EPIDEMIOLOGY OF RADIOGRAPHICALLY-CONFIRMED AND BACTEREMIC PNEUMONIA IN RURAL THAILAND

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Abstract. Pneumonia remains a leading public health concern in Thailand. Using population-based surveillance during January 2004-December 2006, we describe incidence, mortality, and bacterial etiologies of chest radiograph-confirmed pneumonia requiring hospitalization in one rural Thai province. Of 19,316 patients who met the case definition for clinical pneumonia, 9,596 (50%) had a chest radiograph, and 4,993 (52%) of those had radiographically-confirmed pneumonia. The incidence of radiographically-confirmed pneumonia ranged from 199 to 256 per 100,000 persons per year; 151 (3.0%) patients died. The annual average pneumonia mortality rate was 6.9 per 100,000 persons (range 6.2 to 7.8 per 100,000) and was highest in persons aged <1 year (64/100,000) and ≥65 years (44/100,000). Of 4,993 patients with radiographically-confirmed pneumonia, 1,916 (38%) had blood cultures, and 187 (10%) of those had pathogens isolated. Pathogens causing bacteremic pneumonia included *B. pseudomallei* (15% to 24% of bacterial pathogens), *E. coli* (9.2% to 25%), *S. pneumoniae* (7.9% to 17%), *K. pneumoniae* (2.2% to 6.4%), and *S. aureus* (4.3 to 5.3%). Bacteremia was significantly associated with pneumonia mortality after controlling for age, sex, HIV status and measures of disease severity in a logistic regression model (OR=5.2; 95% confidence interval= 2.2 - 12). Pneumonia remains an important cause of morbidity and mortality in Thailand, as in other countries in Southeast Asia. These findings can inform pneumonia clinical management and treatment decisions and guide public health programming, including the development of effective prevention strategies.

INTRODUCTION

Pneumonia remains a leading global infectious disease killer, particularly among young children (Bryce *et al*, 2005; Greenwood *et al*, 2007). Although pneumonia is a reportable disease in many countries, passive reporting systems underestimate true disease incidence and mortality and are often not linked to etiology data, limiting the utility to guide public health programs (Kanlayanaphotporn *et al*, 2004; Olsen *et al*, 2006). In Thailand, where pneumonia is a significant and costly public health problem, more thorough documentation of pneumonia burden and its etiologies is of great interest (Kanlayanaphotporn *et al*, 2004; Olsen *et al*, 2006).

Bacteria cause a substantial proportion of pneumonia cases, especially severe cases, but laboratory confirmation is challenging and

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usually limited to blood culture. Microbiology systems with standardized and reliable quality assurance protocols are needed to maximize the sensitivity of blood culture to detect bacteremic pneumonia. However, modern culture systems are often not in place in hospital laboratories of less wealthy countries, leading to underestimates of the frequency of bacteremic pneumonia. Data on bacterial etiologies of pneumonia are crucial to guide clinical management and inform prevention policies (*eg*, vaccines).

The relative frequency of the pathogens causing bacteremic pneumonia in Thailand is not well understood (Reechaipichitkul *et al*, 2005). To improve understanding of the burden and causes of pneumonia in Thailand, the International Emerging Infections Program (IEIP), a collaboration between the Thailand Ministry of Public Health (MOPH) and the US Centers for Disease Control and Prevention, established active, population-based surveillance for pneumonia requiring hospitalization in Nakhon Phanom Province in 2003. In November 2005, automated blood culture systems were implemented to enhance detection of bacterial pathogens causing pneumonia. We analyzed 3 years of data (January 2004 through December 2006) to describe pneumonia incidence, mortality, and bacterial etiologies among patients with radiographically-confirmed pneumonia requiring hospitalization.

MATERIALS AND METHODS

Population

Nakhon Phanom is located 735 km from Bangkok in the plateau region of northeastern Thailand, bordering Lao PDR. It covers 5,513 km^2, is divided into 12 districts and 99 subdistricts, and had a 2006 population of 734,000 (50,109 <5 years) (National Economic and Social Development Board of Thailand, 2008). Most persons have only a primary school education. The economy is primarily agrarian, and the yearly per capita income was 37,280 Baht (US$ 1,013) in 2005.

