Original Article

# Predicting Positive Blood Cultures in Patients presenting with Pneumonia at an Emergency Department in Singapore

Gregory Cham,[1] *MBBS, FRCSEd, FAMS*, Sun Yan,[2] *PhD (Medical Informatics)*, Heng Bee Hoon,[2] *MBBS, MSc (Public Health), FAMS*, Eillyne Seow,[1] *MBBS, FRCSEd, FAMS*

## Abstract

**Introduction: Routine blood cultures have been recommended for all patients in treatment guidelines for community-acquired pneumonia (CAP). This practice has become a major area of resource utilisation, despite the lack of evidence in its clinical utility. Calls for abandoning the practice is balanced by the occasions of uncovering an unexpected pathogen or an unusual antimicrobial resistance pattern. The aim of this study is to identify factors that predict positive blood cultures among patients hospitalised for pneumonia upon presentation at the Emergency Department (ED). Materials and Methods: A case control study was carried out on patients treated for pneumonia in the ED who had routine blood cultures performed as part of their management. The pneumonia severity index (PSI) was used to categorise patients into low- and high-risk for 30-day mortality. Logistic regression was carried out to determine factors significantly associated with positive blood cultures, from which a predictive probability equation was used to identify patients whose blood cultures were negative at a pre-determined cut-off, with minimum number of culture positive misclassification. A scoring system was devised, with scores predicting which patients would be likely to have a positive or negative blood culture. Results: A total of 1407 patients with pneumonia were treated at ED from May to December 2006, from whom 1800 blood cultures were performed. Of these, 140 cultures (7.8%) grew organisms, comprising 96 (5.3%) true positive cultures and 44 (2.4%) contaminated cultures. Logistic regression analysis identified ill patients with higher PSI classes, smokers and Malay patients to be more likely to have positive blood cultures. Patients who had prior treatment with antibiotics, chronic obstructive pulmonary disease and cough were less likely to have positive blood cultures. An index to predict a negative blood culture resulted in the accurate classification of all but 4 positive patients while still correctly classifying 27.8% of blood culture negative patients. The area under the ROC curve was 0.71 (95% CI, 0.65-0.76). A simplified scoring system was devised based on the predictive model had a sensitivity of 82% and specificity of 38.2% for a positive blood culture. Conclusion: Routine blood cultures yielded negative results in 94% of patients presenting with pneumonia. The development of the clinical scoring system is a first step towards selecting patients for whom blood cultures is performed and improve cost-effectiveness.**

**Ann Acad Med Singapore 2009;38:508-14**

**Key words: Community acquired pneumonia, Emergency department, Positive blood culture, Predictors**

## Introduction

Pneumonia is the fourth leading cause for hospitalisation, and the third leading cause of death in Singapore.[1] Overall, it is consistently one of the most expensive diseases to treat among elderly persons with multiple co-morbid conditions,[2] a challenge to our healthcare system with a rapidly ageing population. Treatment guidelines for pneumonia invariably recommend performing blood cultures. This practice has become a major area of resource utilisation, despite the poor yield of blood cultures.

Blood cultures have good specificity in identifying pathogens. Its poor sensitivity however, renders the chance

[1] Department of Emergency Medicine, Tan Tock Seng Hospital, Singapore
[2] Health Services and Outcomes Research, National Healthcare Group, Singapore
Address for Correspondence: Dr Gregory Cham, Department of Emergency Medicine, Tan Tock Seng Hospital, 11 Jalan Tan Tock Seng, Singapore 308433.
Email: Gregory_Cham@ttsh.com.sg

of altering the therapy directed by the results of the culture very low,[3-5] with questionable cost-effectiveness.[6] On the other hand, false positive blood cultures prolong hospital stay and costs.[6-8]

The evidence base for performing routine blood cultures for all and unqualified patients with community-acquired pneumonia (CAP) had been vigorously challenged and some have argued for the practice to be abandoned.[9,10] Yet the practice of universal blood cultures for patients hospitalised for CAP continues, driven by the occasions of uncovering an unexpected finding. The discovery of an unusual antimicrobial resistance pattern,[11,12] like the shifting drug resistance of pneumococcus[13] and the discovery of community-acquired methicillin-resistant *Staphylococcus aureus* infections[14,15] have been cited as examples for the continuing need to do blood cultures.

