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**Clinical Practice Guidelines for Prevention and Management of
Adults with Hospital-acquired and Ventilator-associated Pneumonia**

Infectious Disease Association of Thailand

Thoracic Society of Thailand

Critical Care Society of Thailand

Infection Control Society of Thailand

Part I. Objectives

This is a guideline directed at healthcare workers to aid in preventing and managing hospital-acquired and ventilator-associated pneumonias. We are not addressing the details of investigations of pulmonary infections nor are we discussing supportive therapy for patients on respirators, oxygen and fluid therapy, as well as intensive care monitoring of critically ill patients. This guideline was approved by a committee of the Infectious Disease Association of Thailand, Thoracic Society of Thailand, Critical Care Society of Thailand, and Infection Control Society of Thailand. The committee made these guidelines mostly on evidence-based data from Thailand (grouped as first priority). Recommendations are grouped as second priority based on evidence-based data from international papers, and are grouped as third priority based on expert opinion. The quality of the evidence and the strength of recommendations are ranked according to the recommendation of the Infectious Diseases Society of America (IDSA) and United States Public Health Service (Table 1).¹ This practice guideline can be modified in many hospitals at different levels because of limitation in diagnosis, instruments, equipment, healthcare workers, and biostatistical data peculiar to that location.

I. Definitions

Hospital-acquired pneumonia (HAP) is defined as pneumonia that occurs 48 hours or more after hospitalization in a patient who is not intubated at the time of diagnosis.¹

Ventilator-associated pneumonia (VAP) is defined as pneumonia that occurs 48 hours or more after endotracheal intubation or within 48 hours after endotracheal tube removal.¹

Healthcare-associated pneumonia (HCAP) refers to pneumonia in any patients who was hospitalized for two or more days prior to onset of 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 as an outpatient or a hemodialysis unit.¹

Early-onset HAP or VAP is defined as HAP or VAP that occurs within the first four days of hospitalization.¹

Late-onset HAP or VAP is defined as HAP or VAP that occurs more than four days after hospitalization.¹

Fever is defined as oral temperature of equal to or greater than 38.3°C, or equal to or greater than 38.0°C for more than one hour, or equal to or greater than 37.5°C by rectal temperature.²

Endotracheal tube includes orotracheal or nasotracheal or tracheostomy tube.¹

Adequate sputum is defined as the sputum that contains neutrophils of more than 25 cells/low-power field (LPF) and squamous epithelial cells of less than 10 cells/LPF on microscopic examination.³

Patients with HCAP and aspiration pneumonia are not included in these clinical practice guidelines. We do not differentiate early-onset or late-onset HAP or VAP because of the absence of epidemiological data in Thailand. Most Thai patients are not living in nursing homes or long term care facilities as is common in foreign countries. These guidelines are for pneumonic patients with suspected bacterial origin and for immunocompetent adults. They are not applicable for severe immunocompromised patients with human immunodeficiency syndrome (HIV), hematologic malignancy, neutropenia, transplantation, and chronic steroid therapy. These guidelines are not to supersede good clinical judgment, but rather only tools for aiding in appropriate management of HAP or VAP.

II. Diagnosis of HAP and VAP¹⁻⁸

2.1 Criteria for clinical diagnosis

We have no gold standard criteria for diagnosing HAP and VAP. Clinical suspicion is raised by the clinical presentations of the patient such as new onset of fever, high spiking temperature, coughing with purulent sputum, and dyspnea.

A diagnosis of HAP or VAP is made from signs and symptoms, along with laboratory data including a complete blood count (CBC), chest X-ray (CXR) and arterial blood gas analysis. HAP or VAP must have a new or progressive infiltration on CXR plus 2 of 3 clinical criteria as follows:

- a. New onset or increase of body temperature
- b. Purulent sputum (defined by an adequate sputum)
- c. White blood cell count of $\geq 12,000$ cells/mm³ (12×10^9 cells/L) or $< 4,000$ cells/mm³ (4×10^9 cells/L)^{1,5,8}

These clinical criteria, if present, should be followed by appropriate further investigations to confirm the diagnosis. The diagnostic criteria for the presence of HAP or VAP with chest infiltrates plus only one of three clinical criterion have high sensitivity but low specificity, resulting in more patients to be treated with empirical antibiotic. In contrast, the diagnosis of HAP or VAP with the presence of chest infiltrates plus all three clinical criteria has increased specificity, and will also result in fewer patients to be treated with antibiotic. The patients with true HAP or VAP are under diagnosed and not received adequate antibiotic therapy. A previous study in which the diagnostic gold standard consisting of histology plus positive microbiologic cultures of immediately collected postmortem lung tissues, the presence of chest infiltrates plus two of three clinical criteria resulted in 69% sensitivity and 75% specificity.⁵ When the three clinical criteria were used, the sensitivity declined, whereas the use of only one criterion led to a decline in specificity. In conclusion, the presence of new or progressive chest infiltrates plus at least two of these three clinical criteria represent the most accurate clinical criteria for initiating empirical antibiotic therapy especially in patients with hemodynamic instability together with careful history taking, physical examination, laboratory tests, and ongoing clinical evaluation of the patient. With this approach, HAP or VAP could be confirmed, and other etiologies mimicking pneumonia such as atelectasis, pulmonary

edema, adult respiratory distress syndrome, pulmonary embolism, drugs-induced pneumonitis, radiation pneumonitis, and pulmonary hemorrhage should be carefully excluded.

Pugin and colleagues developed a clinical pulmonary infection score (CPIS), which combines clinical, radiographic, physiological, and microbiologic data into a single numerical result.⁴ When the CPIS exceeded 6, a high possibility of the presence of HAP or VAP can be assumed as defined by quantitative cultures of bronchoscopic and non-bronchoscopic bronchoalveolar lavage (BAL) specimens. However, in a subsequent study, that used histology plus immediate postmortem quantitative lung cultures as the reference standard, the CPIS had a sensitivity of 77% and a specificity of 42%.⁵ This study left us with the impression that the sensitivity and specificity of the score system were low. Its specificity improved if a Gram stain of endotracheal aspirate or protected specimen brush (PSB) culture was added to the evaluation.⁶

A negative Gram-stained sputum or endotracheal aspirate (absence of bacteria or inflammatory cells) in a patient without a recent (within 72 hours) change in antibiotics has a strong predictive value (94%) for HAP or VAP (IIA).⁹