Pneumonia surveillance

In Nakhon Phanom, all hospital care for acute illness is provided by one provincial general hospital (337 beds), 10 community hospitals (10-90 beds), and one military hospital (10 beds). Surveillance officers screened hospital admission log books from all hospitals daily to identify patients admitted with a diagnosis possibly consistent with pneumonia based on 59 International Classification of Disease codes (A15 - 16, A19, A24, A37, B20, B22 - 24, B59, J10 - 22, J40, J45 - 46, J69, J80 - 81, J84, J90 - 93, J96, J98, P22 - 26, R05 - 06, R09, R50). For each patient identified, they reviewed the medical chart and recorded demographic, clinical, laboratory, and radiographic findings on a standardized surveillance form. HIV status was recorded when noted in the chart. Physicians completed a data section on clinical signs and symptoms. For patients meeting the clinical pneumonia case definition (see below), information was recorded on complications, length of stay, and outcome. Surveillance forms were entered into a computerized database at each hospital and sent via a secure website to a server at the MOPH in Nonthaburi. To ensure complete reporting of pneumonia cases, data audits were conducted monthly by surveillance officers and annually by the Bureau of Epidemiology, MOPH.

Pneumonia case definition

A case of clinical pneumonia was defined as 1) evidence of acute infection [≥1 of the following: reported fever or chills, documented temperature >38.2ºC or <35.5ºC or abnormal white blood cell count (WBC>15,000/µl in patients aged <5 years, >11,000/µl in patients aged ≥5 years, or <3,000/µl for any aged patient) or abnormal differential]; and 2) signs or symptoms of respiratory tract disease (≥1 of the following: abnormal breath

sounds, tachypnea, cough, sputum production, hemoptysis, chest pain, or dyspnea) in a resident who has lived in Nakhon Phanom Province for at least 6 months. Pneumonia was considered radiographically-confirmed when a chest radiograph taken within 48 hours of admission was interpreted as having evidence of pneumonia by the treating clinician. We excluded patients who had been hospitalized during the 3 days prior to their suspected pneumonia diagnosis to prevent inclusion of potential hospital-acquired pneumonia cases.

Specimen collection and laboratory testing

Prior to November 2005, blood cultures were collected at the discretion of the treating physician and processed manually using standard methods. In November 2005, automated blood culture systems were installed at the provincial hospital, and a specimen transport system was implemented to ensure that cultures from community hospitals were processed and incubated in a timely manner. At that time, standing orders were established to collect blood cultures from patients meeting the clinical pneumonia case definition. Patients >5 years of age provided ~20 ml of aseptically collected blood that was equally divided and inoculated into a FA bottle for aerobic growth and a MB bottle for enhanced growth of mycobacteria, fungal pathogens, and other fastidious agents. Patients <5 years of age submitted ≤10 ml of aseptically collected blood that was equally inoculated into a PF bottle for aerobic growth and a MB bottle. All specimens were processed using the BacT/ALERT 3D automated blood culture system (bioMeriéux, Hazelwood, Missouri). Specimens collected at community hospitals were maintained at 15-30ºC and transported to the provincial hospitals for processing within 24 hours of collection. Cultures that turned positive were processed using standard methods. Starting in November 2005, confirmatory identification of bacterial isolates was performed at Thailand's National Institute of Health, the MOPH national reference laboratory. Some pneumonia patients were also tested for tuberculosis at the clinician's discretion by microscopic examination of sputum smears for acid-fast bacilli (AFB).

Statistical analysis

Analyses were performed using SPSS for Windows Version 11 (Chicago, Illinois). Demographic, epidemiologic and clinical data, as well as pathogen type and frequencies, were summarized using counts and percentages. Pneumonia incidence was calculated based on a 3-month moving average using 2004- 2006 data from the estimation of population in Thailand for population denominators (National Economic and Social Development Board of Thailand, 2008). We evaluated demographic, epidemiologic, and clinical factors potentially associated with pneumonia mortality. This analysis was limited to 2006, because microbiology data from 2004-2005 were collected from hospital systems and not integrated into our pneumonia surveillance database. In univariate analysis, differences in proportions were compared using the chi-square or Fisher's exact test and p<0.05 was considered statistically significant. We tested the hypothesis that bacteremia was a risk factor for pneumonia mortality independent of disease severity. We used multivariate logistic regression to control for potential confounders and markers of disease severity including age, sex, HIV status, leukopenia, intubation, need for supplemental oxygen, need for invasive procedure (*eg*, thoracentesis), and intensive care. Covariates remained in the model if their presence changed the odds ratio (OR) describing the bacteremia - mortality relationship by >10%. Because HIV status was missing for so many patients (43% in 2006), we ran the model with and without HIV status as a covariate.

