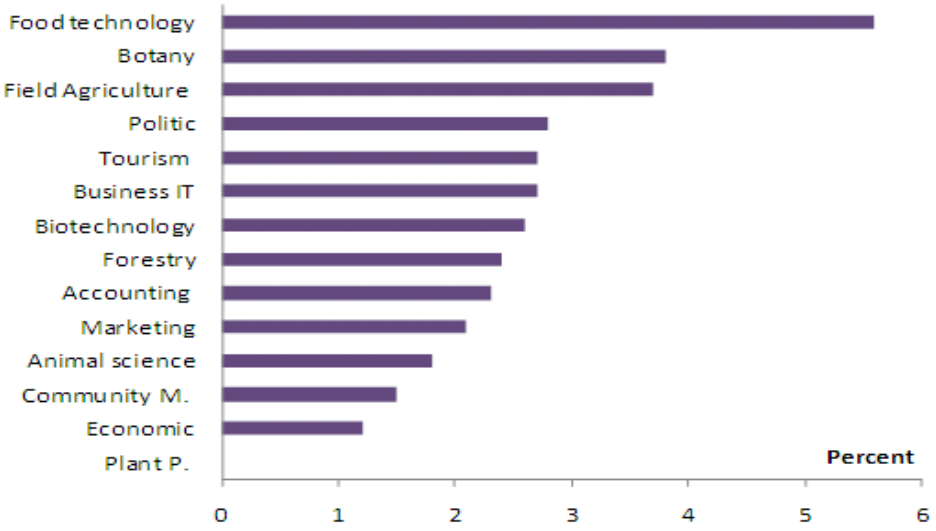

Figure 3. Attack rate of measles among students by departments, Phrae campus, Mae Jo University

A total of 51 symptomatic cases were found, with the attack rate of 3.2%. Among the 51 cases, there were seven reported cases, 35 cases from active case finding and nine cases from surveillance by local health officials. There were other six cases identified in Rong Kwang District, but they were not related to students in the university.

The attack rate was the highest in the first year students (5.5%), followed by the second year students (2.4%), the fourth year students (1.0%) and the third year students (0.3%). The difference was significant (p value <0.05).

The attack rate was the highest in the Food Technology Department (5.6%), while the rates detected in other departments ranged from 0 to 5.6%. Departments of Plant Production had no measles cases.

The youngest student infected with measles was 18 years old, and the oldest at 24 years old. The median of age was 19. The attack rates in male and female students were 2.5% and 3.0% respectively. However, the difference was not significant with 95% confidence interval of 0.5-1.5.

Clinical Manifestations

The most common symptoms of the measles cases were fever and rash (100%), cough (96.1%), coryza (72.0%), conjunctivitis (42.6%) and Koplik's spots (15.2%). In 19.6% of measles cases, diarrhea was a common complication while other kinds of complications were not recorded. Among the measles cases, 71.4% of them had received treatment from out-patient department, yet only 28.6% of them required hospital admission.

From interviews with the first year students about potential factors of getting measles, the results showed that during the outbreak, many students were exposed to the potential risk; as most of them participating in the orientation in Chiang Mai from 8-28 May (98.1%). The other risk factors included having close contact with patients having fever and rash: talking (35.8%), having roommates with fever and rash (15.1%), taking care of measles patients (15.1%), sharing meals with persons having fever and rash (13.7%), staying or sleeping in same bed with a friend having fever and rash (13.0%), and sharing common utensils (6.3%).

We also reviewed history of students getting measles vaccine. However, there were 23.9% of students who could not recall any history of their measles vaccination. Among those who could, their recollection was flimsy.

Environmental Observation in the University

Figure 4. Students in the class and in the laboratory

There were two dormitories for students: one was for male students, and the other for females. A student bedroom was around 20 m^2 in space with three to four students roomed together. Each had own wardrobe and personal belongings. Some students with typical symptoms of measles stayed in separate rooms in the dormitories.

In general, dormitories and rooms of students in the university were clean and ventilated. However, the

classrooms were quite crowded, air conditioned and equipped with electric fans, and students shared glasses for drinking water from water filters.

Laboratory Results

There were six specimens (13.9%) tested positive with measles, and seven specimens (16.3%) were equivocal. Among specimens collected from students who met the case definition, there were 28.5% of specimens tested positive with measles. However, we also realized that there were two specimens (6.9%) collected from students who did not meet case definitions positive with measles IgM. Among specimens collected from students having no measles symptoms, there were 81.1% of them tested positive with measles IgG, another 10.8% of them equivocal and another 8.1% negative with measles IgG (Figure 5). In all throat swabs and urine specimens, measles virus could not be isolated.