Other studies have recommended a more focused and discriminatory approach to doing blood cultures, recommending it for patients with severe CAP with high mortality risk.[6,16] To translate evidence and effect a change in policy and practice for appropriate and cost-effective and safe care, physicians need convincing evidence of the clinical purpose of routine blood cultures in the local context. The aim of this study is to identify factors that predict positive blood cultures among patients hospitalised for pneumonia upon presentation at the Emergency Department (ED).

## Materials and Methods

A case control study was carried out on all patients from the community, who were treated for pneumonia at the ED from May to December 2006. Pneumonia was diagnosed based on symptoms of fever, cough, sputum production, crepitations or consolidation in the lungs with radiological findings suspicious for pneumonia at their initial presentation at the ED. Patients were either hospitalised or discharged from ED. For hospitalised cases, patients were enrolled if the discharge diagnosis concurred with the ED's diagnosis of pneumonia or had a chest x-ray report compatible with pneumonia. This approach was taken because of the absence of a gold standard in the diagnosis of pneumonia[17,18] and high false positives in the diagnosis of pneumonia in the ED.[19] Patients who were not admitted were enrolled if they had a clinical diagnosis of pneumonia and a chest X-ray report compatible with pneumonia.

All patients had routine blood cultures performed as part of their management at the ED. Cases consisted of patients who had positive blood cultures and those with negative or contaminated blood culture results made up the controls. Blood cultures which grew coagulase-negative staphylococcus, micrococcus species, corynebacterium species, clostridium species, bacillus species were considered contaminants. However, coagulase-negative staphylococcus or clostridium species isolated from the blood culture were considered clinically significant if the pneumonia is associated with an infected surgical implant or skin wound.[8]

Case-notes were reviewed for every patient with a diagnosis of pneumonia at ED, by a trained research assistant, and with the approval the ethics committee. Information collected included patients' demographic characteristics (age, gender and ethnic group), symptoms, smoking history, medical history and immunosuppression (receiving immunosuppressant medications, steroids, splenectomy, transplant recipient, HIV status). The pneumonia severity index (PSI) was used to categorise patients into low- and high-risk for 30-day mortality.[20] Information collected for computation of the PSI included (i) whether or not the patient was a nursing home resident, (ii) presence of co-existing illness (neoplastic disease, liver disease, congestive heart failure, cerebrovascular disease, renal disease), (iii) findings on physical examination (altered mental status, respiratory rate, systolic blood pressure, temperature, and pulse rate), (iv) laboratory and radiologic findings (arterial blood pH, blood urea, serum sodium, glucose, haematocrit, $pO_2$ or $O_2$ saturation, pleural effusion on chest X-ray). The PSI scores were summed and patients were grouped into 5 risk classes, from I to V with increasing 30-day mortality from 0.1% to 29%, respectively. In addition, information on hospital admissions in the previous 7 days, intensive care unit admission, prior antibiotic treatment before arrival at the ED, number of blood cultures performed and length of hospital stay were also recorded.

### *Statistical Analysis*

Chi-square and Fisher's exact tests were used to compare categorical variables. The Fisher's exact test was used if the cells in the Chi-square test had less than 5 counts. The T-test and the non-parametric Mann-Whitney U test were used to compare means for continuous variables in univariate analysis. Multivariate analysis by logistic regression was carried out to determine factors significantly associated with positive blood cultures. The stepwise forward method was used to estimate the model. The following variables were considered for inclusion: patients' demographic characteristics (age, gender and ethnic group), PSI class, antibiotics given prior to ED presentation, antibiotics given within 4 hours, symptoms of cough and haemoptysis, smoking history, medical history (COPD, IHD, asthma or DM), and immunosuppression (receiving immuno-suppressant medications, steroids, splenectomy, transplant recipient, HIV status).

