Epidemiology, etiology, and diagnosis of hospital-acquired pneumonia and ventilator-associated pneumonia in Asian countries

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Hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP) are significant public health issues in Asian countries, as they are worldwide. Mortality attributable to HAP and especially VAP can be very high. The present review aims to determine whether the incidence and prevalence of HAP and VAP are higher in Asian countries than in Western countries, whether the organisms causing these nosocomial infections differ etiologically, and whether they are more difficult to treat (ie, demonstrate greater resistance). The implementation of available guidelines can be best achieved through an understanding of local epidemiology, etiology, and resistance patterns, which can facilitate optimal treatment choices. The current review presents data on epidemiology, etiology, and diagnosis of HAP and VAP drawn from an expert panel of clinicians representing 10 Asian countries. (Am J Infect Control 2008;36:S93-100.)

Throughout the world, including Asia, nosocomial infection is an important public health problem, often with pneumonia as a significant consequence. Hospital-acquired pneumonia (HAP) is associated with significant morbidity and mortality and increased costs of treatment. HAP is associated with crude mortality rates of up to 70% and attributable mortality rates as high as 33% to 50%.[1] Many of these deaths may be caused by ventilator-associated pneumonia (VAP), which is believed to be the most frequent infection in patients admitted to the intensive care unit (ICU).[2] Worldwide, point-prevalence studies have reported nosocomial infection rates ranging from 6.1% to 15%. Rates seem particularly high in Asia. In a recent study from Malaysia, 14% of hospitalized patients had a nosocomial infection, and 21% of these infections were pneumonia.[3]

Moreover, the organisms causing nosocomial pneumonia often may be difficult to treat. A study of 200 patients with pneumonia found that 87% of patients with nosocomial pneumonia were infected with Gram-negative bacilli, most commonly *Pseudomonas* spp (31%) and *Klebsiella* spp (20%).[4]

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Although guidelines for treatment are important, they are best used as a framework for the practicing physician. It has been emphasized that the treating physician must always consider local epidemiology, etiology, and resistance patterns when making treatment choices. However, there is a lack of published data from Asian countries regarding the local microbiologic flora and sensitivity patterns. The present review attempts to summarize the findings from an initiative that brought together experts from 10 different Asian countries to share valuable information regarding the prevailing patterns of microbiologic flora, the burden of HAP and VAP, and treatment approaches in their respective setups.

METHODOLOGY

Expert clinicians from 10 Asian countries (China, Hong Kong, India, Malaysia, Pakistan, Philippines, Singapore, South Korea, Taiwan, and Thailand) gathered and exchanged local and published information regarding the epidemiology, etiology, and diagnosis of HAP and VAP in their respective countries. Data presented by each panel member were critically analyzed, along with national and local surveillance data, wherever available. The definitions of HAP and VAP adopted by the panel were those provided by previous guidelines.[5] HAP was defined as pneumonia occurring 48 hours or more after admission that was not incubating at the time of admission. VAP was defined as pneumonia appearing more than 48 to 72 hours after endotracheal intubation. Health care–associated pneumonia (HCAP) was defined as a pneumonia in any patient who was hospitalized in an acute-care

hospital for 2 or more days within 90 days of the infection; resided in a nursing home or long-term care facility; received recent intravenous antibiotic therapy, chemotherapy, or wound care within the past 30 days of the current infection; or attended a hospital or hemodialysis clinic. The panel limited its analysis to cases of HAP and VAP and excluded HCAP, because these patients were considered to have a high probability of infection with multidrug-resistant pathogens, a topic discussed further elsewhere in this supplement.

A relative paucity of recently published epidemiologic data was noted for many Asian countries. Much of the data presented herein is drawn from the local hospitals of the panel members. The need for better epidemiologic studies regarding the incidence and prevalence of HAP and VAP was identified, to allow assessment of the future impact of the proposed treatment guidelines detailed herein. Some of the problems encountered by the panel are intrinsic to any research activity in this area. For example, depending on the criteria used to define VAP in the ICU, its incidence varies from 4% to 48% in the literature.[2] The specific diagnostic criteria used also may explain the differences in outcomes among different published studies and in surveillance data among different hospitals. Identifying deficiencies in our current knowledge base may help inform the direction of future studies.