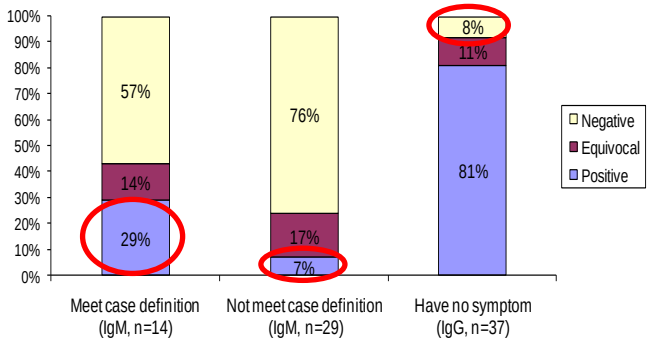

Figure 5. Laboratory results of 80 students

Association of Potential Exposure with Measles during Outbreak

Results of crude analysis showed that there were three exposures significantly associated with getting measles. Students who took care of measles-infected students with fever and rash were 6.4 times more likely to get measles compared to the others (CI 2.5, 16.4). Students who had ever stayed or slept in the same beds with students who had fever and rash were 3.5 times more likely to get measles compared to the others (CI 1.3, 9.4), and students who studied in Department of Food Technology were five times more likely to get measles compared to the others (CI 1.7, 14.6). The other exposures were not significantly associated with getting measles.

Multiple Logistic Regression

To test the association between risk factors and getting measles and the relation among risk factors, multiple logistic regression was employed for only three significant risk factors and one barely significant risk factor; the results are shown below (Table 1).

Table 1. Risk factors of measles in the outbreak

Risk Factor	P value	Adjusted OR	95% CI
Sharing rooms with student having fever and rash	0.610	0.5	0.04, 6.65
Taking care of student having fever and rash	0.002	10.9	2.35, 50.21
Staying/sleeping in the same bed with student having fever and rash	0.803	0.7	0.04, 12.01
Studying in Food Tech Department	0.003	6.2	1.87, 20.62

Consequently, there were two factors significantly associated with getting measles in the outbreak.

Students who took care of measles-infected students with fever and rash were 10.9 times more likely to get measles compared to the others.

Students who studied in Department of Food Technology were 6.2 times more likely to get measles relative to the others.

Discussion

The outbreak was reported rather late to be timely contained, therefore it extended through almost the five-week period. The outbreak affected mostly first year students in the Phrae campus with attack rate of 5.5%; which was much higher than those of the students in the other years. The first case had symptom onset on 4 Jun 2008, one week after participating the orientation in Chiang Mai. In early June 2008, Chiang Mai also recorded an outbreak of measles, which was controlled by the local health authorities. Measles could, therefore, be transmitted from Chiang Mai to Phrae campus.

In this outbreak, one-fourth of measles cases were admitted to hospitals. Moreover, one-fifth had diarrhea complication, which was higher than reported by US CDC as around six percent.[12]

The disease was spread to other students by close contact with an infected person in the university. Taking care of measles patients increased the risk of getting measles, making them about 11 times more likely to get measles compared to others. Studying in the Department of Food Technology significantly increased the risk of getting measles up to about six times more likely to get measles than others. However, no further elaboration could be made because of lack of information about activities of students. The Department of Food Technology which had the largest number of students, its crowded

condition could be a risk factor of measles transmission among students. Nevertheless, association between number of students and attack rate could not be established.

Regarding immunization against measles and history of getting measles, many students however could not recall history of one's own vaccination or ever having measles. Recall bias might be unavoidable in this context. Limitation of immunization against measles was underlined particularly in the early stage of its program launched in 1984. Whereas its coverage was quite low (48%), resulting in outbreaks periodically reported.[8,9,13] Older generation will still be at risk as in the Suphan Buri cases of 9-15 years age group[8]. In addition, interpretation of data was relatively limited as more details on seroprevalence of antibodies to measles were required.

Based on the laboratory results, proportion of positive IgG among students with no symptom was comparable with the seroprevalence of antibodies to measles among 15-19 years Thai population in 2004.[14] With assumption that the sample could be representative for all students in the university, we estimated that mopping up measles vaccine in the university could be effective for 8% of the students. The environment in the university was clean and the classrooms were air conditioned and/or mechanically ventilated with electric fans. However, natural ventilation could still be possible contributing factors in dormitories and other set-ups. However, measles-infected students staying in the university could continue spreading measles to other students. The specimens for viral isolation were not isolated; it needed enhancing techniques in specimen collection especially for viral isolation.