Recently, Singh and colleagues used a modified CPIS (Table 2) that did not rely on culture data to guide the diagnosis of HAP or VAP and the duration of antibiotic therapy.⁷ Reevaluation of the decision to use antibiotics is based on serial clinical evaluations. By day 3 or sooner, is necessary, because patients who are improving will have a good clinical response by this time point. They shown that some patients with a low clinical suspicion of VAP (CPIS of 6 or less) can then have antibiotics safely discontinued after 3 days if their course suggests that the probability of pneumonia is still low. The modified CPIS appears to be an objective measure to define patients who can receive a shorter duration of antibiotic therapy (IA).⁷

Recommendations for the clinical strategy

Conclusion. The committee recommends that a mainly clinical approach is used for the diagnosis of HAP or VAP. The presence of HAP or VAP is defined by new or progressive chest infiltrates plus at least two of three clinical criteria suggesting infection which include the new onset or increase of fever, purulent sputum, and white blood cells count $\geq 12,000$ cells/mm³ or $< 4,000$ cells/mm³. They are the most reliable and practical

clinical criteria for starting empiric antibiotic therapy. Patients with suspected VAP or HAP should have detailed history taking, careful physical examination, and appropriate laboratory tests in order to confirm the diagnosis or exclude other etiologies of chest infiltrates mimicking pneumonia. A reliable Gram stain of sputum or endotracheal aspirate with a careful examination of the morphology of bacteria may improve the diagnostic accuracy when correlated with later culture results. A negative Gram-stained sputum or endotracheal aspirate (absence of bacteria or inflammatory cells) in a patient without a recent (within 72 hours) change in antibiotics has a strong negative predictive value for HAP or VAP, and should lead to a search for alternative sources of fever with chest infiltrates. A modified CPIS of 6 or less for 3 days, as proposed by Singh and colleagues, is an objective criterion to select patients at low risk for early discontinuation of empiric antibiotic therapy of HAP or VAP. The committee suggests that the modified CPIS could be use in clinical practice (Fig. 1).

The committee emphasizes prompt appropriate empirical antibiotic therapy for all patients suspected of having HAP or VAP. If the patients received antibiotics after a suspected diagnosis later than 24 hours, the mortality rate would increase. The committee is aware that the low specificity of these clinical criteria may induce overuse of antimicrobial agents. A modified CPIS of 6 or less by day 3 is a good criterion to select patients at low risk for early discontinuation of empirical antibiotic therapy.

2.2 Bacteriologic evaluation

There are three techniques for culture collection of respiratory specimens (expectorated sputum, endotracheal aspirate, BAL or PBS specimens collected with or without bronchoscope) to define both the presence of pneumonia and the etiologic pathogen.

1. Qualitative culture studies are used routinely. The cultured bacteria may be colonizer or true pathogen from the lower respiratory tract. Diagnostic technique that identify etiologic pathogen based on qualitative cultures usually lead to therapy for more organisms than those base on quantitative cultures (IA).¹⁰⁻¹³

2. Semiquantitative cultures of respiratory specimens cannot be used as reliably as quantitative cultures to define the presence of pneumonia and the need for antibiotic therapy.¹⁰⁻¹³

3. Quantitative culture identifies growth of bacteria above a threshold concentration to define the presence of pneumonia and the etiologic pathogen. Growth below the threshold is assumed to be due to colonization or contamination. This method increases the accuracy of diagnosis HAP or VAP, and decreases the problem of overtreatment with antibiotics. The major concern with this bacteriologic approach is that a false negative culture can lead to a failure to treat a specific patient or a specific pathogen. This approach can also lead to delayed antibiotic therapy. The major factors, causing false negative quantitative cultures, is a recent starting of or changing in antibiotic therapy in the preceding 24 hours, but up to 72 hours, or in the early phase of pneumonia. The use of bronchoscopic quantitative culture has been shown to reduce 14-day mortality, compared with a clinical strategy, in one study of suspected VAP (IIA).⁹

Quantitative cultures of the non-bronchoscopic BAL specimens may be used for diagnosis of HAP or VAP, especially in many clinical settings where bronchoscopist is not available (IIA).¹⁴ At present, the physician has different techniques for collection of BAL specimens without bronchoscopy, and thus the bacteriologic approach by this technique is not recommended in this guideline.

Criteria for diagnosing HAP or VAP by quantitative cultures

1. Quantitative culture from expectorated sputum has never been studied and there are no published references.

2. An endotracheal aspirate can be cultured quantitatively. With a threshold of 10^6 colony-forming units (cfu)/mL or more, the sensitivity of this method for the presence of pneumonia has varied from 38-82%, with a mean of 76 ± 9 %, and with a specificity ranging from 72-85 %, with a mean of 75 ± 28 %.¹⁵

3. Bronchoscopic BAL studies have typically used a diagnostic threshold of 10^4 or 10^5 cfu/mL or more .The sensitivity of this method has varied from 42-93%, with a mean of 73 ± 18 %, and specificity ranging from 45-100%, with a mean of 82 ± 19 %.¹⁶

4. Quantitative culture of PSB samples has used a diagnostic threshold of 10^3 cfu/mL or more. The sensitivity has ranging from 33-100%, with a mean of 66 ± 19 %, and specificity ranging from 50-100%, with a mean of 90 ± 15 %.¹⁶

Recommendations for the bacteriologic strategy

The committee suggests examining respiratory specimens (expectorated sputum, endotracheal aspirate, BAL or PSB specimens) by semiquantitative or quantitative culture. Each technique has its own diagnostic threshold and methodology limitations. The choice of method depends on local expertise, experience, availability, and cost. Clinical judgment decision of the physicians in various clinical settings are important.

Recommendations for the combining clinical and bacteriologic strategies

The clinical approach consists of a measurement of vital signs especially blood pressure (including the dosage of inotropic drugs) and body temperature; a volume and character of the sputum; analysis of white blood cell counts in peripheral blood, arterial oxygen contents, chest radiographic features, and modified CPIS. This is followed by bacteriologic data and culture result analysis on day 2-3.