Based on the significant factors identified by logistic regression, a predictive probability equation was used to

identify patients whose blood cultures were negative at a pre-determined cut-off, with minimum number of culture positive misclassification. Based on the predictive model, a scoring system was devised, with scores predicting which patients would be likely to have a positive or negative blood culture upon presentation at the ED. The receiver operating characteristic (ROC) curve was plotted to determine maximum accuracy. All statistical analyses were performed using SPSS version 15. All tests were conducted at the 5% level of significance. The odds ratios (OR) and corresponding 95% confidence intervals (95% CI) were reported where applicable.

## Results

A total of 1407 eligible patients were treated at the ED from May to December 2006 who had a diagnosis of pneumonia. Patients' characteristics are summarised in Table 1. The overall mean age was 71.6 years, ranging from 16 to 105 years, and the female to male ratio was 1:1.15.

Four hundred and thirty-eight (31.13%) of the study patients had Healthcare-associated Pneumonia (HCAP).[21] This classification was based on 279 patients who were residents of nursing homes, 90 patients who had chronic wounds, 72 immunosuppressed patients, 11 were on dialysis. Forty-five patients were admitted in the preceding 7 days before enrolment in the study.

A total of 1800 blood cultures were performed, of which 140 cultures (7.8%) grew organisms, comprising 96 (5.3%) true positive cultures and 44 (2.4%) contaminated cultures (Table 2). A total of 89 patients (6.3%) had at least one positive blood culture and 44 patients (3.1%) had at least one contaminated blood culture. Twenty-eight (1.99%) of HCAP patients had positive blood cultures.

Thirty patients had either significant *Coagulase Negative Staphylococcus*, or *Staphylococcus aureus*, or methicillin-resistant *Staphylococcus aureus* infection (Table 2). Among them, 15 patients (50%) also had skin lesions, 4 had infective endocarditis, 2 had lung abscesses, 2 had empeyema and 1 patient also had pyogenic arthritis.

*Escherichia coli* infection was found in 18 (18.8%) of the cultures. Among these patients, a total of 13 (72.2%) patients had a neurological defect that could result in aspiration. Eleven (61.1%) had urinary tract infection, out of which 5 patients also had dysphagia or swallowing impairment.

Logistic regression analysis showed that blood cultures were more likely to be positive in sicker patients in higher PSI classes, the odds ratio being 2.0 and 3.0 in PSI Classes IV and V respectively, compared to that of PSI Class II (Table 3). A smoker had 70% higher odds of having positive blood culture than a non-smoker; and Malay and Indian patients were more likely to be positive compared to Chinese patients. Patients who were given antibiotics prior to ED attendance had significantly reduced rate of positive blood cultures. Patients with chronic obstructive pulmonary disease (COPD) or had cough were less likely to have positive blood cultures (Table 3). Patients classified

Table 1. Characteristics of Patients Presenting with Community-acquired Pneumonia