RESULTS

From January 2004 through December

Table 1

Characteristics features of patients with radiographically-confirmed pneumonia, Nakhon Phanom, Thailand, 2004-2006.

	2004 N=1,448 n (%)	2005 N=1,936 n (%)	2006 N=1,609 n (%)
Demographics			
Age (year)			
<5	632 (44)	1,066 (55)	844 (53)
5-19	116 (8.0)	126 (6.5)	94 (5.8)
20-39	129 (8.9)	129 (6.7)	73 (4.5)
40-65	273 (19)	262 (14)	287 (18)
>65	298 (21)	353 (18)	311 (19)
Male	728 (50)	1,055 (55)	901 (56)
Evidence of acute infection			
Reported or documented fever	1,358 (94)	1,822 (94)	1,470 (91)
Reported or documented hypothermia	63 (4.4)	59 (3.0)	28 (1.7)
Leukocytosis[a]	474 (33)	562 (19)	529 (33)
Leukopenia[b]	34 (2.3)	69 (3.6)	55 (3.4)
Respiratory signs and symptoms			
Cough	1,348 (93)	1,843 (95)	1,468 (91)
Sputum production	876 (61)	1,212 (63)	829 (52)
Hemoptysis	39 (2.7)	40 (2.1)	43 (2.7)
Chest pain	204 (14)	168 (8.7)	117 (7.3)
Dyspnea	1,084 (75)	1,457 (75)	1,204 (75)
Tachypnea[c]	1,062 (73)	1,461 (76)	969 (60)
Abnormal breath sounds	1,286 (89)	1,656 (86)	1,346 (85)
Outcome			
Death	45 (3.1)	49 (2.5)	57 (3.5)

[a]Age ≥5 years: WBC>11x 10^3/µl, age <5 years: WBC>15x 10^3/µl
[b]WBC<3 x 10^3/µl; [c]Based on clinician assessment

2006, 19,316 hospitalized patients met the criteria for clinical pneumonia, and 9,596 (50%) had chest radiographs; 4,993 (52%) of those with chest radiographs had radiographically-confirmed pneumonia. Interstitial infiltrates were reported in 3,296 (66%), consolidation in 712 (14%), pleural effusion in 213 (4.3%), cavitations in 144 (2.9%), and atelectasis in 81 (1.6%). The median age of patients with radiographically-confirmed pneumonia was 4 years and 54% were male. The age and sex distribution varied little by year (Table 1). Over 90% of radiographically -confirmed

pneumonia patients had reported or documented fever, and cough was present in 93%. Abnormal breath sounds were documented in over 80%, with rales or crepitation being most common. Approximately 3.0 % (151/4,993) of patients with radiographically-confirmed pneumonia died, and case fatality did not differ substantially from year to year.

HIV status was available for 1,718 (34%) patients, and 9.4% (162/1,718; 3.2% of all patients) were HIV-positive. HIV prevalence differed by age group: age 5 - 15 years (24/307, 7.8%), 16 - 25 years (9/73, 12%), 26 - 35 years

Table 2
Pathogens causing bacteremia among patients with radiographically-confirmed pneumonia,
Nakhon Phanom, Thailand, 2004-2006.