If there is clinical improvement at 48-72 hours after therapy when the microbiologic results are usually obtained. If semi-quantitative ($<3^+$), quantitative (PSB specimen of $<10^3$ cfu/mL or bronchoscopic BAL specimen of $<10^4$ or 10^5 cfu/mL), or qualitative cultures (negative) are below the diagnostic threshold or negative, and antibiotics were not given or changed within 72 hours before culture specimen was collected, this has a strong negative predictive value for HAP or VAP. It should lead to a search for alternative causes of fever or chest infiltrates and discontinuation of antibiotics. In addition, anaerobic bacteria or nonbacterial agents may result in negative routine cultures, and this must be kept in mind. If there is a positive quantitative culture (above the diagnostic threshold), the antibiotic therapy could be changed to focus on a known isolated pathogen. If semiquantitative culture (4^+ , 5^+) or qualitative culture is positive, the physician must make an educated decision whether HAP or VAP is present or not. If pneumonia is suspected, therapy should be focused or narrowed (i.e. de-escalation) on the specific isolated pathogen and susceptibility to a specific antibiotic. If pneumonia is not suspected (for example rapid decline in chest infiltrates within 72 hours), the physician should search for alternative etiologies for fever or chest infiltrates.

In case there is no clinical improvement at 48 or 72 hours after therapy, and the microbiologic results are obtained. If there is a positive quantitative culture (above the diagnostic threshold), the therapy should be changed to a specific antibiotic and

there is also need to search for complications (i.e., empyema, lung abscess, pulmonary embolus). If the quantitative culture is negative (below the diagnostic threshold), the therapy should search for alternative sources of fever or chest infiltrates. If the semiquantitative ($\leq 3^+$) or qualitative culture is negative, one must look for other causes of fever or chest infiltrates. If a semiquantitative (4^+ and 5^+) or qualitative culture yields positive results, the physician should reconsider whether the patients has pneumonia or not. If pneumonia is diagnosed, the therapy should be changed to an antibiotic to the specific isolated pathogen. If pneumonia is not diagnosed, the physician should search for other etiologies for fever or chest infiltrates.

Details of techniques of semiquantitative and qualitative cultures can be found in references number 6, 15, 16 and the appendix.

III. Principles of antibiotic therapy

3.1 Appropriate initial therapy and timing

Timing and appropriateness of initial antibiotic therapy are important in reducing HAP or VAP mortality. Suitable initial antibiotic therapy is defined as being pathogen-specific by susceptibility test as well as using an optimal dose and timing of dosing of antibiotics that correlates to their pharmacokinetics and pharmacodynamics. Initial time for starting antibiotics is defined as the time when patients receive antimicrobial agents after diagnosis of HAP or VAP. Iregui and colleagues documented an adverse outcome when there was a delayed appropriate antimicrobial therapy in 107 patients with VAP.¹⁷ Thirty-three (30.8%) patients received appropriate antibiotic treatment that was delayed 24 hours or more after the patient met the diagnostic criteria for VAP. This was often because there was a delay in recognition of the presence of VAP and in actually writing the orders for antimicrobial therapy (N = 25, 75.8%). Patients receiving delayed antimicrobial therapy had a greater hospital mortality, compared with those without the delay (69.7% versus 28.4%, $p < 0.001$) (IIA).

A prospective study of patients with HAP or VAP at Maharaj Nakorn Chiangmai Hospital in 2005 confirmed the importance of prompt appropriate antibiotic therapy for HAP or VAP.¹⁸ The patients who received appropriate antibiotic therapy within 24 hours after diagnosis of HAP or VAP had a decline in mortality ($p = 0.024$).

They showed more survival than a group that received non-appropriate and delayed antibiotic therapy.

3.2 Selection of antimicrobial agents

Selection of appropriate antibiotics with optimal dose, appropriate pharmacokinetics and pharmacodynamics, and correct route of administration in patients with suspected HAP or VAP decreases mortality and complications (IA).¹⁹⁻²¹ Empirical antibiotics are used before known bacteriologic reports. Antibiotic selection for each patient should be based on the risk factors for multidrug-resistant (MDR) pathogens (summarized in Table 3^{1,22-25}), etiologic bacterial data in the specific clinical setting of HAP or VAP, and the local patterns of antibiotic susceptibility in different areas. If this is done correctly, it decreases mortality and complications (IIA).²⁶⁻²⁸ The respiratory care unit at King Chulalongkorn Memorial Hospital studied the correlation between bacterial cultures from surveillance weekly endotracheal aspirates before the development of VAP and bacterial cultures from BAL specimens after the diagnosis of VAP.²⁹ This study revealed that there was no correlation, and culturing bacterial species and strains were not the same between those that appeared before and at the development of VAP. In a recent prospective study from Maharaj Nakorn Chiangmai Hospital, a surveillance of pathogen and of the local patterns of antimicrobial susceptibility before VAP development resulted in a decline in mortality, compared to individually made decision physicians.³⁰ The better outcomes might result from antibiotic control strategy and correct pharmacokinetics and pharmacodynamics application, rather than from a direct correlation between surveillance bacterial culture from endotracheal aspirate before VAP development and bacterial culture after VAP development. Considering the cost and effectiveness of such a strategy, the committee does not recommend routine surveillance bacterial cultures from endotracheal aspirate before VAP development.

An appropriate empirical combination antibiotic therapy must cover MDR pathogens in clinical setting with a high incidence or prevalence of MDR bacteria and for patients having risk factors for MDR pathogens (IA).³¹ If empirical aminoglycoside is prescribed, it should be stopped after 5-7 days of therapy once the patient has shown an improvement (IIIA).³²

Patients who develop HAP or VAP and have no risk factors for MDR organisms are likely to respond to antibiotic monotherapy.

There are no data to prove good outcomes using aerosolized antibiotics in HAP or VAP therapy (IA).³³ However, aerosolized antibiotics can be used as adjunctive therapy in patients with HAP or VAP caused by MDR pathogens who do not respond to parenteral antibiotics.

Recommendations for antibiotic selection before obtaining bacteriologic results

Empirical antibiotics in patients with suspected HAP or VAP before obtaining the bacteriologic results are selected by considering risk factors of MDR pathogens, etiologic pathogen and their antibiotic susceptibility patterns common at the location (ward and hospital). And, importantly, collecting information and updating these data should be done on a regular basis. Combination antibiotic therapy is recommended if there is a high incidence or prevalence of resistant pathogens at the location.

Antibiotic selection for *Staphylococcus aureus* is based on Gram stained sputum from endotracheal aspirate with Gram-positive cocci in clusters. The selection of either cloxacillin or a glycopeptide antibiotic for *S. aureus* depends on the incidence or prevalence of methicillin-resistant *S. aureus* (MRSA) infection at the location.