Conclusion

The measles outbreak in Mae Jo University's Rong Kwang campus in Phrae Province was confirmed by laboratory with attack rate at 3.2%. Taking care of students having fever and rash, studying in Department of Food Technology were risk factors that could increase risk of getting measles. Eight percent of student without symptoms had no immunity of measles.

Prevention and Control Measures

Protective masks for all students and university staff who had fever in that time period and IEC about measles, mode of transmission and its preventive measures were distributed to all students and university staff in the Phrae campus of Mae Jo University. Vaccination was also provided for all students having no fever during the outbreak.

Recommendations

Local health offices should inform the outbreak in an early stage for timely response. Students should wear protective masks when taking care of the measles-infected patients. Measles patients should be isolated from others. Further details about activities of students in Department of Food Technology are needed to be explored in order to identify the related risk factors.

Limitations of the Investigation

Poor memory of students on their own history of vaccination for measles hampered effective data interpretation. The population of the analytic study was limited to only the first year students, so some risk factors could not be analyzed further. Too little information was available about measles outbreak and student activities in Chiang Mai.

No information about activities of students in Department of Food Technology was available to allow insights into all the risk factors. IgG test for all students could not be performed to get more accurate number of measles immunity among students. Therefore, the reported OR was likely to be underestimated, yet underscored the validity of conclusions.

Acknowledgement

The measles outbreak investigation in Mae Jo University campus in Rong Kwang District of Phrae Province was conducted jointly by an investigation team of IFETP Thailand, with great supports from public health authorities in relevant local offices: the Rong Kwang District Health Office, the Phrae Provincial Public Health Office, the Office of Disease Control and Prevention Region 10, and the Phrae campus of Mae Jo University.

The results of the investigation were contributed by all members of investigation team and Dr. Chuleeporn Jiraphongsa, the FETP Director, who was very active and instrumental in collecting information, performing analyses and contributing to completion of the investigation. The work is attributed to the IFETP Thailand.

Suggested Citation

Long VN, Niramitsantipon A, Jiraphongsa C, Attawong B, Khuankaw W, Tipsriraj S, Pattamadilok S. Investigation on measles outbreak among university students in Phrae Province, Thailand: risk

factors and seroprevalence of antibodies to measles. OSIR. 2011 Apr;4(1):6-12.
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Outbreak, Surveillance and Investigation Reports
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Cholera Outbreak in Village A, Tanjung Keling, Melaka, 2007

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Abstract

On 28 Feb 2007, a cholera case was notified from Village A, Melaka, Malaysia. An epidemiological investigation was conducted to assess the extent of the outbreak and establish control measures. Active case detection was conducted among the case's family and neighbors, work contacts and related food handlers. Passive case detection was enhanced in 10 nearby clinics in the area. A case was defined as a person who developed at least three episodes of watery diarrhea with Vibrio cholerae positive stool culture. A case control study was done to identify risk factors. Controls were healthy household members or neighbors with stool culture negative for Vibrio cholerae. Water and food samples were taken for bacterial analysis. Control measures were immediately initiated and followed up. One hundred and forty two contacts were screened. Seven new diarrhea cases with epidemiological link were detected, clustered among two families with one positive stool culture with no fatality. All cases were Malays; six males and two females. Fifty percent had history of eating ice desserts prepared unhygienically by an infected food handler. Cases were seven times more likely to consume an ice dessert (95% CI = 1.1-44.1). No other food items or water sources were implicated. Immediate control measures effectively contained the outbreak.

Key words: cholera outbreak, Vibrio cholerae, familial clustering, ice dessert.

Introduction

Cholera is an acute bacterial infection of the intestine caused by ingestion of food or water containing *Vibrio cholerae*, serogroup O1 or O139. Its incubation period is from less than one day to five days. The bacteria release an enterotoxin that usually causes painless and copious watery diarrhea. The sudden loss of body fluid can result in severe dehydration. If left untreated, death can occur within hours[1]. Most persons infected with *V. cholerae* are asymptomatic, and the bacteria may be present in their feces for seven to 14 days. Less than 20 percent of ill persons develop the typical rice-water stools with moderate to severe dehydration[2]. Cholera is communicable if the bacteria are present in the stool. Although rare, an asymptomatic carrier state may persist for several months[3].

Cholera case fatality rates as high as 50 percent can occur in an unprepared community[4]. With proper oral or intravenous rehydration treatment, the case fatality rate is less than one percent[1,5].

An epidemic occurs when a community or region has an increase of people with an illness, a specific health related behavior, or another health related event[6]. In Malaysia, a report of one person with cholera is considered as an outbreak[7]. Once the presence of a cholera case in an area is confirmed, it becomes unnecessary to confirm other subsequent cases if there is an epidemiological link[8].