	Number (%) of pathogens		
	2004	2005	2006
Burkholderia pseudomallei	11 (24)	10 (15)	15 (20)
Streptococcus pneumoniae	8 (17)	8 (12)	6 (7.9)
Escherichia coli	9 (20)	16 (25)	7 (9.2)
Acinetobacter species	4 (8.7)	5 (7.7)	1 (1.3)
Acinetobacter baumanii	1 (2.2)	0	2 (2.6)
Klebsiella pneumoniae	1 (2.2)	2 (3.1)	5 (6.6)
Staphylococcus aureus	2 (4.3)	3 (4.6)	4 (5.3)
Streptococcus pyogenes	1 (2.2)	2 (3.1)	0
Bacillus cereus	0	2 (3.1)	2 (2.6)
Nontyphoidal *Salmonella*	0	4 (6.2)	3 (3.9)
Haemophilus influenzae	0	1 (1.5)	1 (1.3)
Cryptococcus neoformans[b]	0	1 (1.5)	3 (3.9)
Pseudomonas species	0	4 (6.2)	2 (2.6)
Mycobacterium tuberculosis	0	0	4 (5.3)
Enterococcus species	3 (6.5)	1 (1.5)	3 (3.9)
Moraxella catarrhalis	0	0	1 (1.3)
Pseudomonas aeruginosa	0	1 (1.5)	1 (1.3)
Enterobacter cloacae	0	0	2 (2.6)
Streptococcus mitis group	0	0	3 (3.9)
Streptococcus salivarius group	0	0	1 (1.3)
Penicillium species[b]	0	0	2 (2.6)
Histoplasma capsulatum[b]	0	0	2 (2.6)
Gram-negative bacilli (not identified)	0	0	3 (3.9)
Other	6 (13)	5 (7.7)	5 (6.6)
Total pathogens	46	65	76[c]
Contaminants[a]	36	67	93
Total positive cultures	82	132	169

[a]Likely contaminants included coagulase negative *Staphylococcus*, *Corynebacterium* species, *Bacillus* species, *Micrococcus* species
[b]Although fungal pathogens, these organisms were included here as potentially important causes of pneumonia, especially in immunocompromised patients, that can be detected by blood culture. [c]76 pathogens in 73 patients. Three patients had two pathogens each: 1) *Burkholderia pseudomallei* and *Enterobacter cloacae*, 2) *E.coli* and *Aeromonas veronii* bv. sobria 3) *Pseudomonas fluorescens* and *Providencia* species

(65/197, 33%), and 36 - 45 years (41/215, 19%), while all other age groups had a prevalence of ≤2%. Nineteen percent (953/4,993) of patients with radiographically-confirmed pneumonia had sputum smears for AFB testing, and 83 (8.7%) were positive. Tuberculosis was diagnosed most commonly in pneumonia patients aged 16 - 25 years (5/73, 6.8%), 26 - 35 years (11/197, 5.6%), 46 - 55 years (16/307, 5.2%) and 56 - 65 (20/390, 5.1%).

Table 3

Age-group distribution of pathogens causing bacteremia among patients with radiographically-confirmed pneumonia, Nakhon Phanom, Thailand, 2004-2006.

	Number (%) of pathogens		
	<5 years	5-15 years	≥16 years[c]
Burkholderia pseudomallei	7 (11)	2 (18)	27 (25)
Streptococcus pneumoniae	7 (11)	0	15 (14)
Escherichia coli	9 (14)	3 (27)	20 (18)
Acinetobacter species	6 (9.1)	1 (9.1)	3 (2.7)
Acinetobacter baumanii	1 (1.5)	0	2 (1.8)
Klebsiella pneumoniae	2 (3.0)	1 (9.1)	5 (4.5)
Staphylococcus aureus	4 (6.1)	1 (9.1)	4 (3.6)
Streptococcus pyogenes	0	0	3 (2.7)
Bacillus cereus	3 (4.5)	0	1 (0.9)
Nontyphoidal *Salmonella*	2 (3.0)	0	5 (4.5)
Haemophilus influenzae	2 (3.0)	0	0
Cryptococcus neoformans[b]	0	0	4 (3.6)
Pseudomonas species	3 (4.5)	1 (9.1)	2 (1.8)
Mycobacterium tuberculosis	0	0	4 (3.6)
Enterococcus species	3 (4.5)	0	4 (3.6)
Moraxella catarrhalis	1 (1.5)	0	0
Pseudomonas aeruginosa	1 (1.5)	0	1 (0.9)
Enterobacter cloacae	0	0	1 (0.9)
Streptococcus mitis group	3 (4.5)	0	0
Streptococcus salivarius group	1 (1.5)	0	0
Penicillium species[b]	0	0	2 (1.8)
Histoplasma capsulatum[b]	0	0	1 (0.9)
Gram-negative bacilli (not identified)	3 (4.5)	0	0
Other	8 (12)	2 (18)	6 (5.5)
Total pathogens	66	11	110
Contaminants[a]	120	6	70
No growth	728	91	714
Total blood cultures	914	108	894