EPIDEMIOLOGY

Incidence

The incidence of HAP has been defined differently based on varying denominators in different studies and institutions. So far, there has been no consensus on a common denominator that would represent the incidence on a uniform basis; it has varied from infection rate to per 100 hospital admissions to 1000 ventilator-days to 1000 patient-days. The overall incidence of HAP, including all VAP cases, is summarized in Table 1. On the other hand reported rates of nosocomial infection in Asian hospitals range from 4% to 43%, of which 45% to 65% are lower respiratory tract infections. A Chinese study of 298 hospitalized critically and seriously ill patients reported an 43.3% incidence of nosocomial infection, with the lower respiratory tract accounting for 65.1% of infections.[6] Another Chinese study of 1826 hospitalized patients reported a nosocomial infection rate of 13.1%, of which 45.2% were lower respiratory tract infections.[7] In Hong Kong, a cross-sectional survey reported that on a single day in the hospital, the nosocomial infection rate among 1042 patients was 4.1%, with approximately 33% of cases due to HAP. A Taiwanese hospital reported an incidence of nosocomial respiratory tract infection (including both HAP and tracheal bronchitis) of 3 cases per 1000 discharged patients.

HAP

The epidemiologic data on HAP are scarce, but various Asian health care facilities have reported incidences ranging from 1 to 21 per 1000 hospital admissions. Specific incidences reported to date include 18 per 1000 admissions to the general ward in an Indian study,[8] 6.3 per 1000 hospital admissions in in a Korean study,[9] 6.0 per 1000 hospital admissions in a 1999 Philippines study (HAP and VAP), and 1.0 per 1000 admissions in a Chinese study (HAP and VAP, with 136 of 562 strains [30.4%] early onset and the remainder late onset [69.6%]), 21.8 per 1000 admissions in Thailand (unpublished data), and 1.76 per 1000 hospital admissions in a tertiary care multispecialty hospital in northern India (unpublished data). In Hong Kong, a cross-sectional survey found that the HAP accounted for 30% of all nosocomial infections.

As would be expected, the incidence of HAP is higher in ICUs. According to various studies in Asian hospitals, the proportion of ICU-acquired respiratory infections ranges from 9% to 23%.[10] A prospective study from Singapore found that 17.7% (24/136) of patients admitted to a medical ICU over a 6-month period developed HAP.[11] A study in Thailand reported an incidence of HAP ranging from 6% to 10% in patients weaned from a ventilator.[12] An Indian study found HAP in 16.7% of patients admitted to the ICU.[8] In another Indian study, over 1-year period, 9.4% (89/948) pf patients admitted to the ICU had HAP.[13] A study in Singapore on nosocomial infection reported that pneumonia represented 9% of cases.[14] In Pakistan, in 1 of the hospitals represented in the panel, HAP constituted 55% of ICU infection cases. A study in Taiwan found that between 1991 and 1996, a significant proportion of patients acquired nosocomial respiratory tract infections more than 72 hours after admission to the surgical, cardiovascular surgical, or neurosurgical ICU.[15] In neurosurgical ICU patients, the rate of nosocomial infection was 4.8%, and HAP accounted for 91% of these infections.[15] In a Korean ICU, 30.3% of infections were HAP, with more than 90% of cases of late onset.

VAP

Published and unpublished data from Asian countries suggest an incidence of VAP varying from 3.5 to 46 per 1000 ventilator days.[16-18] A recent study from Thailand found incidences of VAP of 10.8 per 1000 ventilator days in an adult ICU[16] and 70.3 per 1000 ventilator days in newborn patients.[17] An Indian study of 51 critical care unit patients found an incidence of VAP of 46 per 1000 ventilator days (33% early onset and

Table 1. Overall frequency* of etiologic pathogens in HAP (all cases, including VAP)

	India	Pakistan†	China	Korea	Malaysia†	Taiwan	Thailand†	Philippines†
Incidence of HAP	53.9%		1 per 1000 days	6.3 per 1000 admissions*	1%	0.51 to 0.85 per 1000 patient-days	21.8 per 1000 admissions	6 per 1000 admissions
Incidence of VAP	8.95 per 1000 ventilator days†	55%	41.2%†	3.5 to 7.1 per 1000 ventilator days*	2%		28.3	
Mortality rates	37% to 47.3%	58%	25.8%†				26% to 28%	42.4%

*From Kim JM, Park ES, Jeong JS, Kim KM, Kim JM, Oh HS, et al. Multicenter surveillance study for nosocomial infections in major hospitals in Korea. Nosocomial Infection Surveillance Committee of the Korean Society for Nosocomial Infection Control. Am J Infect Control 2000;28:454-8.
†Local data.

67% late onset).[18] In Korea, the incidence of VAP is 3.5 to 7.1 per 1000 ventilator days.[9] One Indian hospital represented in the panel reported an overall rate of VAP of 8.95 per 1000 ventilator days. From Hong, Kong, surveillance data collected in 2004–2005 from a large tertiary care hospital represented in the panel found an incidence of VAP of 10.6 per 1000 ventilator days. In China, VAP accounts for 2.9% of all nosocomial infections. One Chinese study reported that 41.2% of intubated patients developed VAP, with an incidence of 1 per 1000 ventilator days.

