



An Investigation of Ciprofloxacin-resistant *Neisseria Meningitidis* Serogroup B Infection Outbreak in a Provincial Prison, Nan Province, Thailand, October 2023

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Abstract

Meningococcal infection is a severe illness that can result in organ damage or death. On 23 Oct 2023, a joint investigation team was notified about two inmates diagnosed with meningococcal infection in a provincial prison. The investigation aimed to confirm the outbreak, describe epidemiological characteristics, determine possible source and risks of infection, and provide recommendations and control measures. This study reviewed the situation using surveillance databases. Active case finding was conducted among inmates and prison staff. Close contacts were identified and assessed. Drug sensitivity and serogroup identification were done in the cultured-growth specimens. Surveying inmate rooms, observing inmates' behaviors, and interviewing inmates and prison staff were performed. There were 7 laboratory-confirmed cases identified (attack rate 0.5%). All cases were male inmates with a median age of 46 years (interquartile range 38.5–49.5 years). Common symptoms were fever (100%) and headache (71%). Eight cases required hospital admission and one dead case was found (CFR 14%). Among 609 close contacts, 99% were inmates. All cultured-growth specimens were *Neisseria meningitidis* serogroup B with ciprofloxacin resistance. Crowded inmates and sharing water cups were risk factors for intra-room spreading. Daily activities and the previous influenza outbreak promoted inmates' inter-room contact. This is the ciprofloxacin-resistant serogroup B meningococcal disease outbreak in a provincial prison revealing multiple factors, including environmental, behaviors and daily activities, that promoted the disease's spread. Rifampicin chemoprophylaxis, active surveillance, and limited inmate activities could help reduce disease spread.

Keywords: meningococcal, meningitis, *Neisseria meningitidis*, prison, serogroup B, ciprofloxacin resistance, outbreak, Thailand

Introduction

Meningococcal disease is caused by *Neisseria meningitidis* (*N. meningitidis*). It has 13 serogroups with the invasive serogroups being A, B, C, W-135, X, and Y.¹ It spreads through droplets or close contact with an infected person.² The incubation period ranges from 2 to 10 days. Symptoms include fever, loss of consciousness, vomiting, headache, stiff neck, and purpura fulminans.³ Even with early diagnosis and treatment, case fatality rates can range from 8 to

15 percent.⁴ The prevalence of asymptomatic carriers can vary from 1 to 30 percent.⁵

N. meningitidis stands as a leading cause of meningitis and rapidly fatal sepsis worldwide. Annually, more than 430,000 meningococcal cases and 32,000 deaths were reported.⁶ Thailand has reported sporadic cases of meningococcal disease throughout the year with 1–3 confirmed cases per event.⁷ The major serogroup in Thailand is serogroup B.^{8,9}

To prevent secondary meningococcal disease infection, chemoprophylaxis, involving ciprofloxacin, rifampicin, ceftriaxone, or azithromycin, is recommended for high-risk close contacts.¹⁰ Ciprofloxacin is the commonly used first-line chemoprophylaxis medication in Thailand due to its ease of single-dose oral administration. However, a ciprofloxacin-resistant strain of *N. meningitidis* has been reported globally and these resistant strains are present in all serogroups.^{11–14} The emergence of the resistant strains raises concerns about current recommendations.

On 23 Oct 2023, the Division of Epidemiology, Department of Disease Control was notified about two confirmed meningococcal septicemia patients from Nan Provincial Public Health Office. Both were inmates from a provincial prison. The Department of Epidemiology investigated to confirm the outbreak, describe the epidemiological characteristics, determine possible sources and risks of infection, and provide recommendations and control measures.

Methods

Descriptive Study

To confirm an outbreak and assess the magnitude of meningococcal disease, this study reviewed the situation of meningococcal disease in Nan Province between 1 Jan 2018 and 30 Sep 2023. This study extracted data on reported meningococcal disease patients from the National Disease Surveillance database, Event-based Surveillance, and Health Data Center database (ICD-10 codes “A390”–“A399”). This study also interviewed the laboratory technician at Nan Hospital regarding *N. meningitidis* detection.