| | Blood culture | | *P* value |
|---|---|---|---|
| | **Positive (n = 89)** | **Controls (n = 1318)** | |
| Age (y) | | | |
| Mean | 73 | 72 | 0.59[b] |
| Median | 77 | 76 | |
| Range | 24-104 | 16-105 | |
| Sex (male:female) | 48:41 | 706:612 | 0.95[a] |
| Race, No. (%) | | | 0.12[a] |
| Chinese | 63 (70.8%) | 1028 (78%) | |
| Malay | 16 (18.0%) | 137 (10.4%) | |
| Indian | 8 (9.0%) | 102 (7.7%) | |
| Others | 2 (2.2%) | 51 (3.9%) | |
| Cough | 54 (60.7%) | 1011 (76.7%) | 0.001[a] |
| Smokers | 20 (22.5%) | 234 (17.8%) | 0.26[a] |
| Chronic obstructive pulmonary disease | 3 (3.4%) | 133 (10.1%) | 0.04[a] |
| PSI class, No. (%) | | | |
| II | 13 (14.6%) | 349 (26.5%) | 0.009[a] |
| III | 18 (20.2%) | 307 (23.3%) | |
| IV | 36 (40.4%) | 475 (36%) | |
| V | 22 (24.7%) | 187 (14.2%) | |
| Admitted to intensive care/high dependency unit, No. (%) | 12 (13.5%) | 62 (4.7%) | 0.002[a] |
| Blood cultures obtained | | | |
| Mean | 1.9 | 1.2 | < 0.001[b] |
| Median | 1 | 1 | |
| Range | 1-11 | 1-8 | |
| Length of hospital stay (days) | | | |
| Mean | 17 | 8 | < 0.001[b] |
| Median | 10 | 6 | |
| Range | 1-111 | 0-74 | |
| Hospitalisation in preceding seven days | 0 | 45 | 0.11[a] |
| Received prior antibiotic treatment, No. (%) | 3 (3.4%) | 177 (13.4%) | 0.006[a] |

[a] Chi-square or Fisher's exact test
[b] Mann-Whitney U test

Table 2. Blood Culture Results from Pneumonia Patients

| Organism | Postive blood culture (n = 96) | |
|---|---|---|
| | No. | % |
| Gram positive: | | |
| Coagulase-negative *Staphylococcus* | 14 | 14.6 |
| *Streptococcus pneumoniae* | 13 | 13.5 |
| *Staphylococcus aureus* | 11 | 11.5 |
| Methicillin-resistant *Staphylococcus aureus* | 5 | 5.21 |
| Beta-hemolytic *Streptococcus* | 3 | 3.13 |
| *Streptococcus agalactiae* (Group B) | 1 | 1.04 |
| Gram negative: | | |
| *Escherichia coli* | 18 | 18.8 |
| *Citrobacter koseri* | 6 | 6.25 |
| *Klebsiella* | 6 | 6.25 |
| *Pseudomonas aeruginosa* | 3 | 3.13 |
| *Proteus mirabilis* | 3 | 3.13 |
| *Enterococcus* species | 3 | 3.13 |
| *Acinetobacter* | 3 | 3.13 |
| *Bacteroides fragilis* | 2 | 2.08 |
| *Enterobacter* species | 1 | 1.04 |
| *Fusobacterium* species | 1 | 1.04 |
| *Morganella morganni* | 1 | 1.04 |
| Mixed coliforms | 1 | 1.04 |
| Anaerobic gram-negative rods | 1 | 1.04 |
| | **Contaminated blood culture (n = 44)** | |
| Mixed coagulase negative *Staphylococcus* | 33 | 75.0 |
| *Bacillus* species | 4 | 9.1 |
| *Corynebacterium* species | 3 | 6.8 |
| *Micrococcus* species | 3 | 6.8 |
| *Clostridium* species | 1 | 2.3 |

as HCAP were not significantly predictive of a positive blood culture.

A total of 74 patients were admitted into the intensive care or high-dependency unit. The mean length of stay was longer among those with positive culture results compared to those in the control group (17 days vs 8 days) (Table 1). However, those with contaminated results had a mean length of stay of 12 days.

The discharge diagnosis of 1393 hospitalised patients concurred with the ED diagnosis of pneumonia. Chest x-ray findings were congruent with the diagnosis of pneumonia in 65.2% of those with positive blood cultures and in 54.7% with negative blood cultures. There were 14 patients who were not admitted, of these 13 patients had radiological diagnosis consistent with pneumonia.