[a]Likely contaminants included coagulase negative *Staphylococcus*, *Corynebacterium* species, *Bacillus* species, *Micrococcus* species

[b]Although fungal pathogens, these organisms were included here as potentially important causes of pneumonia, especially in immunocompromised patients, that can be detected by blood culture

[c]Three patients had two pathogens each: 1) *Burkholderia pseudomallei* and *Enterobacter cloacae*, 2) *E.coli* and *Aeromonas veronii* bv. sobria, 3) *Pseudomonas fluorescens* and *Providencia* species

Incidence of radiographically-confirmed pneumonia

Annual incidence of radiographically-confirmed pneumonia ranged from 199 - 256 per 100,000 persons. Incidence varied by age and was highest each year among children aged <1 year (4,312-8,185 per 100,000 persons) and patients aged >65 years (717-877) (Fig 1). Pneumonia incidence also varied by year. Among children aged <1 year, pneumonia

Table 4
Factors associated with mortality among patients with radiographically-confirmed
pneumonia, Nakhon Phanom, Thailand, 2006[a].

	Radiographically-confirmed pneumonia, N	Died, n (%)	Relative risk	95% CI
Age, years				
<5	844	7 (0.8)	referent	
5-19	94	3 (3.2)	3.9	1.0-16
20-39	73	6 (8.2)	11	3.5-33
40-65	287	18 (6.3)	8.0	3.3-19
>65	311	23 (7.4)	9.6	4.1-23
Sex				
Male	708	19 (2.7)	0.6	0.4-1.1
Female	901	38 (4.2)		
Intubation				
Yes	112	42 (38)	59	31-112
No	1,497	15 (1)		
Oxygen therapy				
Yes	662	53 (8)	21	7.4-57
No	947	4 (0.4)		
Bacteremia[b]				
Yes	73	14 (19)	9.1	4.6-18
No	1,266	32 (2.5)		
HIV				
Positive	37	5 (14)	9.3	3.1-28
Negative	730	12 (1.6)		
Leukopenia				
Yes	18	6 (33)	15	5.5-42
No	1,591	51 (3.2)		
Invasive procedure required				
Yes	18	4 (22)	8.3	2.6-26
No	1,591	53 (3.3)		
Intensive care unit stay				
Yes	77	25 (33)	23	13-41
No	1,532	32 (2.1)		

[a]$p < 0.05$
[b]Excluding contaminants as defined in footnote of Table 2.
Note: Additional factors that were assessed and not significantly associated with mortality included smoking addiction (The Alcohol Use Disorders Identification Test, 2001), alcohol consumption Frangerstrom Tolerance Qusstionarie (Fagerström, 2003)], hypothermia, leukocytosis, pleural effusion, consolidation, atelactasis.
CI=confidence interval

incidence in 2005 (8,185 per 100,000) was substantially higher than in 2006 (6,380 per 100,000) and 2004 (4,312 per 100,000).

Seasonal variation was evidenced by consistent peaks in radiographically-confirmed pneumonia cases between July and October each year, as well as by smaller increases between February and March (Fig 2).

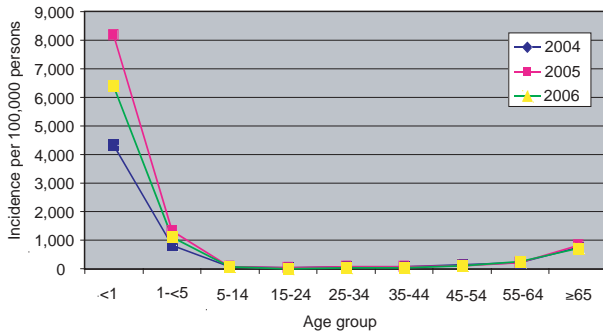During the 3 years studied, the average annual pneumonia mortality rate was 6.9 per