An earlier Thai study of pneumonia in 536 patients on mechanical ventilation in the ICU found a overall rate of 7.5% (17.5% in the pediatric ICU, 6.5% in the medical ICU, and 2.5% in the surgical ICU).[19] In a recent Indian study of 328 patients in the ICU, the overall rate of HAP was reported to be 53.9%, and that of VAP was 81.7%.[20]

Mortality

Local mortality data are given in Table 1. These data are similar to those in previous studies from Asia, in which mortality for HAP (including VAP) ranged from 25% to 54%.[21,22] In China, several epidemiologic studies have been published recently, but the data are generally of poor quality. One limitation to such studies is that much data are drawn from major metropolitan medical centers, such as Shanghai and Beijing, with little date from the relatively underdeveloped areas of China. A Chinese study of 372 patients with HAP found an overall mortality rate of 25.3%. Mortality rates associated with *Pseudomonas* spp and *Staphylococcus aureus* infection were higher, 70.6% and 66.7%, respectively.[21]

A study from Thailand involving 132 patients reported a mortality rate of 47% in immunocompetent patients who acquired nosocomial pneumonia, compared with 54% for immunocompromised patients.[22] A Taiwanese study conducted over a 5-year period reported overall mortality of 42.6% in patients with respiratory tract infections and 61.5% for patients in the surgical ICU.[15] These findings are comparable to those from a study in India on HAP that found an overall crude mortality of 67.4% in ICU patients with pneumonia, with 40% of the mortality in these patients attributable to infection alone.[8] In the Philippines, the crude mortality rate for hospitalized patients with pneumonia was 42.4%, with a mortality rate attributable to infection of 30.1%. In the Philippines, local data presented by the panel demonstrated a mortality rate of 42% for HAP.[4]

Very little data are available on mortality associated specifically with VAP. A prospective study in Singapore reported a mortality rate of 73% for VAP.[11] A Chinese study of 120 patients with VAP reported a 14% mortality rate directly related to this infection.[23] A Thai study of mechanically ventilated patients reported that 22.5% (9/40) of patients died of VAP.[19] A study from India evaluated 51 patients in the critical care unit and found a mortality rate of 37% attributable to VAP, which also correlated very well with higher APACHE III scores; 33% of the cases were early onset, and 67% were late onset.[18] In Thailand, a study of newborn ICU patients on a ventilator found a mortality rate of 29.4% in infants with VAP versus 30.6% in newborn infants in the ICU without VAP.[17]

ETIOLOGY

Data regarding the etiology of HAP, including VAP, are given in Table 2. Reviewing the data reported by the panel reveals 2 prominent trends. First, *Acinetobacter* spp was found to be emerging in several countries, notably Malaysia, Thailand, Pakistan, and India, where it was one of the most common pathogens, being isolated in cases of HAP and VAP. In Taiwan, it represented the second-most common pathogen. However, in China and the Philippines, *P. aeruginosa* was the most common pathogen causing HAP.

Second, methicillin-resistant *S. aureus* (MRSA) has emerged as the most common pathogen causing HAP in Korea and Taiwan, representing a high proportion of all *S. aureus* isolates, 80% to 90% in Korea and

Table 2. Etiology of HAP (all cases including VAP): overall frequency of etiologic pathogens*

Pathogen	India*	Pakistan*	China	Korea	Malaysia*	Taiwan*	Thailand*	Philippines
Pseudomonas spp	20%	15-18%	18%	23%	17.6%	21%	17.8%	42.1%†
A. baumannii	38%	58.5%	16%	9%	23%	20%	28.2%	13.1%†
MRSA	5%	18%	16%	23%	11.8%	18%	7.6%	
K. pneumoniae	23%	No data	14%	11%	5.8%	9%	7.7%	26.3%†
E. coli			6.1%			3.6%	2.8%	
Enterobacteriaceae			8.2%	8%		3.2%		
S. maltophilia					11.8%	3.4%		

*Local data.
†VAP.