During the past decade, the incidence of cholera in Malaysia had decreased from 10.88 per 100,000 population in 1995 to 1.48 per 100,000 population in 2005[7].

On 28 Feb 2007 at 16:00, the Melaka Tengah District Health Office (MTDHO) was notified that a patient at Hospital M had a positive rectal swab for *V. cholerae*

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O1 serogroup El Tor biotype Ogawa serotype. Fellows from the Epidemic Intelligence Program (EIP) and health personnel from MTDHO conducted a joint investigation to determine the source, to assess extent of the outbreak and to establish control measures.

Methods

We conducted a descriptive study by reviewing medical records of acute gastroenteritis (AGE) cases at two government clinics, nearby hospital and eight general practitioners from 19 Feb 2007 to 13 Mar 2007.

Active case finding was done by visiting all 350 houses in the village. Anyone with diarrhea and their contacts were interviewed. The standard questionnaire for Food Water Borne Diseases from Ministry of Health was used to collect demographic information, signs and symptoms, and food consumption during the five days preceding their onset of illness.

Rectal swabs were taken from those with diarrhea and their contacts, cultured for enteric pathogens (*V. cholerae*, salmonella, shigella and campylobacter), and tested for antibiotic sensitivities.

An environmental investigation was carried out by inspecting the outbreak site and observing the conditions in the cases' houses and nearby food premises frequented by the cases one week prior to their illness. Surface swabs were taken from cases' kitchen utensils, toilet bowls, floors and sinks, and food handlers' hands. Food, water and ingredients of ice desserts such as "cendol", "cincau", corn, red and black syrup were also sampled.

A case was a person from Village A with acute onset of watery diarrhea more than three times with or without vomiting and/or dehydration from 19 Feb 2007 until 13 Mar 2007, with the presence of *V. cholerae* in a stool culture. Individuals who had similar signs and symptoms with an epidemiological link were considered as cases, and recruited into the study.

Contact was defined as a person who has a familial or social (working or schooling) relationship with a case within five days before onset (incubation period)[7].

Risk factors were determined by a case-control study. Controls were selected among the household members or neighbors who were healthy (rectal swab was negative for *V. cholerae*). Three controls were collected for each case.

Results

Descriptive Study

Village A was a coastal Malay village about 22 km from Melaka Town, and had 350 houses, with 1,200 residents. Most of population were Malay. Domestic waste was disposed by open dumping, burning or burying. All houses had pour-flush toilets and treated water supply. There was no record of violation water supplies since 2007. Food and water borne diseases was not known to be a health problem in this village, so as AGE from the surveillance data during the same period. No history of cholera cases was reported in this area for the past five years.

There were 18 food premises around the village, and mainly sold ready to eat food, cooked in situ. Food vendors operated small to medium sized stalls that were family owned. Operating hours varied; some were opened the whole day, some only at night, while others opened for breakfast until lunch. One shop sold an ice dessert. The village had night markets every Tuesday, Friday and Sunday, and sold daily usage merchandises and ready to eat food.