This study conducted a descriptive study including active case finding among inmates and staff in a provincial prison. A suspected case was defined as an inmate or staff in a provincial prison who had a history of fever or body temperature $>38^{\circ}\text{C}$, along with at least two of the following symptoms: stiff neck, alteration of consciousness, seizure, headache, vomiting, dyspnea, and purpura fulminans between September and November 2023. A confirmed case was a suspected case that tested positive for *N. meningitidis* through at least one of the following tests: blood culture, cerebrospinal fluid (CSF) culture, serum reverse transcriptase polymerase chain reaction (RT-PCR), or CSF RT-PCR. This study conducted active case finding on 27 Oct 2023 by announcing anyone who had a fever or body temperature $\geq 37.5^{\circ}\text{C}$ would be interviewed using a semi-structured questionnaire. In addition, this study interviewed cases who received medical services at Nan Hospital and reviewed their medical records.

Collected variables were age, gender, underlying disease, inmate room, onset, signs and symptoms, laboratory results, and history of contacts in the past 10 days before symptom onset.

Close contact tracing was conducted to avoid future occurrences by interviewing confirmed cases, prison staff, and nurses at Nan Hospital. Close contact was defined as an inmate living in the same room as the confirmed case or a person who had a history of close contact (caring, talking, working, eating, kissing, hugging, or sharing eating utensils) with a confirmed case without proper protection between 10 days before symptom onset of the confirmed case and one day after the confirmed case received an appropriate antibiotic.

Laboratory Study

This study reviewed blood culture, CSF culture, serum RT-PCR, and CSF RT-PCR results of inmates diagnosed with meningococcal disease. This study collected blood specimens from a suspected case who still exhibited symptoms on the investigation day (27 Oct 2023) for blood culture at Nan Hospital. Furthermore, nasopharyngeal swabs (NPS) for *N. meningitidis* culture were collected on the investigation day, four days after ciprofloxacin prophylaxis. These swabs were randomly collected from 18 close-contact inmates who slept near the confirmed cases to identify asymptomatic carriers. NPS were also collected from all newly transferred inmates from other provinces since September 2023 to identify asymptomatic carriers who might be a source of infection. All cultured-growth specimens were sent to Bamrasnaradura Infectious Disease Institute for drug sensitivity tests and to the National Institute of Health for serogroup identification.

Environmental Study

An environmental study was conducted through surveys, observations, and interviews. This study walkthrough-surveyed and observed personal hygiene such as mask-wearing, social distancing, and hand-washing behavior. This study interviewed inmates and prison staff about inmates' daily activities, behaviors in buildings, and guidelines for respiratory disease screening and contact with inmates from outsiders, including inmates' relatives, doctors, dentists, and prison staff.

Statistical Analysis

This study performed descriptive analysis. Continuous data were presented using median with inter-quartile range (IQR). Categorical data were presented using frequency and proportion.