73% in Taiwan. However, overall, the etiologic pathogens reported herein are somewhat similar to those reported in the international data.[5]

HAP

Some etiologic data were available from the Asian countries represented on the panel. Published studies from China have noted the predominance of Gram-negative bacilli. In a study of 1826 hospitalized patients with nosocomial infection, 67% of isolates were Gram-negative pathogens, of which *P. aeruginosa*, *Klebsiella* spp, *Eschirichia coli*, and *Acinetobacter* spp were most common.[7] Similarly, another Chinese study of 298 patients reported that the most common nosocomial pathogens were Gram-negative bacilli (52.2%),[6] and a study of 372 patients with HAP reported that the most frequent pathogens were *Enterobacteriaceae* spp, *P. aeruginosa*, *S. aureus*, and *Candida albicans.*[21] On the other hand, the panel reported a high incidence of *Acinetobacter* spp (approximately equal to that of *S. aureus*), which is in contrast to a previous study reporting a quite low incidence of *Acinetobacter* spp (approximately 2%). According to the panel, currently the most common pathogen in HAP is *P. aeruginosa* (18%), followed by *S. aureus* (16%), *A. baumannii* (16%), *Klebsiella* spp (14%), *Enterobacteriaceae* spp (8%), and *E. coli* (6%).

The high incidence of *Acinetobacter* spp in nosocomial pneumonia in Malaysia was documented previously.[10] The panel from Malaysia reported that the most common pathogens in HAP are *A. baumannii* (23%), followed by *P. aeruginosa* (18%), *Stenotrophomonas maltophilia* (12%), MRSA (12%), and *Klebsiella* spp (6%).

In Taiwan, the panel identified *S. aureus* (22%), *A. baumannii* (20%), and *P. aeruginosa* (21%) as the 3 most common pathogens, accounting for 20% of HAP cases in a children's hospital. Among neonatal ICU patients, *S. aureus* was the most common pathogen, and nearly 100% of these isolates were MRSA; *A. baumannii* and *P. aeruginosa* followed next in terms of frequency. In the neonatal ICU, approximately 90% of HAP cases were of late onset, and no pathogen could be identified in approximately 50% of tracheal aspirate cultures. This pattern differs from that in a 1998 study of patients with nosocomially acquired respiratory tract infections that found that the most frequently isolated pathogens were *P. aeruginosa* (30%) and *S. aureus* (27%), of which 88% were MRSA.[15]

In Thailand, for HAP cases including VAP, data from the panel indicate that *A. baumannii* represents 28% of isolates, followed in order of frequency by *P. aeruginosa* (18%), *Klebsiella* spp (7.7%), *E. coli* (both extended spectrum beta lactamase [ESBL]–producing and non-ESBL producing), MRSA (7.6%), and nonfermentative Gram-negative bacilli. Moreover, most of these isolates are multidrug-resistant. In a recent study from Thailand, the most common organisms isolated from newborn ICU patients with VAP were *P. aeruginosa*, *Klebsiella pneumoniae*, and *Acinetobacter* spp, constituting 13% of endotracheal aspirate culture isolates.[17] A prospective study in Singapore reported that in cases of HAP, including VAP, the etiologic organisms were polymicrobial, mainly *K. pneumoniae*, *P. aeruginosa*, MRSA, and coagulase-negative *Staphylococcus.*[11]

In a study of nosocomial pneumonia in 51 ICU patients in India, the most commonly isolated organisms were *P. aeruginosa* (46%), *Acinetobacter* spp (8%), *Klebsiella* spp (29%), *S. aureus* (25%), and *E. coli* (12%). In earlier studies, the most commonly isolated organisms in HAP were *Pseudomonas* spp (44%), *Klebsiella* spp (34%)[8] enteric Gram-negative organisms, and *S. aureus.*[13] In another Indian study of HAP, including VAP cases, *P. aeruginosa* was the most common organism, and polymicrobial infection was found in 16.3% of cases.[20] A recent Indian study found *A. baumannii* to be responsible for 41.8% of all nosocomial infections.[24]

In Korea, the data indicate that MRSA is the most common pathogen in HAP, accounting for 23.5% of isolates. Other common pathogens include *P. aeruginosa* (22.7%), *Klebsiella* spp (11.1%), *Acinetobacter* spp (8.9%), and *Enterobacteriaceae* spp (8%). In ICU

cases, including both HAP and VAP, the most prevalent organisms were *S. aureus* (34.9%), *Acinetobacter* spp (19.2%), and *P. aeruginosa* (13.3%). MRSA accounted for 80% to 90% of the *S. aureus* isolates.

In the Philippines, in patients with HAP excluding VAP, the panel noted that the etiologic scenario has not changed much over time. *P. aeruginosa* was reported to be the most common pathogen (19% of isolates), followed by *E. coli*. Earlier studies also identified *P. aeruginosa* (31.1% of isolates) and *E coli* (15.5%) as highly prevalent organisms.