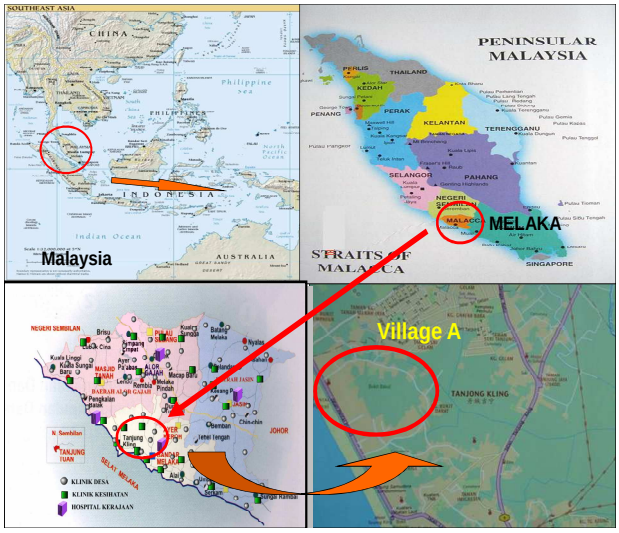

Figure 1. Map of Malaysia with the inset of Village A

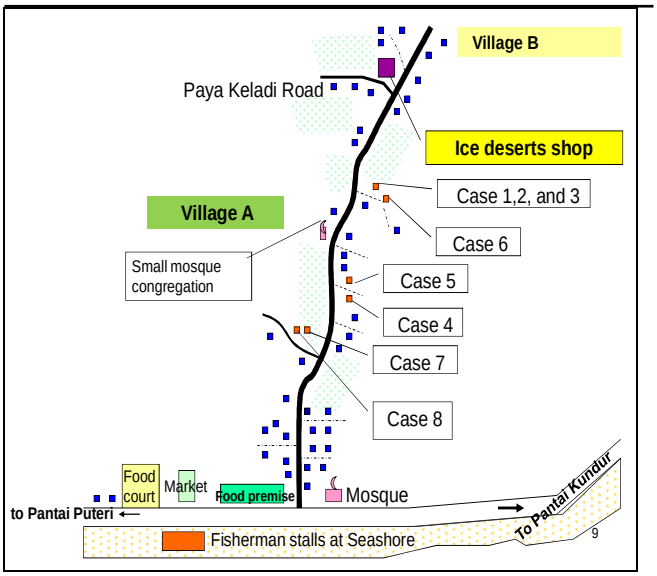

Figure 2. Spot map showing location of cases' houses in relation to food premises in the cholera outbreak

Communal activities in the village included "surau" (mini mosque) congregation every Tuesday and Friday evenings. Food was prepared in a pot-luck manner. The most recent gathering was on 23 Feb 2007, five days prior to the outbreak, and attended by 43 people.

All cases resided near the ice dessert shop and 50 percent of the cases ate ice dessert prior to their illness.

Two were *V. cholerae* positive. All eight symptomatic cases had a very strong epidemiological link[8].

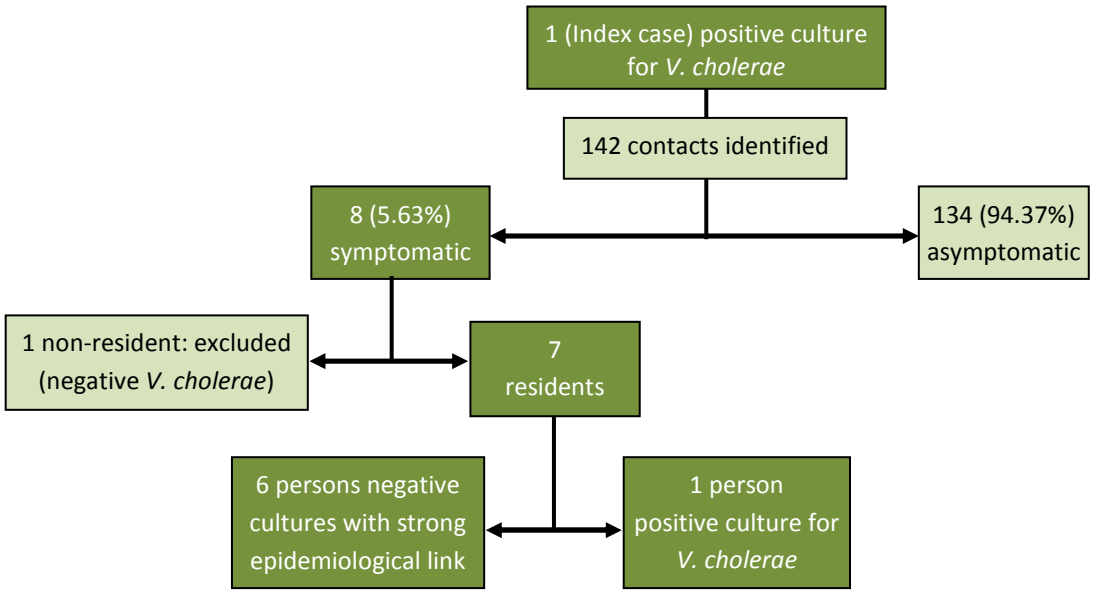

Figure 3. Outcome of cholera outbreak contact tracing in Village A, Melaka.

23 Feb 2007	24 Feb 2007	25 Feb 2007	26 Feb 2007	27Feb 2007	28 Feb 2007	1 Mar 2007
18:00	03:00	05:00		11:00	08:00	09:30
C2 and C3 consumed ice desserts bought from C5 shop. C4 and C5 also consumed ice desserts.	C2 developed diarrhea, vomiting and lethargy 06:00 C3 (C1 & C2's mother) developed diarrhea, vomiting and lethargy	C1 (brother of C2) developed diarrhea, vomiting and abdominal discomfort after taking care of C2 including his toilet care. They also shared toiletries. Went to Melaka Hospital. Rectal swab was positive on the 28 Feb 2007. 23:00 C4 developed painless spurious watery diarrhea, vomiting and lethargy. Received metronidazole (flagyl) from private doctor before stool swab taken.		C5 had diarrhea and abdominal discomfort. C5 had Doxycycline prior to stool swab taken as initially a contact for C4 (son).	C6 (C1's nephew) developed diarrhea, vomiting, lethargy. C6 hared chicken with C1 prior to illness. C7 (C4's relative) had diarrhea. C7 visited C4 and had meal prepared by her prior to illness.	C8 (C4's relative) developed diarrhea and abdominal pain. C8 visited C4 and had meal prepared by her prior to his illness.