Ethics

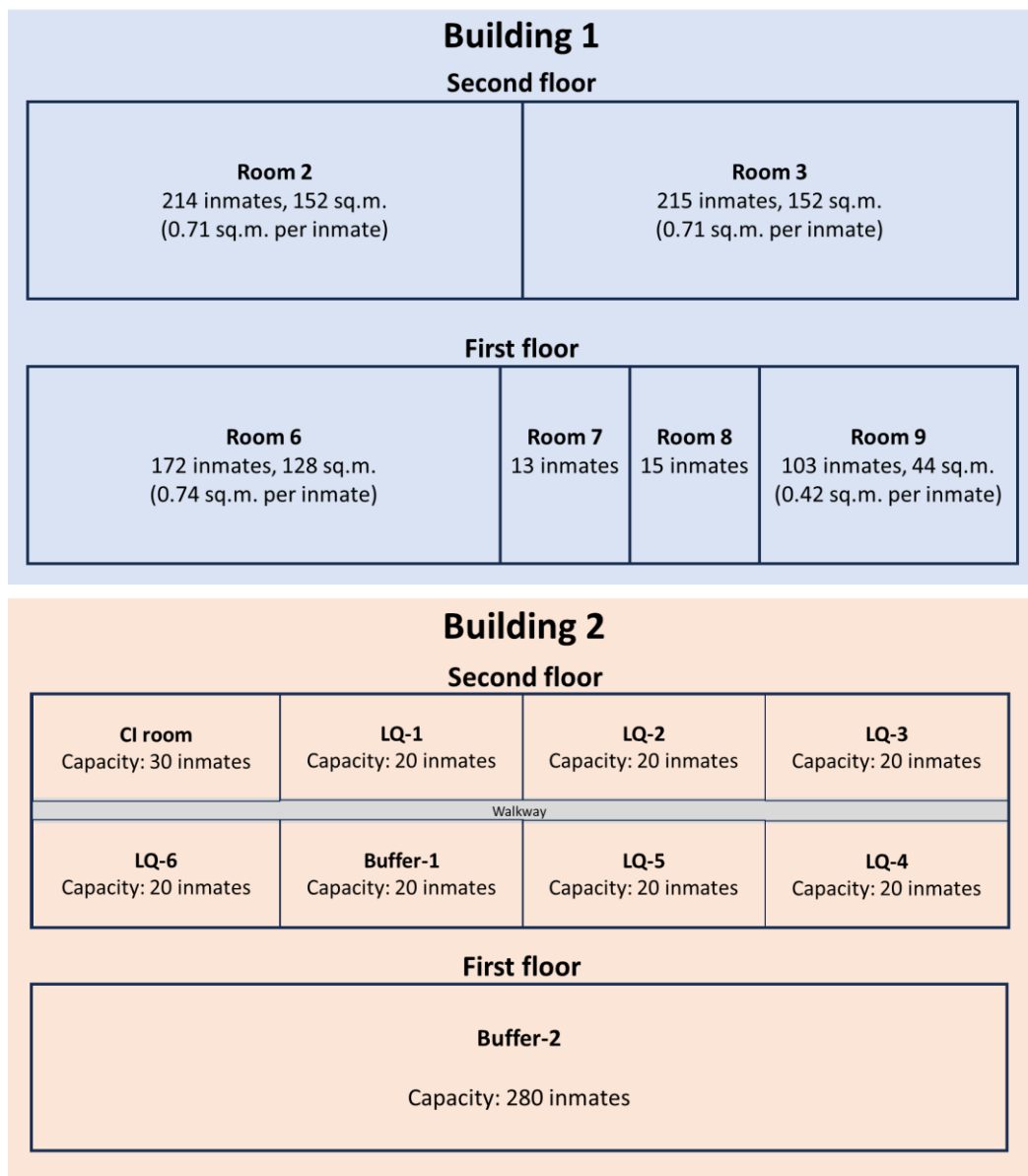
This investigation was conducted in response to a disease outbreak. The results do not include personal details. Confidentiality regarding case information was maintained throughout the study.

Results

The Prison and Its Responses to Previous Respiratory Disease Outbreaks

The provincial prison had 94 staff and 1,202 inmates. Among the inmates, 1,063 were male and 139 were female. Male and female inmate zones were completely separated. There were two buildings in the male zone, including Building 1 and Building 2.

Building 1 has six inmate rooms. The four main rooms were rooms 2, 3, 6, and 9. The inmate density was between 0.42 and 0.74 square meters per inmate. Building 2 served as a COVID-19 quarantine unit at least three months before the current outbreak to quarantine new inmates entering the prison who had COVID-19 or upper respiratory tract infection symptoms. The first floor was a common quarantine room called “Buffer-2” that could hold 280 inmates. The second floor was divided into six Local Quarantine rooms (LQ), one COVID-19 isolation room (CI), and one common quarantine room (Buffer-1) that could accommodate 20–30 inmates. All rooms were separated (Figure 1).