Fig 1–Incidence of radiographically-confirmed pneumonia by age and year, Nakhon Phanom, Thailand, 2004-2006.
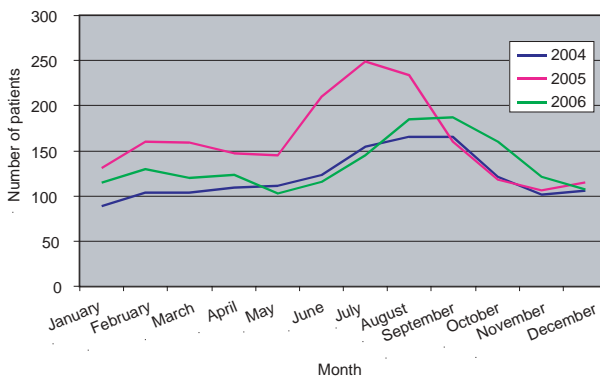

Fig 2–Number of radiographically-confirmed pneumonia patients by month.
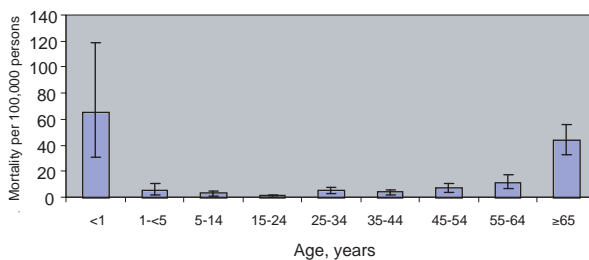

Fig 3–Average annual mortality (per 100,000 persons) of radiographically-confirmed pneumonia, Nakhon Phanom, Thailand, 2004-2006. Bars = 95% confidence intervals.

100,000 persons (range 6.2 to 7.8 per 100,000). Mortality rates were highest in children aged <1 year (64 per 100,000) and ≥65 years (44 per 100,000) (Fig 3).

Bacteremic pneumonia

Blood cultures were obtained from an increasing proportion of patients with radiographically-confirmed pneumonia: 14% (199/1,448) in 2004, 20% (378/1,936) in 2005, and 83% (1,339/1,609) in 2006. Therefore, 1,916 of 4,993 (~38%) patients with radiographically-confirmed pneumonia had blood cultures performed over 3 years. After excluding patients with likely contaminants (eg, coagulase-negative *Staphylococcus*, *Corynebacterium* species, *Bacillus* species, and *Micrococcus* species), pathogens were isolated from 184 patients, including 46 (23%) patients in 2004, 65 (17%) in 2005, and 73 (5.5%) in 2006 (three patients in 2006 had two pathogens each for a total of 76 pathogens isolated). The most common pathogens isolated were *Burkholderia pseudomallei* (15% to 24% of all bacterial pathogens), *Escherichia coli* (9.2% to 25%), *Streptococcus pneumoniae* (7.9% to 17%), *Klebsiella pneumoniae* (2.2% to 6.6%), and *Staphylococcus aureus* (4.3% to 5.3%). (Table 2). The distribution of pathogens causing bacteremia differed slightly by age group (Table 3).

Bacteremia and mortality

In univariate analysis, several factors were associated with pneumonia death, including older age, HIV positivity, selected measures of disease severity, and bacteremia (Table 4). In multivariate logistic regression, after controlling for age, sex, and measures of disease severity, bacteremia remained associated with pneumonia death [OR=5.2; 95% confidence interval (CI)= 2.2 - 12]. The relationship did not change when HIV status was included in the model, but the confidence interval widened (OR=12, 95% CI=3.0 - 48).

DISCUSSION

Using active, population-based surveillance we documented the incidence and mortality rate of radiographically-confirmed pneumonia requiring hospitalization in a rural

Thailand province. Similar to other settings (Jokinen *et al*, 1993; GutiéORez *et al*, 2006), we found that pneumonia incidence was highest in young children and the elderly, with the highest incidence found in children aged <1 year (4,312 to 8,185 per 100,000 persons). Pneumonia mortality was also highest among children aged <1 year (annual average 64 per 100,000 persons), highlighting further the burden of pneumonia. The age-specific pneumonia incidence rates described herein are consistent with those found in another rural province in eastern Thailand (Sa Kaeo), which used the same active surveillance protocol (Olsen *et al*, 2006). In contrast, the incidence of pneumonia we found in rural Thailand is higher than what has been reported in some western countries, such as Canada, England and Finland (Jokinen *et al*, 1993; Marrie *et al*, 2000; GutiéORez *et al*, 2006), although comparisons are limited by differences in case definitions.