In Pakistan, the panel determined that the most common organisms were *Acinetobacter* spp (58.5%), MRSA (18%), and *P. aeruginosa* (3.5%). According to the data, the incidence of *Pseudomonas* is currently decreasing, whereas the incidences of ESBL-producing *E. coli* and *Klebsiella* spp are increasing.

VAP

As is the case for HAP, *A baumannii* was found to be the most common pathogen in VAP in Malaysia, Pakistan, India, Thailand, and the Philippines. In India, a study from a hospital represented by the panel (local data) found that the most common isolate was *Acinetobacter* spp (38%), followed by *Klebsiella* spp (23%), *P. aeruginosa* (20%), *S. aureus* (5%), *Candida* spp (3.5%), and *S. maltophilia* (2%). Polymicrobial infections accounted for 7.3% of isolates, and MRSA represented 20% of *S. aureus*. Similarly, *A. baumannii* dominated in Thailand, accounting for 30% of VAP cases, followed by *Pseudomonas* spp (18%), MRSA (8%), and *Klebsiella* spp (7%). However, the incidence of polymicrobial flora was higher (48%). Fungal infections, mostly *Candida* spp, were also common. The overall rate of multidrug-resistant organisms was 48.4% in cases of VAP, compared with 2.3% in HAP. In Malaysia, the panel reported that the most common pathogens causing VAP were *Acinetobacter* spp (23%), *Pseudomonas* spp (17.6%), MRSA (11.8%), *Klebsiella* spp (5.8%), and *S. maltophilia* (11%). Approximately 1/2 of all *Acinetobacter* isolates, as noted in 1 hospital, are multidrug-resistant, susceptible only to polymyxin and amikacin. From Pakistan, local data demonstrated that *Acinetobacter* spp was most common (58%), followed by *Pseudomonas* spp (19%) and MRSA (18%). The panel also noted that in the Philippines, *A. baumannii* was the most common organism in VAP, accounting for 13% of cases, but *P. aeruginosa* was the most common pathogen in HAP. From China, the panelists reported that the most common organisms isolated from patients with VAP were *Pseudomonas* spp (18%), *S. aureus* (16%; mostly MRSA), *A. baumannii* (16%), *Klebsiella* spp (14%), *Enterobacteriaceae* spp (8.1%), and *E. coli* (6%).

In Korea, the panel reported data from a single medical center. The most common pathogens isolated were *S. aureus* (34.4%; almost all MRSA), *A. baumannii* (26.2%), *P. aeruginosa* (18.1%), *Klebsiella* spp (9%), *S. maltophilia* (6%), and *E. coli*. In Taiwan, the organisms most often responsible for VAP were *Pseudomonas* spp (21%), *Acinetobacter* spp (20%), *S. aureus* (18%), *Klebsiella* spp (9%), *E. coli* (3.6%), other *Enterobacteriaceae* spp (3.2%), and *S. maltophilia* (3.4%). Nationwide surveillance data from ICU units are available in Taiwan through the SMART network. SMART data collected from 9 centers in Taiwan between 2000 and 2005 reveals that approximately 73% of *S. aureus* was MRSA. Overall, the most common organisms in ICU units were *S. aureus*, *P. aeruginosa*, *Klebsiella* spp, and *A. baumannii*.

It is important to note that the much of the present data reported in this article revolves around the hospitals represented in the panel in a dearth of well-published studies. Nevertheless, there is a striking similarity in the emerging trends throughout Asia. The data also clearly demonstrate that the incidence and prevalence of multidrug-resistant pathogens are rising in Asian countries. *A. baumannii–calcoaceticus* complex is emerging as a major pathogen in most of the ICUs in these countries. MRSA, although present, is not as big a problem as in the Western world; however, it is interesting that more developed countries like Korea and Taiwan reported MRSA as the predominant pathogen isolated.

RISK FACTORS FOR HAP AND VAP

The panel agreed that the risk factors predisposing a patient to the development of HAP in Asian countries were likely to be similar to those detailed in previous guidelines.[5] Previously noted risk factors include male sex, preexisting pulmonary disease, multiple organ system failure, the presence of intubation or enteral feeding, mechanical ventilation, and supine position. In addition to these, the panel considered elderly age, APACHE II score > 15, previous use of antibiotics for more than 2 weeks, diabetes, immunosuppression, dialysis, reintubation due to failed weaning, use of paralytic sedative, and length of ICU stay to be additional risk factors. The panel also concurred that certain factors may increase the incidence of infection with multidrug-resistant pathogens, including regular dialysis, immunosuppression, heart disease, renal failure, hepatic failure, a high incidence of antibiotic resistance in the community, and/or the presence of a family member colonized with a multidrug-resistant pathogen. As always, the time of onset of pneumonia is an important epidemiologic factor for specific pathogens and clinical outcomes in HAP. Early-onset HAP

or VAP occurs within the first 5 days of hospitalization and carries a better prognosis. Late-onset HAP or VAP occurs after 5 days or more of hospitalization and is more likely associated with multidrug-resistant pathogens and increased morbidity and mortality.