Due to the high turnover rate of inmates in Building 2, the inmate density could not be calculated.

Figure 1. Room plan and inmate capacity in Building 1 and Building 2 in a provincial prison, Nan Province, October 2023

During normal situations, all new inmates or returned from outside inmates had to complete a 15-day quarantine. This started with the first 5 days in LQ followed by Buffer-1 and Buffer-2 for 5 days each. Then inmates can enter Building 1 (Figure 2A).

The influenza outbreak in a provincial prison occurred on 27 Sep 2023, and there were 494

influenza-like illness cases which were male inmates. The highest number of cases was found on 1 October. Therefore, between 3 and 13 October, prison staff used the Buffer-2 room for the isolation of influenza-like illness cases and changed the quarantine flow to stay 10 days in LQ, then 5 days in Buffer-1 before moving to Building 1 (Figure 2B).

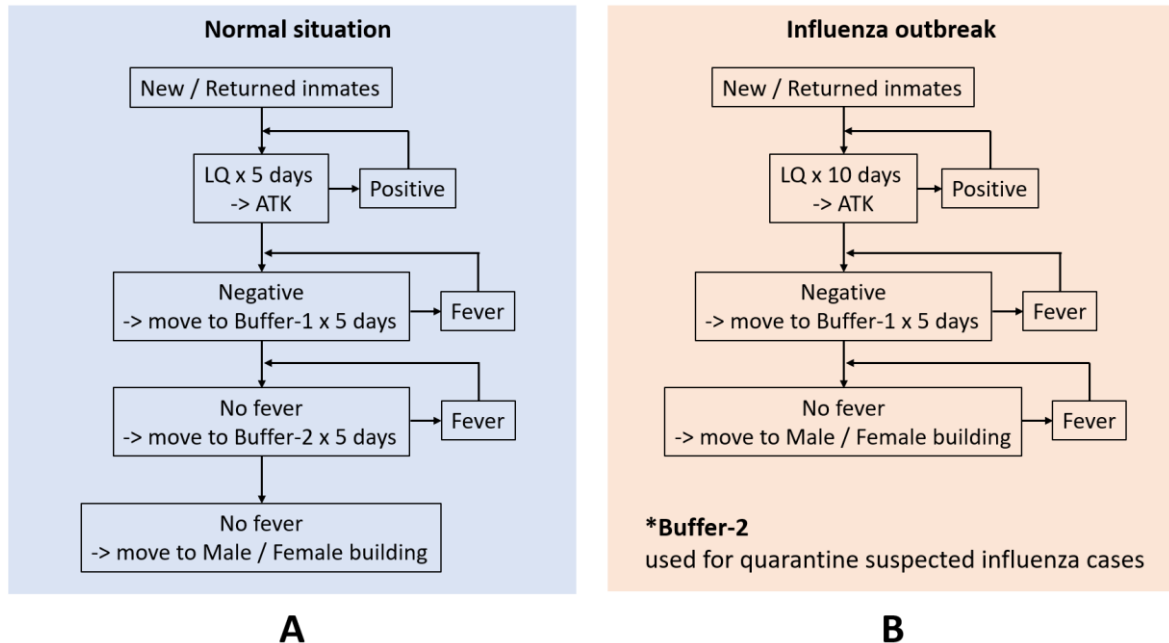


Figure 2. Diagram of quarantine guidelines during normal situation (Diagram 2A) and during influenza and meningococcal outbreak situation (Diagram 2B) in a provincial prison, Nan Province, October 2023

Descriptive Study

Between 2018 and September 2023, there were no reported cases of meningococcal disease in Nan Province in all databases. In addition, there was no detection of *N. meningitidis* in Nan Hospital's laboratory during this period.

Through active case finding, five confirmed and seven suspected cases were identified. Therefore, the total cases were 14, including the first two confirmed cases from notification. Considering only confirmed cases, the overall attack rate was 0.5% (7/1,296). All cases were Thai male inmates with a median age of 46 years (IQR 38.5–49.5 years). All confirmed cases stayed in Building 1 and lived in rooms 2, 3, and 6, which had room-specific attack rates of 0.9%, 0.5%, and 2.3%, respectively.

