Eur J Clin Microbiol Infect Dis (1998) 17:78–84

Article

Low Specificity of the Bacterial Index for the Diagnosis of Bacterial Pneumonia by Bronchoalveolar Lavage

R. Speich, M. Hauser, T. Hess, J. Wüst, E. Grebski, F. H. Kayser, E. W. Russi

Abstract The bacterial index (BI) as defined by the sum of $\log_{10}$ colony-forming units (cfu) of microorganisms per milliliter of bronchoalveolar lavage (BAL) fluid, i.e., a multiplication of the single cfu/ml, has been used to distinguish between polymicrobial pneumonia ($BI \geq 5$) and colonization ($BI < 5$). Since many false-positive results are to be expected using this parameter, the diagnostic value of the BI was studied prospectively by obtaining bacteriologic cultures of BAL fluid in 165 consecutive unselected patients. In 27 cases the diagnosis of bacterial pneumonia was established on clinical criteria. In 133 patients pneumonia could be excluded, and in five patients the diagnosis remained unclear. Using a cut-off of $\geq 10^5$ cfu/ml BAL fluid, sensitivity and specificity for the diagnosis of pneumonia were 33% (9/27) and 99% (132/133), respectively. Sensitivity was mainly influenced by prior treatment with antibiotics, being 70% (7/10) in untreated and 12% (2/17) in treated patients. Applying the BI methodology at a cut-off of ≥ 5, however, resulted in an unacceptably high rate of 16 additional false-positive results, thus lowering the specificity to 87% (116/133; $P < 0.0001$) while increasing the sensitivity to only 41% (11/27; $P = 0.77$). In conclusion, given the high rate of false-positive results, the methodology of the BI is of doubtful value for the diagnosis of bacterial pneumonia by BAL in an unselected patient group. By applying the absolute number of cfu/ml BAL fluid, however, positive bacteriologic cultures of BAL fluid are highly specific for the diagnosis of pneumonia. Their sensitivity is limited by previous antibiotic therapy.

Key words Pneumonia · Bronchoalveolar lavage · Diagnosis

Introduction

The diagnosis of bacterial pneumonia remains difficult. Clinical findings such as fever, physical exam, leukocytosis, or abnormal chest radiographs are often nonspecific or even misleading, especially in the ventilated patient [1]. Microscopic examination and cultures of sputum or tracheobronchial secretions retrieved by aspiration or bronchoscopy are nonspecific due to contamination by flora from the upper respiratory tract [2]. Transtracheal aspirates also do not allow differentiation between infection and colonization of the lower respiratory tract, especially in patients with chronic bronchitis [3]. Furthermore, transtracheal aspiration cannot be performed in mechanically ventilated patients.

During recent years the reliability of bronchoalveolar lavage (BAL) for the diagnosis of bacterial pneumonia has been studied intensively. Kahn and Jones [4] and Thorpe et al. [5] have demonstrated that quantitative bacterial cultures of BAL fluid from nonventilated patients allow differentiation between colonization and infection of the lower respiratory tract at a cut-off of 10^5 colony-forming units (cfu) per milliliter of BAL fluid. The sensitivity for detecting bacterial pneumonia was reported to range from 87–100%, with specificity

R. Speich (✉), T. Hess, E. Grebski, E. W. Russi
Department of Internal Medicine, Zurich University Hospital, Raemistrasse 100, CH-8091 Zurich, Switzerland

M. Hauser
Department of Medical Radiology, Zurich University Hospital, Raemistrasse 100, CH-8091 Zurich, Switzerland

J. Wüst, F. H. Kayser
Institute of Medical Microbiology, Zurich University Hospital, Raemistrasse 100, CH-8091 Zurich, Switzerland

ranging from 70–100% [4, 5]. The importance of BAL for the early recognition of ventilator-associated bacterial pneumonia has also been documented [6, 7]. Lately, innovative techniques of performing BAL, such as nonbronchoscopic "blind" [8, 9] and protected BAL [10], have been described. Furthermore, we have recently evaluated a novel bedside technique for quantitative cultures of BAL fluid using dip slides [11]. These methods will presumably propagate the use of BAL as an important diagnostic tool [12–17].