Table 3. Significant Independent Factors by Logistic Regression Associated with Positive Blood Culture Positive Results

| Independent factors | *P* value | Odds ratio | 95% confidence interval | |
|---|---|---|---|---|
| | | | Lower | Upper |
| Ethnic group | | | | |
| Malay | 0.002 | 2.6 | 1.4 | 4.8 |
| Indian | 0.201 | 1.7 | 0.8 | 3.7 |
| Others | 0.787 | 0.8 | 0.2 | 3.5 |
| [Chinese] | | | | |
| PSI class | | | | |
| PSI class III | 0.184 | 1.7 | 0.8 | 3.5 |
| PSI class IV | 0.049 | 2.0 | 1.0 | 4.0 |
| PSI class V | 0.004 | 3.0 | 1.4 | 6.5 |
| [PSI class II] | | | | |
| Chronic obstructive pulmonary disease | | | | |
| Yes | 0.012 | 0.2 | 0.1 | 0.7 |
| [No] | | | | |
| Smoker | | | | |
| Yes | 0.051 | 1.7 | 1.0 | 3.0 |
| [No] | | | | |
| Cough | | | | |
| Yes | 0.005 | 0.5 | 0.3 | 0.8 |
| [No] | | | | |
| Prior antibiotic treatment | | | | |
| Yes | 0.023 | 0.3 | 0.1 | 0.8 |
| [No] | | | | |

The reference category is denoted in parenthesis [].

*Development of the Predictive Model*

Based on the above regression model, an index to predict a negative blood culture was created. The predicted probability of positive blood culture $(p_i)$ was calculated using the following equation,

$$\ln \frac{p_i}{1-p_i} = -2.90 - 1.36x_{1i} - 1.53\,x_{2i} - 0.69x_{3i} + 0.55x_{3i} + 0.51x_{5i} + 0.69x_{6i} + 1.11x_{7i} + 0.96x_{8i} + 0.51x_{9i} - 0.20x_{10i}$$

For each individual *i*, x1 to x10 are covariates or dependent variables. x1 represents prior treatment with antibiotics; x2 represents presence of COPD; x3 cough; x4 smoker; x5-7 represent PSI classes III-V; and x8-10 represents Malay, Indian or Other ethnic groups, respectively. $P_i$ is the probability of a positive blood culture. A cut-off point was

established by minimising the number of misclassification of positive culture while maintaining a high proportion classified as negative culture. The relevant statistical measures and overall accuracy showed that if $p_i$ is below the cut-off, patient *i* is predicted to have a negative blood culture. Using a cut-off of $P = 0.027$, the model had a sensitivity of 95.5% and a specificity of 27.8%. The cut-off resulted in the accurate classification of all but 4 positive patients while still correctly classifying 27.8% of blood culture negative patients. The area under the ROC curve was 0.71 (95% CI, 0.65-0.76) (Fig. 1), indicating that the model had a good ability to discriminate between patients with positive and those with negative blood culture.

*A Scoring System to Identify Pneumonia Patients With Positive or Negative Blood Cultures*

Using the above predictive model, a simplified scoring system that could be easily applicable was devised based on the predictive model above. The scores were derived from the regression coefficients and their clinical importance is as follows:

The range of the predictive score is from -5 to 5. Patients

| Predictor | Score |
|---|---|
| PSI class V | 3 |
| PSI class IV | 2 |
| Prior antibiotic treatment | -2 |
| COPD | -2 |
| Malay | 1 |
| Smoker | 1 |
| Cough | -1 |

scoring ≥-1 is predicted to have a positive blood culture. The area under the ROC curve was 0.64 (95% CI, 0.58-0.70) (Fig. 2). This model had a sensitivity of 82% and specificity was 38.2% for a positive blood culture. The negative likelihood ratio is 0.47; and the positive likelihood ratio is 1.33.

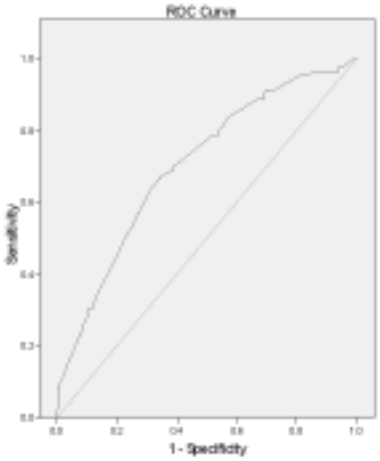


Fig. 1. ROC curve of the predictive model for identifying patients with positive blood cultures.