All confirmed cases and one suspected case were hospitalized and received treatment at the standard internal medicine ward of Nan Hospital. Two were diagnosed with meningitis, five with meningococemia, and one with unexplained sepsis. One fatality (case fatality rate 14%) and two severe cases requiring endotracheal intubation were found. Among the cases, only one severe case had an underlying disease which

was hypertension. The most common symptoms were fever (100%) and headache (71%), respectively (Figure 3).

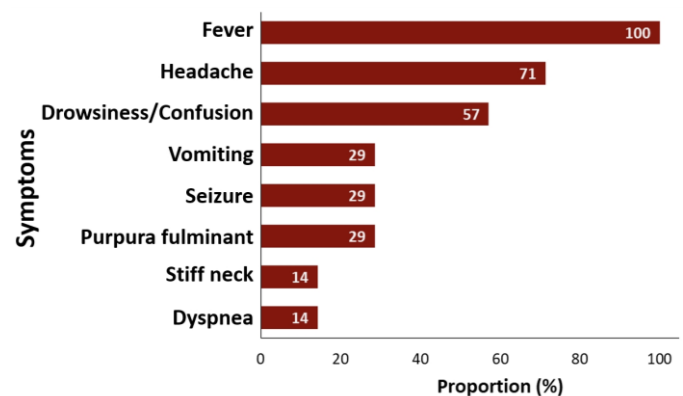


Figure 3. Symptoms of confirmed meningococcal disease cases in a provincial prison, Nan Province, 20 Sep–28 Nov 2023 (n=7)

The first confirmed case had the onset of symptoms on 12 Oct 2023. He had lived in this prison for one year in Room 2 and had not gone outside the prison in the past month. The next four cases developed symptom onset between 13 and 16 October. They all lived in Room 6 and had stayed in this prison for one to four months, two of them were suspected of influenza and were moved to the Buffer-2 room for quarantine on

3 October, and another two of them were new inmates who were isolated in Building 2 for two weeks (23 September–7 October) before they were moved to Building 1 Room 6. The fifth case had onset on 19 October, he was also a new inmate. In the first two weeks at Building 2 (20 September–4 October), he lived in the same room as one of the confirmed cases who moved to Building 1 Room 3. The last confirmed case reported onset on 28 October, he was a 53-year-old Thai male with an unknown underlying disease. He developed symptoms consisting of fever, seizure, and purpura fulminant. Although he was immediately transferred to Nan Hospital, he ended up dying in the

Emergency Department. The doctor gave his provisional diagnosis of severe sepsis; *N. meningitidis* was the most suspected pathogen which was confirmed with a blood culture result in the next three days.

The results of meningococcal infection were not available until 22 October. Despite administering ciprofloxacin prophylaxis to all inmates on 23 October, one confirmed case emerged after that. It was later discovered that *N. meningitidis* was ciprofloxacin-resistant. Subsequently, on 28 October, all inmates received rifampicin as a second-time prophylaxis (Figure 4).