Recommended empirical antibiotic treatment for Gram-negative bacteria and *S. aureus* appears in Table 4¹ and includes type, optimal dose, and method of administration for each drug in Table 5.¹

3.3 Changing antibiotics after obtaining the bacteriologic results

The selected empirical antibiotic usually has a broad spectrum and covers common and MDR pathogens. If the therapy with such a broad-spectrum antibiotic is of long duration, it will encourage colonization of antibiotic-resistant bacteria. Such secondary infection with antibiotic-resistant bacteria results in spread of such resistant strains to other wards, and increases the hospitals budget for antibiotics. This is why therapy should be adjusted as soon as the antibiotic susceptibility pattern is known. Adjustment of antibiotics consists of using a specific narrow-range agent at optimal dosage, appropriate duration of therapy, and good penetration to the site of infection.

A study of 60 culture confirmed VAP patients, 66.1% should receive adjusted antibiotics after obtaining the microbiologic results. However, the antibiotics were

adjusted in only 24.4% of those patients, and most adjustments were delayed until day 4 after reporting.³⁴

3.4 Duration of antimicrobial agents

Many studies revealed that the duration of antibiotic therapy in responding cases of VAP was not necessary to be 14-21 days as previously recommended. Dennesen and colleagues demonstrated that when VAP was caused by *Haemophilus influenzae* and *Streptococcus pneumoniae*, the organisms could be rapidly eradicated from endotracheal aspirates, whereas Enterobacteriaceae, *S. aureus*, and *P. aeruginosa* persisted longer despite in vitro susceptibility to the antibiotics administered.³⁵ Significant improvement was observed in all clinical parameters, usually within the first 6 days of appropriate antibiotics. Luna and colleagues, used serial CPIS evaluation and found that patients who survived VAP after receiving adequate therapy tended to show a clinical improvement by day 3-5 of therapy.³⁶ Chastre and colleagues, in a multicenter randomized controlled study, demonstrated that patients who received appropriate initial empirical therapy of VAP for 8 days, had outcomes similar to those of patients who received therapy for 14 days.³⁷ There was, however, a trend to greater rates of relapse for short-duration therapy if the etiologic agent was *P. aeruginosa* or an *Acinetobacter* spp. (IA).

However, a small study in Thailand found that patients with HAP or VAP caused by *P. aeruginosa* or *Acinetobacter* spp. who received appropriate antibiotics had an average duration of treatment of 8 days, but did not show an increased mortality, relapse rate, and duration of hospitalization.³⁸

Recommendations for the duration of antimicrobial agent

The committee recommends that appropriate antibiotic treatment for HAP or VAP patients with a good initial clinical response should be continued for 7-10 days, provided that the etiologic pathogen is not *P. aeruginosa* or *Acinetobacter* sp.

3.5 Antibiotic therapy for some types of bacteria

Pseudomonas aeruginosa

P. aeruginosa has the capacity to readily develop resistance to all known classes of antibiotics. This can develop in 30-50% of patients receiving monotherapy, but no data show that this problem can be avoided by the use of combination therapy. A

meta-analysis evaluating the addition of an aminoglycoside to a β -lactam monotherapy did not show benefit for the therapy of *P. aeruginosa* in patients with sepsis (IA).³¹ But all studies in this meta-analysis have not used once daily dosing of the aminoglycoside.

No randomized controlled study has compared a fluoroquinolone combination with β -lactam monotherapy of HAP or VAP. The committee can therefore not conclude that β -lactam plus fluoroquinolone is better than β -lactam monotherapy.

***Acinetobacter* spp.**

At present, there is an increased incidence of carbapenem-resistant or MDR *Acinetobacter* spp. in Thailand. Based on susceptibility testing, some antibiotics can be used to treat such resistant strains. These are sulbactam, polymyxin B, colistin, tigecycline and fosfomycin. This statement is based on case series or case reports publications.³⁹ To date, no randomized controlled studies has been performed.

Extended-spectrum β -lactamase (ESBL)-producing Enterobacteriaceae

There is no randomized controlled trial of treatment of patients with HAP or VAP caused by extended-spectrum β -lactamase (ESBL)-producing Enterobacteriaceae. A reliable choice is a carbapenem including ertapenem (where there is no risk factors for *P. aeruginosa* and *Acinetobacter* spp.), imipenem and meropenem. There are small studies comparing fosfomycin⁴⁰, colistin⁴¹, or tigecycline⁴¹ for the treatment of ESBL-producing organisms.

Methicillin-resistant *Staphylococcus aureus* (MRSA)

Vancomycin or teicoplanin has been accepted as a standard therapy for this pathogen. However, many centers have reported clinical failure rates of 40% or greater. A prospective randomized trial of quinupristin–dalfopristin for Gram–positive nosocomial pneumonia found worse clinical success than with vancomycin for MRSA HAP (IA).⁴² Quinupristin–dalfopristin is not yet available in Thailand. Two recent large multicenter studies in patients with HAP or VAP due to MRSA found that linezolid had a significant association with both clinical cure and lower mortality rates (IIA).⁴³ At present, there is as yet no published randomized controlled study.

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Table 1. Quality of evidence and strength of recommendations (adapted from the Infectious Diseases Society of America (IDSA) and United States Public Health Service).¹

Category, grade	Definition
Strength of recommendation	
A	Good evidence to support a recommendation for use, should always be offered.
B	Moderate evidence to support a recommendation for use, should generally be offered.
C	Poor evidence to support a recommendation, optional.
D	Moderate evidence to support a recommendation against use, should generally not be offered.
E	Good evidence to support a recommendation against use, should never be offered.
Quality of evidence	
I	Evidence from ≥ 1 properly randomized, controlled trial.
II	Evidence from ≥ 1 well-designed clinical trial, without Randomization, from cohort or case-controlled analytic studies (preferably from > 1 center), from multiple time-series, or from dramatic results from uncontrolled experiments.
III	Evidence from opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