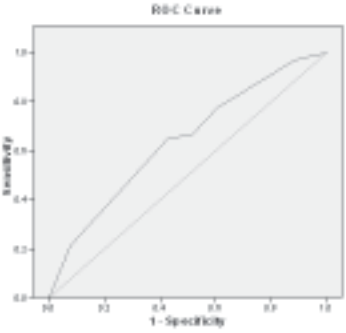


Fig. 2. ROC curve of the scoring system to identify patients likely to have positive blood cultures.

## Discussion

This study had shown that routine blood cultures were negative in 93.7% of patients presenting with pneumonia. Blood cultures were more likely to be positive in patients who were in PSI class IV or V; of Malay origin; or smokers. Prior treatment with antibiotics significantly rendered the blood cultures negative. The presence of COPD or cough were also negative predictors.

Chest X-rays is not a robust gold standard to make a diagnosis of pneumonia. The reliance on subjective radiological features is fraught with poor interobserver reliability. Radiologists only agree moderately about the presence of infiltrates and pleural effusions on chest X-rays of patients with pneumonia. Kappa was 0.37 (95% CI, 0.22-0.52) for infiltrates; and 0.46 (95% CI, 0.33-0.50) for pleural effusion. Radiologists do not agree about the presence of lobar vs. bronchopneumonia or air bronchograms, 0.09 (95% CI, -0.04-0.22) and 0.01 (95% C.I. -0.12-0.14) respectively.[18] Kappa was considerably lower if chronic obstructive pulmonary disease was present (κ 0.20) or *Streptococcus pneumoniae* (κ -0.29) was the infective agent.[22] Clinical features of pneumonia are not unique, but a measure of the clinician's judgment over time, is crucial despite also being similarly affected by subjectivity.[17] In practice, the diagnosis of pneumonia is arrived at on the balance of the two.

Coagulase-negative staphylococcus and clostridium species isolated from blood culture are usually considered contaminants. However they were clinically significant in patients who had pneumonia and infected surgical implants, heart valves or significant skin infection.[8] The rate of 14.6% of blood cultures with significant coagulase-negative staphylococcus bacteremia in this study was comparable with that in other studies.[8,23]

Likewise, the rates of infection from gram-negative

organisms like *Escherichia coli*, klebsiella, *Pseudomonas aeruginosa* and enterococcus species were comparable to another study.[24] Micek's study showed that *Escherichia coli* infection was present in 5.8% of CAP; 4.2% in HCAP patients and made up a total of 4.7% of pathogens.[25]

*Burkholderia pseudomallei* infection was not found in the cohort. Melioidosis is a relatively uncommon infection locally, with an incidence rate of 1.7 per 100,000 population annually.[26] Melioidosis should be suspected in severe community-acquired pneumonia.[27-29] The severity of melioidosis infection would likely prompt a blood culture and a serology test.

The study population involved prospective pneumonia patients, some of whom were eventually found to have more than one source of infection. It reflected the realities of medically heterogeneous patients arriving at an ED, diagnosed against an imperfect gold standard and an unreliable blood culture yield. This regression model was translated into a clinical scoring system for use by physicians faced with such patients, with a specificity of 38.2% while retaining a higher sensitivity of 82% for a positive blood culture. Retrospectively applying the model created in the current study on the cohort of 1407 patients, 535 blood cultures, or 38%, could have been saved while missing 16 positive blood cultures.

Other prediction models for blood cultures in CAP have been put forth. Metersky's model reported slight differences in independent positive predictors of bacteremia,[24] the factors identified were actually individual components that added to the total PSI score. Metersky's model was able to identify 88% to 89% of patients with bacteremia and reduced the blood cultures by 38%. Another model[30] also identified slightly different predictors comprised of PSI components. The yield of blood cultures increased with the PSI class, was similarly found in other studies.[31,32] A significant similarity between these models and the current study is that PSI is a prominent predictor of bacteremia and its use in a predictive modeling tool for bacteremia.