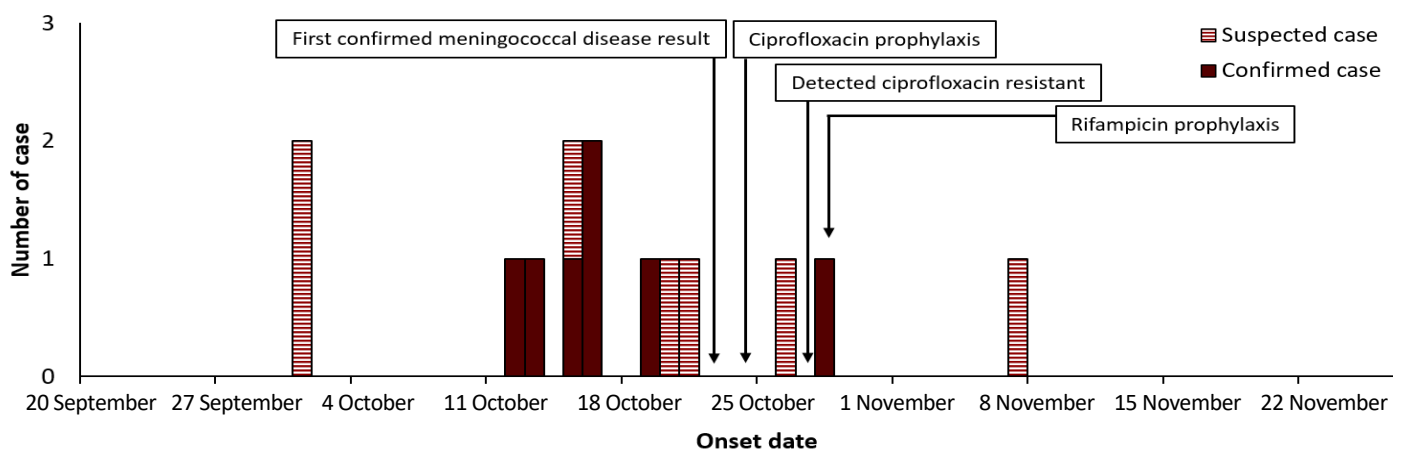


Figure 4. Number of meningococcal disease inmates in a provincial prison, Nan Province, 20 Sep–28 Nov 2023 (n=14)

There were two patterns of epidemiological linkage. The first was epidemiological linkage by close contact in the same room, while the second was close contact by sharing activities during the day. This study found three pairs of cases with the second pattern, either between suspected-confirmed cases or confirmed-confirmed cases (Figure 5).

Through contact tracing, at least 609 close contacts were identified, including 605 from close contact

inmates and four from inmate's relatives who visited Nan Hospital. Additionally, there were nurses and other healthcare workers in the Emergency Department and male internal medicine ward where confirmed cases were admitted, but the exact number was not known due to data unavailable. No prison staff were identified as close contact. None of the close contact developed symptoms after prophylaxis with rifampicin.

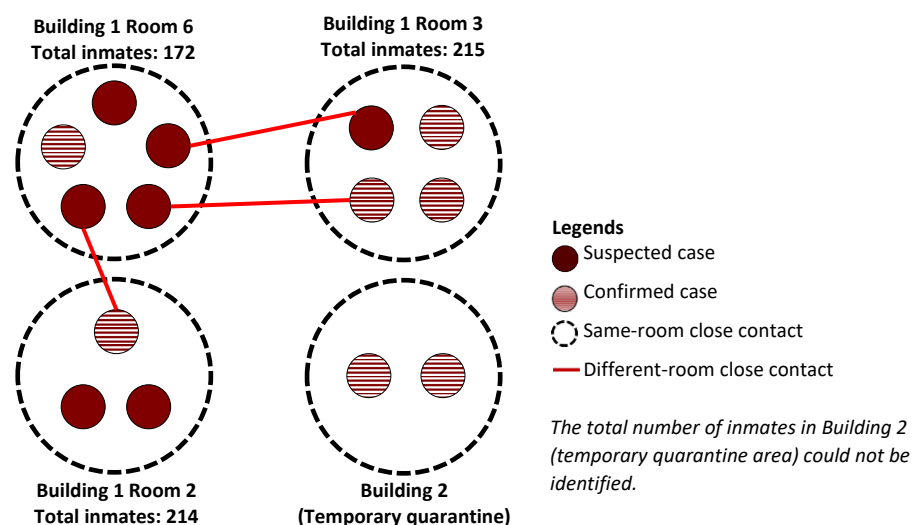


Figure 5. Epidemiological linkage among cases of meningococcal disease in a provincial prison, Nan Province, 20 Sep–28 Nov 2023 (n=14)

Laboratory Study

Neisseria meningitidis was detected from blood culture of five confirmed cases and CSF RT-PCR of the remaining two confirmed cases. No *N. meningitidis* was found from close contact inmates, and newly transferred inmates from other provinces (Table 1).