Table 2. Components of modified clinical pulmonary infection scores (CPIS).⁶

Factors	Points
1. Temperature ($^{\circ}\text{C}$)	
36.5–38.4 $^{\circ}\text{C}$	0
38.5–38.9 $^{\circ}\text{C}$	1
≤ 36.0 $^{\circ}\text{C}$ or ≥ 39.0 $^{\circ}\text{C}$	2
2. WBC (cells/mm ³)	
4000–11,000	0
< 4000 or > 11,000	1
Band forms $\geq 50\%$ WBC	2
3. Sputum	
No sputum	0
Non-purulent sputum	1
Purulent sputum	2
4. Oxygenation: $\text{PaO}_2/\text{FIO}_2$ (mmHg)	
> 240 or presence of ARDS ($\text{PaO}_2/\text{FIO}_2 \leq 200$ or PAWP ≤ 18 mmHg plus new chest infiltrate)	0
≤ 240 and no ARDS	2
5. CXR	
No infiltrate	0
Diffuse or patchy infiltrate	1
Localized infiltrate	2
6. Progression of infiltration from CXR	
No infiltrate progression	0
Infiltrate progression (no ARDS or CHF)	2
7. Culture from tracheal aspirate	
No, light, or rare growth of pathogenic bacteria	0
Moderate or heavy growth of pathogenic bacteria	1
Growth of pathogenic bacteria similar to that from Gram stain	2

ARDS: adult respiratory distress syndrome, PAWP: pulmonary artery wedge pressure, $\text{PaO}_2/\text{FIO}_2$: arterial oxygen pressure divided by fraction of inspired oxygen, CXR: chest X-ray, CHF: congestive heart failure.

Table 3. Risk factors for multidrug-resistant strains causing hospital-acquired pneumonia or ventilator-associated pneumonia.^{1,22-25}

1. Antimicrobial therapy in the preceding 90 days.
2. Current hospitalization of 5 days or more.
3. High frequency of antibiotic resistance in the specific hospital unit.
4. Immunosuppressive disease and/or therapy.

Table 4. Empirical therapy for hospital-acquired pneumonia (HAP) or ventilator-associated pneumonia (VAP).¹

Pathogens	Combination antibiotic therapy ¹
1. Gram-negative bacilli	Antipseudomonal cephalosporin
<i>Pseudomonas aeruginosa</i>	or
<i>Acinetobacter</i> spp ²	Antipseudomonal carbapenem
<i>Escherichia coli</i> ³	or
<i>Klebsiella pneumoniae</i> ³	β -lactam/ β -lactamase inhibitor
Other Enterobacteriaceae ³	
	And/or
	Antipseudomonal fluoroquinolone
	or
	Aminoglycoside
2. <i>Staphylococcus aureus</i>	Cloxacillin or glycopeptide ⁴

¹See Table 5 for the type and dosage of antibiotics used. Initial empirical antibiotic therapy should be selected on the basis of local bacteriologic data and the presence of risk factors for multidrug-resistant bacteria (Table3).

²If *Acinetobacter* sp. is suspected, a carbapenem is a reliable choice except there is a high frequency of carbapenem-resistant strains.

³If there is a high frequency of extended-spectrum β -lactamase-producing strains, a carbapenem is a reliable choice.

⁴A glycopeptide is selected if there is a high frequency of methicillin-resistant *Staphylococcus aureus*.

Table 5. Types and doses of intravenous antibiotics for the therapy of hospital-acquired pneumonia (HAP) or ventilator-associated pneumonia (VAP) in adults with normal liver and renal functions.

Antimicrobial agents	Dosage
1. Non-antipseudomonal third-generation cephalosporins	
Ceftriaxone	2 g every 24 hrs
Cefotaxime	1 g every 6-8 hrs
2. Antipseudomonal cephalosporins	
Ceftazidime	2 g every 8 hrs
Cefepime ¹	1-2 g every 8-12 hrs
Cefpirome ¹	1-2 g every 8-12 hrs
3. Carbapenems	
Ertapenem ²	1 g every 24 hrs
Imipenem	500 mg every 6 hrs or every 8 hrs
Meropenem	1 g every 8 hrs
4. β -lactam/ β -lactamase inhibitors	
Piperacillin/tazobactam	4.5 g every 6 hrs
Cefoperazone/sulbactam ³	1-2 or 1.5-3.0 ⁶ g every 12 hrs
5. Aminoglycosides	
Gentamicin	7 mg/kg every 24 hrs
Amikacin	20 mg/kg every 24 hrs
Netilmicin	7 mg/kg every 24 hrs
Tobramycin	7 mg/kg every 24 hrs
6. Antipseudomonal fluoroquinolones	
Ciprofloxacin	400 mg every 8 hrs
Levofloxacin	750 mg every 24 hrs
7. Cloxacillin	2 g every 4-6 hrs ⁷
8. Glycopeptides	
Vancomycin	15 mg/kg every 12 hrs
Teicoplanin	6 mg/kg every 24 hrs (first 3 doses at 6-12 mg/kg every 12 hrs for 3 times)
9. Linezolid	600 mg every 12 hrs
10. Fosfomycin ⁴	2-4 g every 8-12 hrs
11. Tigecycline ⁵	First dose at 100 mg, followed by 50 mg every 12 hrs

¹Maximum dosage in case of *Pseudomonas aeruginosa* and *Acinetobacter baumannii*.

²Ertapenem is used for empirical therapy of HAP or VAP caused by extended-spectrum β -lactamase (ESBL)-producing Enterobacteriaceae.

³Sulbactam dosage for the therapy of HAP or VAP caused by *Acinetobacter baumannii* is 4-6 g/day