The result of the study is limited by the retrospective derivation cohort and is yet to be validated prospectively. Many of the patients in this study were old and had other co-morbidities, contributing to a high proportion of patients with PSI classes of IV or higher. A younger cohort of pneumonia patients may not show similar predictive characteristics.

It was also found that 44 patients (3.1%) had contaminated culture results, and these patients had an associated four-day extended length of stay on average compared to those with negative cultures, translating to resource utilisation and cost. Although the clinical utility of positive blood culture results was not studied, the cost-effectiveness of the subset of patients with correctly identified positive blood cultures needs to be clarified in future studies.

The lack of a significant yield from blood culture in all patients with pneumonia and the re-investigation required to clarify contaminated blood culture results, lead to longer hospital stays and higher resource utilisation. Targeting the scope of patients for whom blood cultures is performed for pneumonia is a first step towards better cost-effectiveness.

REFERENCES


1. Ministry of Health Singapore. Top 10 Conditions of Hospitalisation. Available at: http://www.moh.gov.sg/mohcorp/statistics.aspx?id=5528. Accessed 27 April 2009.
2. Ministry of Health Singapore. Hospital Bill Size. Available at: http://www.moh.gov.sg/mohcorp/billsize.aspx. Accessed 27 April 2009.
3. Campbell SG, Marrie TJ, Anstey R, Dickinson G, Ackroyd-Stolarz S. The contribution of blood cultures to the clinical management of adult patients admitted to the hospital with community-acquired pneumonia: a prospective observational study. Chest 2003;123:1142-50.
4. Campbell SG, Marrie TJ, Anstey R, Ackroyd-Stolarz S, Dickinson G. Utility of blood cultures in the management of adults with community acquired pneumonia discharged from the emergency department. Emerg Med J 2003;20:521-3.
5. Theerthakarai R, El-Halees W, Ismail M, Solis RA, Khan MA. Non value of the initial microbiological studies in the management of non severe community-acquired pneumonia. Chest 2001;119:181-4.
6. Chalasani NP, Valdecanas MA, Gopal AK, McGowan, JE, Jurado RL. Clinical utility of blood cultures in adult patients with community-acquired pneumonia without defined underlying risks. Chest 1995;108:932-6.
7. Corbo J, Friedman B, Bijur P, Gallagher EJ. Limited usefulness of initial blood cultures in community acquired pneumonia. Emerg Med J 2004;21:446-8.
8. Souvenir D, Anderson, DE Jr, Palpant S, Mroch H, Askin S, Anderson J, et al. Blood cultures positive for coagulase-negative staphylococci: antisepsis, pseudobacteremia, and therapy of patients. J Clin Microbiol 1998;36:1923-6.
9. Sanyal S, Smith PR, Saha AC, Gupta S, Berkowitz L, Homel P. Initial microbiologic studies did not affect outcome in adults hospitalized with community acquired pneumonia. Am J Respir Crit Care Med 1999; 160:346-8.
10. Walls RM, Resnick JB. The Joint Commission on Accreditation of Healthcare Organizations and Center for Medicare and Medicaid Services Community-Acquired Pneumonia Initiative: What Went Wrong? Ann Emerg Med 2005;46:409-11.
11. Berk SL. Justifying the use of blood cultures when diagnosing community-acquired pneumonia. Chest 1995;108:891-2.
12. Ostergaard L, Andersen PL. Etiology of community-acquired pneumonia. Evaluation by transtracheal aspiration, blood culture, or serology. Chest 1993;104:1400-7.
13. Doern GV, Richter SS, Miller A, Miller M, Rice C, Heilmann K, et al. Antimicrobial resistance among *Streptococcus pneumoniae* in the United States: have we begun to turn the corner on resistance to certain antimicrobial classes? Clin Infect Dis 2005;41:139-48.
14. Frazee BW, Salz TO, Lambert L, Perdreau-Remington F. Fatal community-associated methicillin-resistant *Staphylococcus aureus* pneumonia in an immunocompetent young adult. Ann Emerg Med 2005;46:401-4.