Table 1. *Neisseria meningitidis* testing result among samples from confirmed cases, suspected cases, close contacts, and newly transferred inmates in a provincial prison, Nan Province, 20 Sep–28 Nov 2023 (n=37)

Type of individual	Type of Specimen	Number of samples send for testing	Result	Number of samples with pathogen (% positive)
Cases of meningococcal disease*	Blood culture	9	<i>N. meningitidis</i>	5 (55.56)
	CSF culture	2	-	0
	CSF RT-PCR	2	<i>N. meningitidis</i>	2 (100.00)
Close contact†	NPS culture	18	-	0
Newly transferred inmate	NPS culture	6	-	0

*Samples were collected from thirteen cases of meningococcal disease. A sample from one suspected case was not collected because he did not have any symptoms on the investigation day (28 Oct 2023). †There were 18 of 42 close contacts who slept near confirmed cases were randomly tested. CSF: cerebrospinal fluid. NPS: nasopharyngeal swab. RT-PCR: reverse transcriptase polymerase chain reaction.

Environmental Study

Regarding the behavior of inmates, this study observed that there were less than 20 inmates among more than 200 inmates wearing facemasks during activities outside buildings. They often gathered in groups of 4–5 people. During meals, they used individual plates and spoons but shared water cups. Inside buildings, each room had only 1–2 water cups; therefore, inmates in the same room shared these water cups. In addition, inmates from different rooms could meet each other for about eight hours per day in some activities, such as breakfast time and factory work.

The guidelines for outsiders entering a provincial prison, in case of inmate's relatives visit, were as follows: relatives could visit through a tightly partitioned room and communicate with inmates by telephone. Bringing food for visits was not allowed. However, prison staff, vocational trainers, doctors, or dentists could enter the prison if they passed the fever screening and could contact directly with inmates. Through observation, no prison staff wore facemasks while working in this prison except staff who worked in an infirmary.

Action Taken

This study developed guidelines for surveillance of meningococcal infection for a provincial prison, starting with a daily check of whether inmates had symptoms that met meningococcal meningitis or meningococcemia criteria. Inmates who met the criteria were referred to Nan Hospital for diagnostic confirmation and close contacts were identified. Rifampicin re-prophylaxis would be given to these

Drug sensitivity test showed that all five blood culture-growth specimens were sensitive to ceftriaxone, ceftazidime, and azithromycin; but resistant to ciprofloxacin and trimethoprim/sulfamethoxazole. Serogroup test also showed all five specimens were *N. meningitidis* serogroup B.

contacts if the suspected inmates had a diagnosis confirmed.

The provincial prison staff had done active surveillance for 20 days after the last confirmed case was identified and temporarily rescheduled inmate activities to reduce inter-room contact. Nan Public Health officers informed all close contacts about the symptoms of meningococcal disease and advised a hospital visit if symptoms occurred. After the end of 20 days of surveillance on 28 Nov 2023, no additional case was notified from a provincial prison.

Discussion

This event was a meningococcal disease outbreak in a provincial prison and its extent was limited to the prison. The pathogen was ciprofloxacin-resistant *N. meningitidis* serogroup B which, based on a published literature review, has never been reported in Thailand. Although there was documentation of ciprofloxacin-resistant *N. meningitidis* in Southern Thailand, the serogroup from that report was W-135.¹⁵ There were reports of ciprofloxacin-resistant *N. meningitidis* serogroup B in many countries, potentially linked to the widespread use of fluoroquinolones.^{11–13} In Thailand, ciprofloxacin was widely used to treat urinary tract infections.¹⁶ The wide usage of ciprofloxacin can cause drug-resistant strains.¹⁷ Since ciprofloxacin is commonly used for *N. meningitidis* chemoprophylaxis in Thailand, the occurrence of ciprofloxacin-resistant strain found in this event might indicate reduction in the prophylaxis effectiveness of the drug. The US-CDC and Thai Clinical Practice Guideline recommended that

rifampicin, azithromycin, or ceftriaxone could be used for chemoprophylaxis of *N. meningitidis* in case of ciprofloxacin-resistant strain.^{10,18}