To account for the fact that nosocomial pneumonia is often due to polymicrobial infection, Johanson et al. [6] proposed the calculation of a so-called bacterial index (BI) by adding up the $\log_{10}$ converted numbers of colony-forming units of individual organisms per BAL specimen. For instance, a BI of 6 may represent a single organism in a concentration of 10^6 cfu/ml BAL fluid or may stand for the detection of three different species, each at a concentration of 10^2 cfu/ml BAL fluid. Since a BI of ≥ 5 is considered sensitive and specific for the diagnosis of a lower respiratory tract infection [6, 9], low concentrations of several bacterial strains would erroneously suggest the diagnosis of pneumonia. We believe the concept of the BI to lack a sound microbiological basis. Moreover, according to our experience, the use of the BI reduces the specificity of BAL in the diagnosis of bacterial pneumonia. Therefore, we decided to study prospectively the diagnostic value of the BI as introduced by Johanson et al. [6] and used by others [8, 9] compared to the absolute number of the cfu/ml BAL fluid in an unselected patient group undergoing bronchoscopy for a variety of indications.

Patients and Methods

Patients. One hundred sixty-five patients (mean age, 45 years; range, 18–77 years; 55 women, 110 men) consecutively underwent fiberoptic bronchoscopy with BAL for the following indications: evaluation of pulmonary complications during immunosuppression (54 HIV-infected patients, 27 patients after solid organ transplantation, 18 patients with hematologic malignancies), suspected pneumonia in non-immunosuppressed patients ($n=33$), bilateral infiltrative lung disease of unknown origin ($n=22$), and suspected bronchogenic carcinoma ($n=11$). Eight patients were lavaged twice, and each BAL was considered separately. Nine patients were intubated and mechanically ventilated, and 59 patients were treated with antibiotics prior to bronchoscopy.

Bronchoalveolar Lavage. The fiberoptic bronchoscope (Olympus type; Olympus Opticals, Switzerland) was inserted through a nostril in nonintubated patients and through an endotracheal tube via a sterile swivel adaptor (single-use 15 mm swivel adaptor; Portex, Hythe, UK) in ventilated patients. Nonintubated patients received 0.5 mg of atropine sulfate 15 min before bronchoscopy. Intravenously administered hydrocodone 7.5–15 mg and flunitrazepam 1–2 mg were used for additional sedation. The patients received 5–10 ml of nebulized 4% lidocaine with 10 drops of salbutamol followed by 10 ml of 1% lidocaine injected through the bronchoscope onto the vocal cords. Suctioning through the bronchoscope channel and injecting lidocaine onto the airways was avoided whenever possible. During the examination the patients were given supplemental oxygen 2–6 l/min through the unused nostril or a face mask. Intubated patients received additional sedation with midazolam and morphine sulfate intravenously as required. Before BAL was started, the ventilator settings were changed. The FIO_2 was switched to 1.0 and the tidal volume was increased by 20%. The oxygen saturation was monitored by a transcutaneous pulse oximeter (Ohmeda Biox 3740 Pulse Oximeter; Ohmeda, USA) through a finger probe. The bronchoscope tip was wedged into the subsegmental bronchus leading to the area showing the most prominent infiltrations on the chest radiograph. Four 50 ml aliquots of sterile isotonic saline were injected then gently hand-aspirated with a syringe. The recovery ranged from 40–80%. The BAL fluid was filtered through a double layer of sterile surgical gauze and pooled into a sterile graduate cylinder. The BAL samples were immediately submitted for microbiologic analysis.

Bacteriology. The quantitative bacterial cultures of the pooled BAL fluid were performed by plating 0.001 ml of the original specimen with a calibrated loop according to a widely accepted standard [18] onto sheep blood agar, chocolate agar, CNA agar (blood agar containing colistin and nalixidic acid), and MacConkey agar. After inoculation the plates were incubated at 37 °C in 5% CO_2; MacConkey agar was incubated aerobically without CO_2. Culture plates were examined for growth after 24 and 48 h. Colonies with distinct morphologies were enumerated separately and the results were expressed as cfu/ml BAL fluid. Identification of organisms was performed according to standard recommendations [19]. The BI was calculated according to Johanson et al. [6] for each of the BAL specimens by adding up the $\log_{10}$ of the concentrations of the individual organisms per BAL specimen. A value of ≥ 5 was considered diagnostic for bacterial pneumonia [6, 9]. Furthermore, the absolute number of cfu/ml BAL fluid of the single microorganisms and the sum of cfu/ml per BAL sample were calculated for each patient, and a value $\geq 10^5$ was considered diagnostic for pneumonia [4, 5].

Clinical Variables. Bacterial pneumonia was diagnosed clinically if all of the following criteria were present: (i) fever >38.5 °C or purulence of tracheobronchial secretions; (ii) a new or progressive localized infiltrate on chest radiographs; and (iii) improvement after adequate antimicrobial therapy. The diagnosis of pneumonia as well as the alternative diagnosis in the nonpneumonia cases was made prospectively by the treating physicians, independent of the study team. The quantitative cultures were performed for the study purposes only.