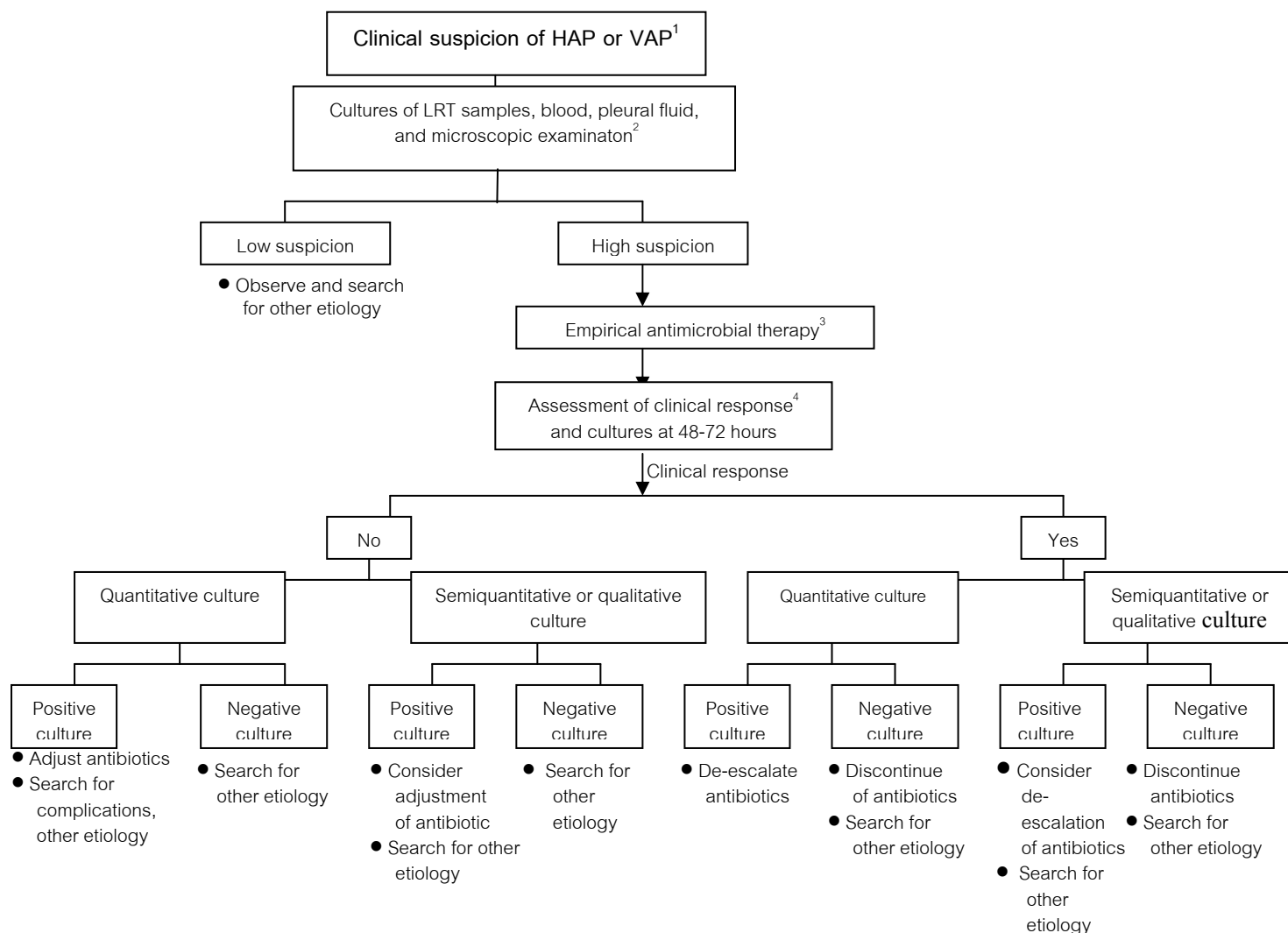
⁴Fosfomycin should be used in combination with other drugs except vancomycin in case of HAP or VAP caused by Gram-positive bacteria; the dosage should be 4 g every 8 hours for therapy of Gram-negative infections.

⁵Tigecycline should be used for therapy of HAP or VAP caused by multidrug-resistant bacteria except *Pseudomonas aeruginosa*.

⁶For drug preparation containing 1 g of cefoperazone and 0.5 g of sulbactam.

⁷Levofloxacin use in therapy of HAP or VAP caused by *P. aeruginosa* increases risk of failure if the MIC >1 µg/mL.

Figure 1. Algorithm for the management strategies for an adult patient with suspected hospital-acquired pneumonia (HAP) or ventilator-associated pneumonia (VAP).



LRT: lower respiratory tract.

¹Clinical suspected HAP or VAP include new or progressive chest infiltrate plus at least 2 of 3 criteria as follows: a, new or increase of fever b, purulent sputum and c, white blood cell count of $\geq 12,000$ or $< 4,000$ cells/mL.

²See text for detailed in methods for bacterial cultures and microscopic examination.

³See text and Tables 3, 4, and 5 for details.

⁴Clinical evaluation consists of vital signs especially blood pressure and body temperature, character and volume of respiratory secretion, white blood cell count, arterial oxygen contents, and chest radiographic features.

Appendix

I. Semiquantitative culture of endotracheal aspirate.¹

Criteria for rating scales of semiquantitative of endotracheal aspirate.

0: no bacterial colony on agar plate.

1+ (rare growth, <10 colonies on agar plate): bacterial colonies on quadrant 1.

2+ (a few growth, 10-10² colonies on agar plate): bacterial colonies on quadrants 1 and 2.

3+ (moderate growth, >10²-10³ colonies on agar plate): bacterial colonies on quadrants 1, 2, and small amount on quadrant 3.

4+ (numerous growth, >10³-10⁴ colonies on agar plate): bacterial colonies on quadrants 1, 2, and 3.

5+ (numerous growth, >10⁴ colonies on agar plate): bacterial colonies on quadrants 1, 2, 3, and 4.

II. Quantitative culture of endotracheal aspirate (ETA) and bronchoalveolar lavage (BAL)²⁻⁴

Processing of endotracheal aspirate (ETA).

1. Use catheter with 22-inch, 12-F size for endotracheal aspirate.
2. Pass catheter through endotracheal tube at least 30-cm long.
3. Percuss and vibrate at chest wall at least 10 minute duration.
4. Softly suck secretion without pouring normal saline in bronchus.
5. Do not use first ETA, but use the second ETA by connect catheter with Lukian tube.
6. Volume of ETA should be at least 1 mL.

Processing of bronchoalveolar lavage (BAL).

1. Pass bronchoscope (or protected system) through endotracheal tube until subsegmental bronchus (normal position at third or fourth bronchus). Occlude proximal respiratory tract at the lesion in chest radiography.
2. Do 7 aliquots, pour 20 ml. of normal saline into the bronchus, and gently suck BAL for each aliquot.
3. Do not use the first 2 aliquots.

4. Collect the latter 5 aliquots together as one sample.

Microbiological processing.

1. Sent ETA or BAL to microbiological laboratory room immediately (or within 15 minutes and no later than 60 minutes).
2. Test ETA or BAL for a good quality sample by microscopic examination (Table 1).
3. Centrifuge ETA or BAL with glass beads by vortex for 1-minute duration.
4. Then, centrifuge at 3,000 cycles/min for 10-minute duration.
5. Dilute content with sterile normal saline for the final concentration of 1:10, 1:1,000, and 1:100,000 (Figure 1).

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Table 1. Criteria of good quality of endotracheal aspirate (ETA) and bronchoalveolar lavage (BAL) samples for quantitative culture.