Seasonal trends for pneumonia occur in other parts of the world, including North America (Macey *et al*, 2002; Maorie and Wu, 2005) and Europe (Almirall *et al*, 1993; Roger and Woodhead, 1998). Our data demonstrate that pneumonia is also a seasonal disease in Thailand, with large peaks occurring consistently between July and October (rainy season), and smaller peaks occurring between January and March. These seasonal trends are consistent with findings from Sa Kaeo Province, and from Khon Kaen Province in northeastern Thailand (Wongpratoom *et al*, 1990). These peaks likely reflect disease incidence fluctuations associated with specific respiratory pathogens. For example, influenza contributes substantially to the increase in pneumonia cases in July through October (Simmermana *et al*, 2004). Further, unpublished data from our surveillance platform suggest that respiratory syncytial virus (RSV) cases peak during this same period. Knowledge of seasonal peaks and specific etiologies can be important for timing appropriate

prevention messages, vaccine delivery (*eg*, influenza vaccine) and guiding clinical management in Thailand. Reinforcing public health education messages, such as respiratory etiquette and hand hygiene, during Thailand's rainy season may also help reduce transmission (Jefferson *et al*, 2007). In addition, anticipation of clinical presentations and medical resource needs may improve triage and patient care and outcome.

Documenting bacterial pneumonia is difficult, because available diagnostic tests can lack sensitivity (*eg*, blood culture) or specificity (*eg*, sputum culture) or are challenging to perform (*eg*, lung aspirate). Therefore, although a relatively small proportion of patients with bacterial pneumonia have bacteremia, documenting bacteremia is important in order to understand the relative frequency of bacterial causes of pneumonia and to inform pneumonia clinical management guidelines and prevention strategies. High quality microbiology systems are critical to achieve this end, but are often not available in less wealthy countries. We implemented automated blood culture systems in Nakhon Phanom in November 2005 to improve detection of pathogens causing bacteremic pneumonia. Enhancing microbiology capacity in a province with ongoing pneumonia surveillance allowed us to collect blood cultures from most pneumonia patients (>80% in 2006) and thereby characterize the bacterial causes of pneumonia in a way that is unlikely to be biased by culturing practices. However, it is difficult to compare the 3 years of bacteremia data, because blood culture results from 2004 and 2005 were not confirmed by the national reference laboratory, as was done in 2006.

The distribution of agents causing bacteremic pneumonia was different from that found in other parts of the world (Bovic *et al*, 2003; Reechaipichitkul, 2005). We demonstrated that *B. pseudomallei* was the most common pathogen causing bacteremic pneu-

monia (15 - 24%) in Nakhon Phanom. Although melioidosis is known to be endemic in northeastern Thailand (Apisarnthanarak and Mundy, 2005), province-level data are lacking from many areas. Reporting such local prevalence estimates should help to ensure early and appropriate treatment of this often fatal disease. *E. coli* was also a common cause of bacteremic pneumonia; 32 pneumonia patients had *E. coli* isolated from blood culture over 3 years. Previous work from our surveillance sites showed that patients with *E. coli* pneumonia were older (median age 67 years) and more likely to be female than other bacteremic pneumonia patients (Henchaichon *et al*, 2008), which raises questions about risks for infection that were not detected by our surveillance, such as recent healthcare exposure or urinary tract infection. Data were not available to definitively determine whether these patients had underlying conditions or healthcare exposures more than 72 hours before admission that may have predisposed them to this pathogen more often associated with nosocomial infections or urinary tract disease. In North America, Europe and Japan, *S. pneumoniae* has typically been the most commonly identified bacterial pathogen isolated from blood cultures among pneumonia patients, and *E. coli* is rare (Ruize *et al*, 1999; Luna *et al*, 2000; Apisarnthanarak and Mundy, 2005). Although *E. coli* has been described as an uncommon cause of community-acquired pneumonia (Ruize *et al*, 1999), our findings may suggest a larger role for this pathogen, and deserve further study (Ruize *et al*, 1999; Luna *et al*, 2000; Apisarnthanarak and Mundy, 2005). Additional data are needed to better understand the role of *E. coli* in pneumonia patients in rural Thailand.