PREVENTION OF HAP OR VAP

Existing guidelines[5] suggest several measures to reduce the incidence of HAP and VAP. The panel suggested adopting the following measures to reduce HAP and VAP:

- Strict infection control policies
  - Alcohol-based hand disinfection
  - Collection of timely microbiologic surveillance data on multidrug-resistant pathogens
  - Monitoring and early removal of invasive devices
  - Programs to reduce antibiotic prescribing practices
  - Continuous aspiration of subglottic secretions
  - Detection of pneumonia and deescalation of drug treatment
- Use of oral rather than nasal endotracheal tubes
- Maintenance of endotracheal cuff pressure $>$ 20 cm H_20
- Limited use of sedative and paralytic agents
- Positioning of the patient
  - Semirecumbent positioning (30 to 45 degrees) is recommended to reduce the risk of aspiration.
  - Proper care should be taken when turning the patient or the bed rail is raised to avoid inadvertently flushing the condensate that collects on the ventilator circuit into the lower airway or to inline medication nebulizers.
- Intensive insulin therapy to maintain normal blood glucose level
- Emphasis on bleeding prophylaxis; use of H_2 antagonists or sucralfate
- Avoidance of intubation by using noninvasive ventilation wherever possible, particularly in patients with chronic obstructive pulmonary disease and cardiogenic pulmonary edema
- Avoidance of blood transfusion
- Adequate nurse-to-patient ratios
- Staff education

DIAGNOSIS

The panel considered that the diagnosis of pneumonia should include the detection of a new or progressive radiographic infiltrate, along with clinical signs of infection. At least 2 of 4 signs of infection (ie, fever above 38°C, purulent secretions, leukocytosis or leukopenia, decreasing oxygenation) must be present. The presence of these findings suggests that the patient should be evaluated for HAP or VAP. Routine investigation includes a blood culture or, for intubated patients, a semiquantitative/quantitative endotracheal aspirate culture.

MANAGEMENT

The aims of managing a patient with VAP are to identify pulmonary infection, to ensure collection of appropriate specimens, and to promote early, effective therapy. Recently, 2 different approaches to management have been suggested, a clinical strategy and a bacteriologic strategy.

Clinical strategy

In this approach, as described in existing guidelines,[5] the presence of pneumonia is defined by new lung infiltrate plus clinical evidence that the infiltrate is of an infectious origin. The presence of a new or progressive radiographic infiltrate plus at least 2 of 3 clinical features (ie, fever above 38°C, leukocytosis or leukopenia, purulent secretions) represents the most accurate combination of criteria for starting empiric antibiotic therapy.[25] This strategy emphasizes prompt empiric therapy for all patients suspected of having VAP. This is based on the consistent findings that a delay in initiating appropriate antibiotic therapy for patients with VAP is associated with increased mortality. Inappropriate therapy is also an important correlate of high mortality.[25,26] The initial antibiotic is chosen based on risk factors for specific pathogens modified by knowledge of local patterns of antibiotic resistance and organism prevalence. After starting treatment, the patient is reevaluated after 48 to 72 hours as findings of semiquantitative cultures of lower respiratory tract secretions become available.

The advantage of this approach is that it does not require specialized methods, and it ensures that all patients with suspected pneumonia are treated. The approach's major disadvantage is that it will lead to overuse of antibiotic therapy even when a noninfectious process is responsible for clinical features. The semiquantitative culture cannot differentiate between colonization and true pathogens. These cultures are of greatest value if they are negative and the patient has not received any antibiotics.

Bacteriologic strategy

This approach uses quantitative cultures of the lower respiratory tract secretions (endotracheal aspirates, bronchoalveolar lavage [BAL], or protected specimen brush [PSB] specimens collected with or without a bronchoscope) to define the presence of pneumonia and the etiologic pathogen. Growth above a threshold

concentration is necessary to allow a diagnosis of HAP or VAP and to determine the causative microorganism. Growth below the threshold is thought to be due to colonization or contamination. This approach emphasizes avoiding the problem of overtreatment with antibiotics by separating colonizers from pathogens.