	ETA	BAL
1. Neutrophils	> 25/LPF	77-82%
2. Squamous epithelial cells	< 10/LPF	< 1%
3. Intracellular organisms	ND	≥ 5%
4. Quantitative culture threshold (cfu/ml)	≥ 10 ⁵ -10 ⁶	≥ 10 ⁴

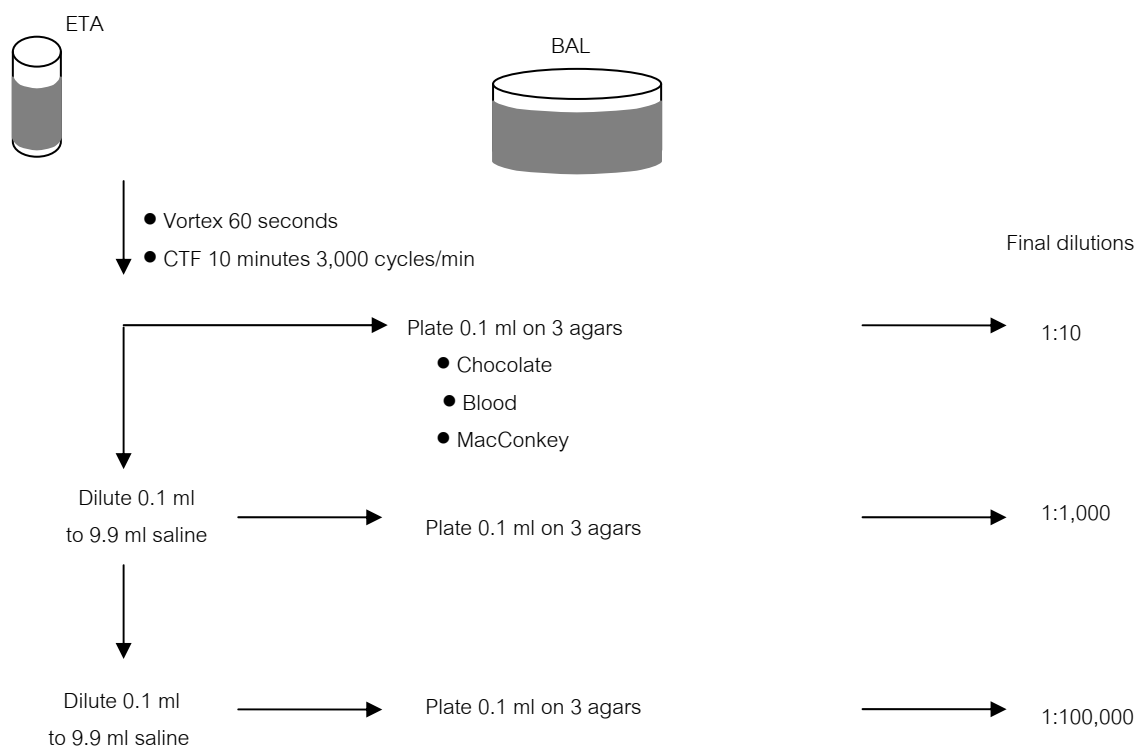
LPF: low-power field, ND: no data, cfu: colony-forming units

Table 2. Sensitivity and specificity of endotracheal aspirate (ETA) and bronchoalveolar lavage (BAL) for diagnosis of hospital-acquired pneumonia (HAP) or ventilator-associated pneumonia (VAP).

	ETA (%)	BAL (%)
1. Sensitivity	38-100	42-93
2. Specificity	14-100	45-100

Figure 1. Technique for quantitative culture of endotracheal aspirate (ETA) and bronchoalveolar lavage (BAL).

CTF: centrifugation.



Part II. Prevention hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP)

I. Epidemiology

In 2001, an epidemiological study of nosocomial infections from 42 hospitals in Thailand found that the most common was lower respiratory tract infection including pneumonia and bronchitis (34.1% of nosocomial infections). An average antibiotic cost for the treatment of lower respiratory infection was 9,938 baht per infection, and an average duration for the treatment was 12.4 days. HAP and VAP were the most common nosocomial infections in Thailand, and were associated with high budget and duration of treatment. Intubation was the most common risk factor for lower respiratory tract infections. The patients who received endotracheal tube and ventilator had a 2.2-fold higher risk than those who did not receive mechanical ventilator (95% confidence interval = 18.6-26.6)¹. A recent study in Thailand revealed the average incidence of VAP was 12.6 per 1,000 ventilator-days. The VAP incidence varied among different types of hospitals, ranging from 11.5 to 14.3 per 1,000 ventilator-days.²

II. Principles of prevention

Education of healthcare workers regarding preventing of HAP or VAP is the most important strategy. During 2003 and 2004, a study from 12 hospitals in Thailand revealed a decline in the incidence rate of HAP and VAP when healthcare workers had competency and responsibility in the healthcare setting, instructed by infection control nurses (ICN). The main activities of ICN consisted of educating the healthcare workers regarding hand washing before and after contacting patients, suctioning of respiratory secretions, and hand washing before using respiratory devices. These activities decreased the morbidity of HAP and VAP from 40.5% to 24.0%, and decreased mortality from 12.5% to 8.7%³. A study from Maharaj Nakorn Chaing Mai Hospital showed that hand washing before contacting patients decreased the incidence of VAP to 50%.⁴

III. Clinical practice guidelines for prevention of HAP and VAP

From the above data, the committee recommends clinical practice guidelines for prevention of HAP and VAP. This guideline should be applied only for bacterial pathogen and not for higher bacteria such as *Nocardia* spp.

Activities	Management
0 General practice	<p>Educate healthcare workers continuously about preventive measures for HAP or VAP.</p> <p>Conduct surveillance patient care every steps including hand washing with alcohol-based hand rub before and after contacting patients, wearing gloves before and after contacting infected part of the body, and washing hands contaminated with blood or secretion with soap and water.⁵⁻⁸</p>
1 Intubation	<p>Hygienic hand antiseptics before and after intubation (IA).⁵⁻⁸</p> <p>Oral intubation (IA).⁵⁻⁷</p>
2 Tracheostomy	<p>Use aseptic technique (II).⁷</p> <p>Wear a gown if changing tracheostomy tube with aseptic technique (IB).⁷</p> <p>Should perform in the operating room(III).</p>
3 Management patients with endotracheal or tracheostomy tube	<p>Decontaminate hands before and after giving care to or touching a patient or touching a patient's respiratory secretions, whether or not gloves are worn (IA).</p> <p>After contact any parts of a patient's body, hand washing followed hand hygiene practice was done before giving respiratory care at the same patient (IIIA).⁷⁻⁸</p> <p>Check cuff pressure of endotracheal tube at least every 12 hours; the pressure should be 20-30 mmHg.⁹⁻¹¹</p>
4 Suction of respiratory tract secretions	<p>When there is an indication as follows:</p> <ol style="list-style-type: none"> 1. Signs and symptoms of large amount of secretions in the respiratory tract. 2. Before deflating cuff of endotracheal tube for extubation (II).⁷ 3. Before feeding enteral tube (IIIA). <p>The in-line suction catheter of a closed-suction system does not decrease morbidity of pneumonia. Its use reduce the</p>

budget especially in a patient who requires frequent suction of respiratory tract secretions.