Figure 4. Diagrammatic representative of the chronology of the outbreak event

Family A: C1, C2, C3, C6 were family members. C2 was the primary case. C1 was the index case. He had poor personal hygiene practices, especially after taking care of C2.

Family B: C4 and C5 were mother and son. C7 and C8 were relatives. C5 sold five to ten packs of ice desserts per evening. He was symptomatic when he sold the ice desserts to C2 and C3, five days prior to the outbreak.

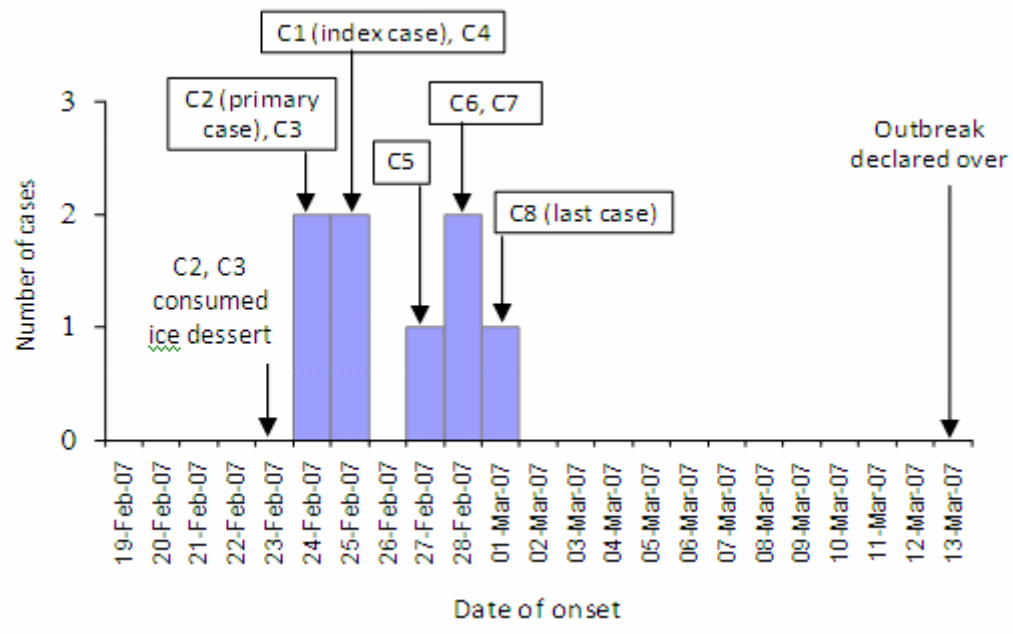

Figure 5. Epidemic curve of cholera outbreak in Village A, Melaka

This was a propagated cholera outbreak with eight cases which was declared over after no new case reported within two incubation period (after 13 Feb 2007). Six were male, and two were female. The youngest was 12 years old, and the oldest was 57 years old. All were Malays.

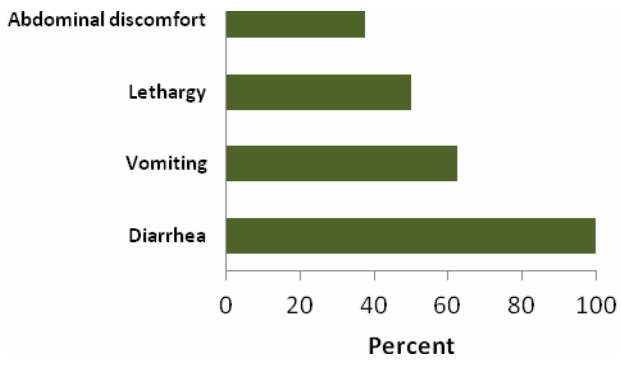

Figure 6. Symptoms of cholera cases in Village A, Melaka

Environmental Study

All houses in the village were made of brick, supplied with treated water, had sanitary toilets, and disposed their solid wastes in the backyard and burned it.

There were nine family members in the index case's house. The house had one toilet which was clean and separated from the bathroom. The waste disposal dumping area was unsanitary.

Figure 7. The house, the pour-flush toilet and the unsanitary dumping area of the index case house

(a) Diced ice (b) Ready to eat ice dessert

Figure 8. Pictures showing the preparation of ice desserts

Diced ice was added with "cendol", "cincau", corn, milk, and black and red syrup. The ice cubes were made from unboiled water. The red and black syrup was prepared by C4. "Cendol" and "cincau" were properly packed, labeled and produced abundantly by a factory, bought from a nearby shop. The milk and corn were from cans.