Quantitative cultures have been demonstrated to have good diagnostic utility for the presence of pneumonia. A major concern with their use is the occurrence of false-negative results, which may result from a recent start of or change in antibiotic therapy, especially in the preceding 24 to 72 hours. In addition, in VAP the disease process is often multifocal, and thus BAL and endotracheal aspirates may provide more representative samples than PSB, which samples only a single bronchial segment. Another problem with this approach is that the culture results are not available immediately, which can be a serious issue in clinically unstable patients. Ancillary tests, such as Giemsa stain, Gram stain, or differential cell counts, can be used to increase the likelihood of a subsequent positive culture and to guide the decision for antibiotic therapy. Clinically, factors that come into play are the certainty of the diagnosis of pneumonia and the severity of illness. Many clinicians would agree that therapy should be initiated in all clinically unstable patients with signs of infection, regardless of the initial bronchoscopic findings.

The panel endorsed the use of BAL, either bronchoscopically or nonbronchoscopically, to diagnose HAP or VAP. When done with a quantitative culture, this approach has proven to be quite sensitive and specifically accurate for lower respiratory tract infections. The sensitivity of bronchoscopic BAL in suspected VAP has been reported to range from 42% to 93% (mean, 73% ± 18%); the specificity, from 45% to 100% (mean, 82% ± 19%).[27] Blind bronchial suction or blind mini-BAL also may be used. Previous studies have shown that the sensitivity and specificity of these 2 methods are comparable to those of bronchoscopic BAL (sensitivities of 74% to 97% vs 63% to 100%, respectively, and specificities of 74% to 100% vs 66% to 96%, respectively).[28]

The panel noted that most members were not using PSB, although it remains a recommended modality. It may not be available in some Asian countries, and it is much more costly than nonbronchoscopic BAL. Quantitative endotracheal culture or quantitative nonbronchoscopic BAL culture was considered preferable to bronchoscopic BAL or PSB, because the former may be done at any time without a clinical specialist, and they offer the advantages of comparable sensitivity and specificity at a reduced cost. These factors are of relatively greater significance in Asian countries compared with Western countries and often come into play in clinical practice decisions. The panel also noted that in most Asian countries, quantitative cultures were usually preferred over semiquantitative cultures. Thresholds of 10^3 colony-forming units (cfu)/mL for PSB, 10^4 cfu/mL for BAL, and 10^6 cfu/mL for endotracheal aspirates were suggested as representative of infection.

SUMMARY

Data from the panel and a review of the literature reveals that overall, HAP occurs at a rate of 5 to 10 cases per 1000 hospital admissions in Asian countries, similar to the rate reported in developed countries.[29-31] Mortality rates reported by the panel and in the literature are also comparable to those reported in the United States. Furthermore, risk factors for HAP and VAP were found to be similar to those reported in previous guidelines.[5] Asian countries had relatively higher incidences of *Acinetobacter* spp. In all but a few countries, the prevalence of MRSA was not as high as in Western countries. Quantitative nonbronchoscopic BAL and endotracheal aspirate cultures were the preferred diagnostic modalities over other procedures, such as PSB. In many Asian countries, national surveillance data on the epidemiology of HAP and VAP are not available, and clinicians must rely on local data.

References

1. Mandell LA, Campbell GD Jr. Nosocomial pneumonia guidelines: an international perspective. Chest 1998;113:188S-93S.
2. Chinsky KD. Ventilator-associated pneumonia. Is there any gold in these standards? Chest 2002;122:1883-5.
3. Hughes AJ, Ariffin N, Huat TL, Abdul Molok HM, Hashim S, Sarijo J. Prevalence of nosocomial infection and antibiotic use at a university medical center in Malaysia. Infect Control Hosp Epidemiol 2005;26:100-4.
4. Luo B, Huang Y, Qiu W, Wu ES. A prospective study on etiologic bacteria in 200 patients with pneumonia. Hunan Yi Ke Da Xue Xue Bao 1998;23:453-7.
5. American Thoracic Society and Infectious Disease Society of America. Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. Am J Resp Crit Care Med 2005;171:318-416.
6. Liu MD, Cheng P. Analysis of nosocomial infection in hospitalized critical and serious patients. Zhonghua Liu Xing Bing Xue Za Zhi 1995;16:231-3 [in Chinese].
7. Zhang Y. A two-year prospective survey on nosocomial infections. Zhongua Yi Xue Za Zhi 1991;71:253-6 [in Chinese].
8. Merchant M, Karnad DR, Kanbur AA. Incidence of nosocomial pneumonia in a medical intensive care unit and general medical ward patients in a public hospital in Bombay India. J Hosp Infect 1998;39:143-8.
9. Kim JM, Park ES, Jeong JS, Kim KM, Kim JM, Oh HS, et al. Multicenter surveillance study for nosocomial infections in major hospitals in Korea. Nosocomial Infection Surveillance Committee of the Korean Society for Nosocomial Infection Control. Am J Infect Control 2000;28:454-8.
10. Rozaidi SW, Sukro J, Dan A. The incidence of nosocomial infection in the intensive care unit, Hospital Universiti Kebangsaan Malaysia: ICU-acquired nosocomial infection surveillance program, 1998–1999. Med J Malaysia 2001;56:207-22.