The case fatality rate for pneumonia requiring hospitalization was 3% (151/4,993), which is lower than what was documented in Sa Kaeo Province in 2002 - 03 (9.3%, 72/777) (Olsen *et al*, 2006). Reasons for this lower case fatality rates are unclear but might include improved access to medical care and earlier treatment in Nakhon Phanom, lower HIV prevalence among pneumonia patients, or improved pneumonia management over time. Alternatively, severely ill patients may not make it to the hospital and thus die at home, but this assumption is not supported by a recent health utilization survey in Nakhon Phanom (Jordan HA, 2006, publication in process). In both provinces, pneumonia case fatality rates were high among young adults, which may be related to higher frequency of HIV in these age. In Nakhon Phanom, among pneumonia patients aged 26 - 35 years and 36 - 45 years with HIV status available, HIV prevalence was high [65/197 (33%) and 41/215 (19%), respectively]. Tuberculosis infection was also common in these age groups, which likely contributed further to the high pneumonia mortality in these groups. Thailand ranks 18th among countries with a high TB burden as designated by the World Health Organization, and it is known that HIV and TB play an important role in pneumonia progression and death (Health and Development networks, 2007). These findings are consistent with other studies in Thailand demonstrating the importance of TB, especially among HIV-infected persons (Yanai *et al*, 1996; Ngamvithayapong *et al*, 2001; Putong *et al*, 2002; Olsen *et al*, 2006).

In 2006, pneumonia patients with HIV infection were more likely to die than those without HIV (RR=9.3; 95% CI= 3.1 - 28); there were 37 patients known to be HIV infected and 5 (14%) died. Although HIV infection increased the risk of pneumonia mortality, the mortality was lower than what has been reported in previous studies, which may reflect increased use of anti-retrovirals as part of a national anti-retroviral drug program for HIV in infected persons (Arozullah *et al*, 2003; Olsen *et al*, 2006; Kaewkasikij, 2008). In Nakhon Phanom, 95% of patients with HIV infection who registered and qualified for the

anti-retrovirals program received medications (Nakhon Phanom Province, 2007). Bacteremia was also associated with pneumonia mortality independent of HIV status and measures of disease severity. This highlights both the importance of reliable blood culture systems to ensure early and accurate diagnosis of bacteremic cases, and epidemiologic data to guide empiric treatment when the diagnosis is not immediately known.

This analysis has several limitations. Although citizens of Thailand have excellent access to health care and the active pneumonia surveillance system includes all hospitals in the province, the system captures only pneumonia cases resulting in hospitalization. Although the majority of persons with pneumonia seek healthcare in Thailand, a recently conducted health utilization survey suggested that only 58% of pneumonia patients in this province seek care at a hospital (Jordan HA, 2006, publication in process). Therefore, our findings underestimate the true incidence of pneumonia. By limiting our analysis to patients with radiographically-confirmed pneumonia, we may have further underestimated incidence because only 50% of patients with clinical pneumonia had chest radiographs. Further, we relied on the radiograph interpretations of local clinicians, who are less likely to interpret chest radiographs as having evidence of pneumonia than trained radiologists (Javadi *et al*, 2006; Novack *et al*, 2006). Finally, we focused our analyses on pathogens causing bacteremic pneumonia because these pathogens often cause severe disease, are usually responsive to therapy if initiated early, and some are vaccine preventable. These findings, however, do not provide a comprehensive picture of pneumonia etiology, as we did not include other frequent causes of pneumonia, including viral pathogens (*eg*, influenza and RSV) and atypical bacteria, such as *C. pneumoniae, M. pneumoniae* or *Legionella.* Testing for viral pathogens and atypical bacteria is ongoing in Nakhon Phanom, but results are not yet available.

Pneumonia is a leading cause of death worldwide, but information on burden and etiology are lacking in many settings. Standardized collection of surveillance data, and linkage of epidemiologic and laboratory testing results, are crucial to guide public health program and policy decisions. The data documenting pneumonia incidence and etiology presented herein can be used to guide clinical management, refine treatment guidelines, and inform prevention strategies.

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