15. Hageman JC, Uyeki TM, Francis JS, Jernigan DB, Wheeler JG, Bridges CB, et al. Severe community-acquired pneumonia due to *Staphylococcus aureus*, 2003-04 influenza season. Emerg Infect Dis 2006;12:894-9.
16. Chambers DC, Waterer GW. Are blood cultures necessary in community-acquired pneumonia? Clin Pulm Med 2005;12:146-52.
17. Metlay JP, Kapoor WN, Fine MJ. The rational clinical examination: does this patient have community-acquired pneumonia? Diagnosing pneumonia by history and physical examination. JAMA 1997;278:1440-5.
18. Albaum MN, Hill LC, Murphy M, Li YH, Fuhrman CR, Britton CA, et al. Interobserver reliability of the chest radiograph in community-acquired pneumonia. Chest 1996;110:343-50.
19. Kanwar M, Brar N, Khatib R, Fakih MG. Misdiagnosis of community-acquired pneumonia and inappropriate utilization of antibiotics, side effects of the 4-h antibiotic administration rule. Chest 2007;131:1865-9.
20. Fine MJ, Auble TE, Yealy DM, Hanusa D, Weissfeld LA, Singer DE, et al. A Prediction Rule To Identify Low-Risk Patients With Community acquired Pneumonia. N Engl J Med 1997;336:243-50.
21. American Thoracic Society; Infectious Diseases Society of America. Guidelines for the Management of Adults with Hospital-acquired, Ventilator-associated, and Healthcare-associated Pneumonia. Am J Respir Crit Care Med 2005;171:388-416.
22. Hopstaken R, Witbraad T, van Engelshoven J, Dinant G. Inter-observer variation in the interpretation of chest radiographs for pneumonia in community-acquired lower respiratory tract infections. Clin Radiol 2004;59:743-52.
23. Mirrett S, Weinstein MP, Reimer LG, Wilson ML, Reller LB. Relevance of the number of positive bottles in determining clinical significance of coagulase-negative staphylococci in blood cultures. J Clin Microbiol 2001;39:3279-81.
24. Metersky ML, Ma A, Bratzler DW, Houck PM. Predicting bacteremia in patients with community-acquired pneumonia. Am J Respir Crit Care Med 2004;169:342.
25. Micek ST, Kollef KE, Reichley RM, Roubinian N, Kollef MH. Health care-associated pneumonia and community-acquired pneumonia: a single-center experience. Antimicrob Agents Chemother 2007;51:3568-73.
26. Heng BH, Goh KT, Yap EH, Loh H, Yeo M. Epidemiological surveillance of melioidosis in Singapore. Ann Acad Med Singapore 1998;27:478-84.
27. Lee KH, Hui KP, Tan WC, Lim TK. Severe community-acquired pneumonia in Singapore. Singapore Med J 1996;37:374-7.
28. Tan YK, Khoo KL, Chin SP, Ong YY. Aetiology and outcome of severe community-acquired pneumonia in Singapore. Eur Respir J 1998; 12: 113-5.
29. Poulose V. Severe community-acquired pneumonia requiring intensive care: a study of 80 cases from Singapore. Singapore Med J 2008;49:458-61.
30. Benenson RS, Kepner AM, Pyle DN, Cavanaugh S. Selective use of blood cultures in Emergency Department pneumonia patients. J Emerg Med 2007;33:1-8.
31. Stalnikowicz R, Block C. The yield of blood cultures in a department of emergency medicine. Eur J Emerg Med 2001;8:93-7.
32. Waterer GW, Wunderink RG. The influence of the severity of community-acquired pneumonia on the usefulness of blood cultures. Respir Med 2001;95:78-82.