The unsanitary surrounding of the ice dessert shop

Ice dessert machine was not well kept when it was not in use

Storage of left-over ingredients in the refrigerator

Ice made from unboiled water

Figure 9. Pictures showing the unhygienic surroundings of the ice dessert shop and the storage of the desserts

The ice dessert shop was unsanitary. There was no proper bin for waste disposal. Rubbish was dumped beside the concrete slab where the ice dessert was prepared. The slab was dirty. The ice dessert machine was kept unhygienically. Hand washing facility was in a toilet beside the shop.

Laboratory Study

One hundred forty-two rectal swabs were taken from contacts, one was positive for *V. cholerae*.

All cultures were negative for salmonella, shigella and campylobacter.

All 153 surface swabs (45 cooking utensils, 46 hand swabs and 62 surface swabs from tables, bathrooms, toilets, freezers, etc) were negative for *V. cholerae*, shigella and salmonella.

All 96 food samples were negative for *V. cholerae*, shigella and salmonella.

All 58 water samples from the ice dessert shop, food stalls and school canteens were negative for *V. cholerae*, shigella and salmonella.

Case-control Study

Table 1. Percentage of cases with exposure to potential risk factors

Risk factors	Number of cases (n=8)	Percent affected
Ate ice desserts*	4	50.0
Ate food from various places outside the Village A	3	37.5
Ate food from various night markets	3	37.5
Ate food at *"surau"* or mosque congregation	2	25.0

Given the data in table 1, a hypothesis postulated was that ice dessert was the potential source of the cholera outbreak. This was tested via case-control study, in which 32 respondents were enrolled, eight were cases and 24 were controls (1:3 case and control ratio). Cases and controls were comparable in terms of sex and age group (p-value >0.05). All of them were Malays. Mean age for cases was 31.6±16.1 years, and control was 29.7±15.4 years.

Table 2. Result of case-control study

Food eaten before get sick	Case (n=8)		Control (n=24)		Odds Ratio	95% CI
	Ate	Did not eat	Ate	Did not eat		
Ice desserts*	4	4	3	21	7.0	1.1 – 44.1
Food bought from places outside the Village A	3	5	11	13	0.7	0.1 – 3.7
Food bought from various night markets	3	5	4	20	3.0	0.5 – 18.0
"Surau" or mosque congregation food	2	6	11	13	0.4	0.7 – 2.3

Cases were seven times more likely to consume the ice desserts. Stratification by ingredients could not be done because all cases ate all ingredients (Table 2).

Public Health Actions

Cases were promptly identified and referred to hospital for treatment. Doxycycline was given to all contacts as selective chemoprophylaxis because they were easily identified[9]. The unhygienic ice dessert shop was temporarily closed on 2 Mar 2007 under Communicable Disease Control Act 1988, and reopened on 6 Mar 2007. Enhanced AGE surveillance was done to identify new cases. No new cholera case was reported after 1 Mar 2007. The community was given health education and health promotion on personal hygiene, food safety, preparation of only hot and freshly cooked food hygienically and drinking of boiled water. They were taught to dispose their waste disposal in a hygienic manner. Food hygiene inspections were carried out for food handlers. Individual health education was given during house to house active case detection (ACD) activities. Posters and flyers of cholera were also explained.

Discussion

The Cholera Outbreak

Cholera outbreak in Village A showed clustering of cases among members of two families (eight people). Half had history of eating ice desserts prepared unhygenically by a symptomatic individual. Only two were positive for *V. cholerae* O1 serogroup El Tor biotype Ogawa serotype. One person had classical cholera symptoms, but stool culture was negative because she took metronidazole (flagyl) prior to hospital admission.

V. cholerae is a facultatively anaerobic gram-negative bacillus[11]. *V. cholerae* may not be isolated from stool samples of cholera patients if the sample collected late in an illness or after microbial therapy is started. Vibriocidal antibody titers peak 10-21 days after infection, and can be used to confirm *V. cholerae* infection. *V. cholerae* infection occur when vibriocidal antibody titers were greater than or equal to 1:1280[12]. In this study, test for vibriocidal antibody titer was not done because of lack of facility for this.

This cholera outbreak was self-limiting and occurred as a small cluster in a family or gathering. Examples of similar outbreaks occurred among husband and wife in Louisiana[13], 12 cases among nine families in New Orleans[14] and eight patients in Hudson and Union Counties[12]. There was no fatal case in this outbreak because of early ACD and prompt treatment.