11. Stebbings AE, Ti TY, Tan WC. Hospital acquired pneumonia in the medical intensive care unit: a prospective study. Singapore Med J 1999;40:508-12.
12. Bumroongkit C, Liwsrisakun C, Deesomchok A, Theerakittikul T, Pothirat C. Efficacy of weaning protocol in medical intensive care unit of a tertiary care center. J Med Assoc Thai 2005;88:52-7.
13. Trivedi T, Shejale SB, Yeolekar ME. Nosocomial pneumonia in a medical intensive care unit. J Assoc Physicians India 2000;48:1070-3.
14. Johan A. The diagnosis of nosocomial pneumonia. Singapore Med J 1999;40:498-9.
15. Wang FD, Chen YY, Liu CY. Prevalence of nosocomial respiratory tract infections in the surgical intensive care units of a medical center. Zhonghua Yi Xue Za Zhi (Taipei) 1998;61:589-95.
16. Thongpiyapoom S, Narong MN, Suwalak N, Jamulitrat S, Intaraksa P, Boonrat J, et al. Device-associated infections and patterns of antimicrobial resistance in a medical-surgical intensive care unit in a university hospital in Thailand. J Med Assoc Thai 2004;87:819-24.
17. Petdachai W. Ventilator-associated pneumonia in a newborn intensive care unit. Southeast Asian J Trop Med Public Health 2004;35: 724-9.
18. Rakshit P, Nagar VS, Deshpande AK. Incidence, clinical outcome and risk stratification of ventilator-associated pneumonia: a prospective cohort study. Indian J Crit Care Med 2005;9(4):211-6.
19. Thanamee N, Sujaritjan N, Techasena W. Pneumonia in mechanically ventilated patients in Nan hospital intensive care unit. J Med Assoc Thai 1995;78(Suppl 2):S102-4.
20. Mukhopadhyay C, Bhargava A, Ayyagari A. Role of mechanical ventilation and development of multidrug resistant organisms in hospital acquired pneumonia. Indian J Med Res 2003;118:229-35.
21. Hou SR, Xu XJ, Yi P. Nosocomial pneumonia: a report of 372 cases. Zhonghua Nei Ke Za Zhi 1992;31:338-40 [in Chinese].
22. Saenghirunvattana S, Charoenpan P, Kiatboonsri S, Aeursudkij B. Nosocomial pneumonias in Thailand. Southeast Asian J Trop Med Public Health 1994;25:332-4.
23. Zhou P, He H, Liu JD, Wu XH. Impact of clinically related factors on the outcomes of ventilator-associated pneumonia. Zhonghua Liu Xing Bing Xue Za Zhi 2003;24:216-9 [in Chinese].
24. Prasanth K, Badrinath S. Nosocomial infections due to *Acinetobacter* species: clinical findings, risk and prognostic factors. Indian J Crit Care Med 2006;24(1):39-44.
25. Kollef MH, Sherman G, Ward S, Fraser VJ. Inadequate antimicrobial treatment of infections: a risk factor for hospital mortality among critically ill patients. Chest 1999;115:462-74.
26. Luna CM, Vujacich P, Niederman MS, Vay C, Gherardi C, Matera J, et al. Impact of BAL data on the therapy and outcome of ventilator-associated pneumonia. Chest 1997;111:676-85.
27. Torres A, El-Ebiary M. Bronchoscopic BAL in the diagnosis of ventilator-associated pneumonia. Chest 2000;117:198S-202S.
28. Campbell GD. Blinded invasive diagnostic procedures in ventilator-associated pneumonia. Chest 2000;117:207S-11S.
29. Chastre J, Fagon JY. Ventilator-associated pneumonia. Am J Respir Crit Care Med 2002;165:867-903.
30. Celis R, Torres A, Gatell JM, Almela M, Rodriguez-Roisin R, Agusti-Vidal A. Nosocomial pneumonia: a multivariate analysis of risk and prognosis. Chest 1988;93:318-24.
31. Torres A, Aznar R, Gatell JM, Jimenez P, Gonzalez J, Ferrer A, et al. Incidence, risk, and prognosis factors of nosocomial pneumonia in mechanically ventilated patients. Am Rev Respir Dis 1990;142:523-8.