Previous studies showed that infection sources of droplets or close contact transmission disease outbreaks in prison probably came from outsiders or outside activities of inmates.^{19,20} The NPS results from transferred prisoners showed no growth which means they were less likely to be an infection source. The possible explanation was *N. meningitidis* might have been introduced to a provincial prison by other asymptomatic carriers such as returned inmates from outside, outside staff, or prison staff.

Blood culture results of suspected cases, including the latest case were no growth. This indicated low infection probability among them.²¹ Despite excluding suspected cases, there were still seven confirmed cases in this outbreak. It was considerably high compared to previous outbreaks in Thailand, which typically had 1–3 confirmed cases in closed environments such as prisons, military camps, and boarding schools.^{7,22}

Several factors might have contributed to this outbreak's widespread infection, consisting of intra-room factors, inter-room factors, and the previous influenza outbreak. In a provincial prison, rooms in Building 1 had a density range 2–3 times higher than the standard (1.6 square meters per inmate).²³ This overcrowding increases the transmission of contagious diseases.^{20, 24} Additionally, inmates shared water cups and rarely wore facemasks when doing their activities, further facilitating the spreading of disease. Inter-room factor was the inmates' daily schedules. Almost all activities during the day provided opportunities for inmates from different rooms to interact whether through talking, working, sharing meal, or other close-contact activities. Furthermore, the preceding influenza outbreak might also have promoted contact among inmates from different rooms when they were quarantined in the Buffer-2 room. There might have been carriers of *N. meningitidis* who were quarantined during the same period, potentially causing disease transmission. However, this study could not identify any carriers in this outbreak, so this remains a hypothesis to support the possibility of transmission among inmates from different rooms.

Limitations

This study had several limitations. First, information bias might have occurred due to confirmed cases forgetting the names of their close contacts, leading to difficulty in establishing a strong epidemiological linkage and close contact finding. Second, this study

could not apply the NPS test in all close contacts due to limited resources and the nature of the carrier stage which may be transient.²⁵ For these reasons, the detection of asymptomatic carriers was limited, so it might have been difficult to identify how *N. meningitidis* entered the prison. Third, limitations to accessing CSF study results in hospitals made us unable to develop probable case definitions. Last, we could only walkthrough survey Building 2 of the provincial prison due to the regulation of the prison, so Building 1 environment description was limited. This study used data provided by prison staff such as the number of inmates, room plan, and asking inmates about the environment inside the building instead.

Public Health Recommendations

The provincial prison should encourage prison staff and outside staff to wear facemasks upon entry into the prison. Nan Provincial Public Health Office should monitor the situation of meningococcal disease in the community setting closely and continuously by starting with risk communication about the occurrence of this outbreak, then emphasizing all hospitals to be aware of meningococcal disease in patients with sepsis or meningitis symptoms. Drug sensitivity results in confirmed cases should be checked before starting antibiotic chemoprophylaxis to close contacts. However, in settings where close contact isolation is difficult, consider reviewing the drug-resistant situation in the area before starting antibiotics prophylaxis.

Conclusion

This event was the first meningococcal infection outbreak in a provincial prison and Nan Province in the past five years. The pathogen was *Neisseria meningitidis* Serogroup B with ciprofloxacin resistance. There were multiple possible sources of infection, which included personal hygiene, inmates' behaviors, daily activities, and the previous influenza outbreak appeared to be the factors that promoted the disease's spreading. Chemoprophylaxis with rifampicin, active surveillance, and limited inmate activities could help reduce disease spreading in the prison.

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Conflicts of Interest

The authors of this study have no conflicts of interest.

Suggested Citation

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