The spread of infection was from contaminated food and direct person-to-person contact due to poor hygiene. The suspected food was ice desserts prepared by C5 on 23 Feb 2007. There could also be other villagers who consumed the contaminated food, but were asymptomatic. This was because *V. cholerae* El Tor is more likely to cause unapparent or asymptomatic infection as compared to the classical biotype[1,11]. El Tor *V. cholerae* infection in both endemic and non-endemic countries showed mild or clinically inapparent infection for every hospitalized patient[11]. In Louisiana 1986, toxigenic *V. cholera* O1 was detected in sewer systems of several towns; however, there was no case identified[14]. In Maryland in 1991, a cholera outbreak due to *V. cholerae* O1 serogroup El Tor biotype Ogawa serotype was detected involving four people who consumed contaminated coconut milk in a party. Three out of four were symptomatic. One asymptomatic patient had an elevated vibriocidal antibody titer[15].

C1 probably contracted cholera from C2 through direct person-to-person contact (possible to occur[16]) because they were sharing the same bed, toilet and fomites[11] (like towels and other personal utilities). This is seen in the El Tor biotype; facilitated by its characteristic of longer persistent in the environment, high infectivity, low virulence and greater hardiness[1,11]. Spread might have also occurred during C1 taking toilet care of C2 due to poor personal hygiene practice. There was no spread to the other

family members by home cooked food because none of the other five family members in the household had symptoms and their rectal swabs were negative for *V. cholerae*. Moreover, food was prepared by the healthy sister. There was also availability of safe drinking water and proper sewage system in their homes.

Source of the Outbreak

Case-control study results showed that those who consumed ice desserts were seven times more likely to develop symptoms than those who did not (OR=7; 95% CI=1.1-44.1). The individual ice desert ingredients were tested negative for *V. cholerae* because these were not the ingredients used during the outbreak. A possible source of contamination was from the poor hygienic practice of the handler (C5) with unsanitary environmental condition of the shop. He could be an asymptomatic carrier whose status could persist for several months[3], and later became symptomatic. His rectal swab was *V. cholerae* negative because he took doxycycline prior to his rectal swab taken.

All environmental samples were negative for *V. cholerae*. Sea water samples to prove cholera endemicity was also negative. Those samples were tested by standard culture and sensitivity procedure which can only detect viable organisms. There is a laboratory procedure using Polymerase Chain Reaction (PCR) technique which can detect cholera DNA from nonviable organism[16]. However, such test was not available in Malaysia.

Public Health Actions and Follow Up

The early ACD with enhanced surveillance managed to identify all suspected cases and referred to hospital for early proper management. Health education and promotion resulted change in community behavior; "surau" or mosque congregation did not prepare food as they usually did, waste disposal was disposed of in hygienic manner. The backyards of houses were cleaned. Inspection of food premises was done as scheduled. Their rating was satisfactory (>75%). Doxycycline prophylaxes, which were done selectively to all contacts of symptomatic cases as selective chemoprophylaxis, might be useful for household members who shared food and shelter with cholera patient[9].

Limitations

The sample size was small, thus, limiting analysis to the primary hypothesis. Recall bias was inevitable. However, respondents were given ample time to recall their dietary intakes and allowed help from other family members as most of them ate home-cooked food. Food samples collected for microbiological culture were not the actual food items eaten by cases. There was a limited capability in swab culture and sensitivity to detect cholera antigen as compared to vibriocidal antibody titer test and PCR technique, which can detect DNA from nonviable organism[17]. *V. cholerae* may not be present if the swab is taken late in their illness. Swab culture and sensitivity was subjected to stringent processes. Contamination might affect the result.

In conclusion, the cholera outbreak caused by *V. cholerae* serogroup O1 biotype El Tor serotype Ogawa in Village A, Melaka occurred among members of two families who were linked epidemiologically to a food handler who prepared ice desserts unhygienically. There were no deaths in this outbreak.

Recommendations

The environmental health team should continuously promote hygienic and proper waste disposal methods to the community. Regular inspection of food premises should be carried out. Unhygienic premises should be closed. It will be useful to have vibriocidal antibody titer testing to complement the standard culture and sensitivity procedure so that confirmation of cases would be easier if stool or rectal swab negative for *V. cholerae*. It will also be helpful to have PCR technique to test for *V. cholerae* DNA in a non-viable condition to identify the vehicle. Good communication and cooperation among staff of hospital, health personnel and community members are essential for an effective control and prevention of the outbreak.

Suggested Citation

Ujang N, Kamaluddin A, Kamaludin F, Syed Sheikh SH, CM Din SNA, Ariffin R, Suleiman A. Cholera outbreak in Village A, Tanjung Keling, Melaka, 2007. OSIR. 2011 Apr;4(1):13-20. <http://osirjournal.com/issue.php?id=24>.

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