The single-use open-system suction catheter can be used. In case of using of repeated-use open-system catheter, suction of catheter with sterile normal saline should be done before reuse to the same patient (II).⁷

Use aseptic technique for suction respiratory tract secretions (II).

Clean joints of respiratory equipments with 70% alcohol before and after opening joint circuit (III).

- | | | |
|---|-----------------------------|--|
| 5 | Prevention of aspiration | <p>of Remove respiratory device such as endotracheal tube, tracheostomy tube, enteral feeding tube as soon as possible when there is no indication (IB).⁷</p> <p>Use non-invasive positive-pressure ventilation (NIV) instead of endotracheal tube, or try to reduce the duration of endotracheal intubation, if there is no indication (IB).⁷</p> <p>Patients with endotracheal or enteral tube feeding should be kept in the semirecumbent position (30°-45°) if no contraindication (II).</p> <p>Oropharyngeal cleaning and decontamination with 0.12% chlorhexidine oral rinse is used for prevention of pneumonia in preoperative cardiac surgery patients (II).⁷</p> <p>Prophylaxis of stress ulcer is not suggested in every patient with intubation. If the patient has a major risk, including receiving mechanically assisted ventilation more than 48 hours and abnormal coagulopathy, he should be considered the risk and benefit for the opportunity of pneumonia versus upper gastrointestinal bleeding.⁶</p> <p>Check proper position of enteral tube before feeding (IB).⁷</p> |
| 6 | Prevention of postoperative | <p>of Instruct preoperative patients about taking deep breaths and ambulating as soon as medically indicated in the post-</p> |

pneumonia	operative period, if there is no contraindication (IB). ⁷
7 Respiratory equipments	<p data-bbox="614 257 1390 414">Wash medical device completely before sterilization (visibly dirty or proteinaceous material or soiled with blood or body fluids).</p> <p data-bbox="614 436 1390 996">Use high-level disinfection or sterilization for processing semicritical equipment or devices. Whenever possible, the first choice should be the physical method (wet heat pasteurization at $>70^{\circ}\text{C}$ or $>158^{\circ}\text{F}$ for 30 minutes). And the chemical method (soaking the device in glutaraldehyde, rinsing with filtered or tap water, then rinsing with isopropyl alcohol, and then drying and packaging with contaminate precaution) should be the alternative choice (IB).⁷ Respiratory device or equipment must be sterilized or high-level disinfected (Table1).</p> <p data-bbox="614 1019 1390 1120">Use sterile water in humidifier or nebulizer in open system with aseptic technique (IA).⁷</p> <p data-bbox="614 1142 1390 1243">Do not change sterile water routinely because there is no supporting (IIIB).</p> <p data-bbox="614 1265 1390 1355">Change sterile water in the empty humidifier or nebulizer in closed system with aseptic technique (IA).⁷</p> <p data-bbox="614 1377 1390 1590">Do not change breathing circuit (i.e. ventilator tubing and exhalation valve and the attached humidifier) routinely. Change the circuit when it is visibly soiled or mechanically malfunctioning (IA).⁷</p> <p data-bbox="614 1612 1390 1825">Use aerosolized medications in single-dose vials. If multidose medication vials are used, follow manufacturers' instructions for handling, storing, and dispensing the medications (IB).⁷</p> <p data-bbox="614 1848 1390 2002">Do not routinely change the circuit of heated-moisture exchange (HME). Change immediately when there is a malfunction (II).⁷</p>

There is no data for recommendation of changing the circuit of heated-wire circuit or heated humidifier.

Periodically drain and discard any condensate that collects in the tubing of a mechanical ventilator, taking precautions not to allow condensate to drain toward the patient (IA).⁷

Other respirator equipment including mist-tent nebulizers, reservoirs, and tubings that are used on the same patient should be low-level disinfected daily (soaking with 2% acetic acid) or pasteurized (II).⁷

Resuscitator bag and connection port for each patient should be cleaned before and after reuse to the same patient. Between their uses on different patients, they should be sterilized or high-level disinfected (IB).⁷

Use oxygen humidifier closed system and follow manufacturers' instructions for use of oxygen humidifiers. Change the humidifier-tubing (including any nasal prongs or face mask) when it malfunction or becomes visibly contaminated (II).⁷

Small-volume medication nebulizers, both in-line and hand-held nebulizer, between treatments on the same patient should be cleaned, disinfected, rinsed with sterile water (if rinsing is needed), and dried with alcohol (IB).⁷

8 Surveillance nosocomial pneumonia

Conduct surveillance for nosocomial pneumonia in patients who are at high risk for healthcare-associated pneumonia (e.g. patients with mechanically assisted ventilation, post-operative chest or upper abdominal surgery, ICU patients). Express data as rate (e.g. number of infections per 1,000 ventilator-days) to facilitate intrahospital comparison and trend determination. Link the rates and prevention efforts and return data to appropriate healthcare workers for quality development.

Table 1. Respiratory devices or equipment that requires sterilization or high-level disinfection.

:

- Face mask or tracheal tube
 - Inspiratory and expiratory tubing
 - Y-piece
 - Reservoir bag
 - Humidifier
- Breathing circuits of mechanical ventilators
- Bronchoscopes and their accessories, except for biopsy forceps and specimen brush
- Endotracheal and endobronchial tubes
- Laryngoscopes blades
- Mouthpieces and tubing of pulmonary-function testing equipment
- Nebulizers and their reservoirs
- Oral and nasal airways
- Probes of CO₂ analyzers, air-pressure monitors
- Resuscitation bags
- Stylets
- Suction catheters
- Temperature sensors

¹Items that directly or indirectly contact mucous membranes of the respiratory tract should be sterilized or subjected to high-level disinfection before reuse.

²Considered critical items and should be sterilized before reuse.

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