Statistical Analysis. Frequencies and categories were compared with the use of Fisher's exact test. A P value of <0.05 was considered significant. Sensitivity and specificity were calculated according to standard formulas. Confidence intervals (CI) of 95% were calculated by standard methods [20]. The performance of the diagnostic tests was determined by a receiver operating characteristic (ROC) curve analysis according to the recommendations of Hanley and McNeil [21]. Briefly, sensitivity and 1 – specificity are plotted at multiple cut points, and a curve is generated. The area under the curve (AUC) represents the diagnostic performance of the test relative to the diagnostic performance of a hypothetical perfect test (100% specificity; 100% sensitivity; AUC 1.0). By comparing the AUC of the various tests, it is possible to judge the performance of the tests as a diagnostic and screening tool. Most clinically useful diagnostic tests have an AUC of 0.8–0.9.

Results

In 27 of the 165 patients (16.4%), the diagnosis of bacterial pneumonia was established according to clinical criteria. These criteria were not fulfilled in 133 cases (80.6%), and an alternative diagnosis was made in most instances: sepsis or fever of unknown origin with nor-

mal chest radiograph ($n=19$); *Pneumocystis carinii* pneumonia in HIV-infected ($n=12$) and non-HIV immunosuppressed patients ($n=12$); nonspecific interstitial pneumonia not treated with antibiotics ($n=12$); vasculitis with pulmonary alveolar hemorrhage ($n=8$); pulmonary tuberculosis ($n=7$); pulmonary lymphoma ($n=7$) and other neoplasias ($n=8$); sarcoidosis ($n=6$); mucus plugging ($n=5$); bronchiolitis obliterans ($n=4$); pulmonary embolism ($n=4$); left heart failure ($n=3$); eosinophilic pneumonia ($n=2$); pneumonia due to *Aspergillus fumigatus* ($n=6$), *Legionella pneumophila* ($n=3$), cytomegalovirus ($n=3$), *Nocardia asteroides* ($n=2$), *Cryptococcus neoformans* ($n=2$), or *Mycoplasma pneumoniae* ($n=1$); herpetic tracheobronchitis ($n=1$); chemotherapy-induced lung diseases ($n=2$); and chronic bronchitis with normal chest radiography ($n=3$). Five patients (3%) were lost to follow-up. They were excluded from further analysis.

The distribution of the colony counts per milliliter of BAL fluid in patients with and without pneumonia, respectively, is shown in Figure 1A. In nine of the 27 patients with pneumonia, at least one bacterial strain at a count of $\geq 10^5$ cfu/ml BAL fluid was detected: *Haemophilus influenzae* ($n=5$), *Pseudomonas aeruginosa* ($n=2$), and viridans streptococci ($n=2$). Only in one patient without pneumonia (Table 1, case 17) was *Streptococcus pneumoniae* at a concentration of $\geq 10^5$ cfu/ml BAL fluid found. Thus, with regard to pneumonia diagnosed by clinical criteria (see Methods), a threshold of 10^5 cfu/ml BAL fluid resulted in a sensitivity of 33% (9/27; CI, 23–57%) and a specificity of 99% (132/133; CI, 98–100%). Lowering the cut-off point to 10^4 cfu/ml BAL fluid increased the sensitivity to 59% (16/27; CI, 49–84%; not significant compared to a cut-off point of 10^5 cfu/ml, $P=0.10$) but significantly reduced the specificity to 82% (108/133; CI, 77–90%; $P<0.0001$). Due to low case numbers, an analysis of the various subgroups of underlying diseases was possible only in the 54 HIV-infected patients. Using the criteria mentioned above, the sensitivity of BAL with regard to pneumonia was 36% (4/11; CI, 27–54%; not significant compared to the non-HIV group), and the specificity was 100% (43/43).

The low sensitivity of BAL for the diagnosis of bacterial pneumonia in our study population with a relatively low prevalence of pneumonia was mainly due to antimicrobial pretreatment. This important issue is illustrated by the distribution of the colony counts per milliliter of BAL fluid in patients with and without pneumonia, respectively, who had not been treated previously with antibiotics (Figure 1B) compared to those who had been receiving antimicrobial agents before BAL (Figure 1C). In patients without antibiotics prior to BAL, the sensitivity for the diagnosis of pneumonia improved to 70% (7/10; CI, 64–100%; $P=0.067$ compared to all patients; $P=0.0037$ compared to those pretreated with antibiotics), and the specificity remained at 99% (94/95;

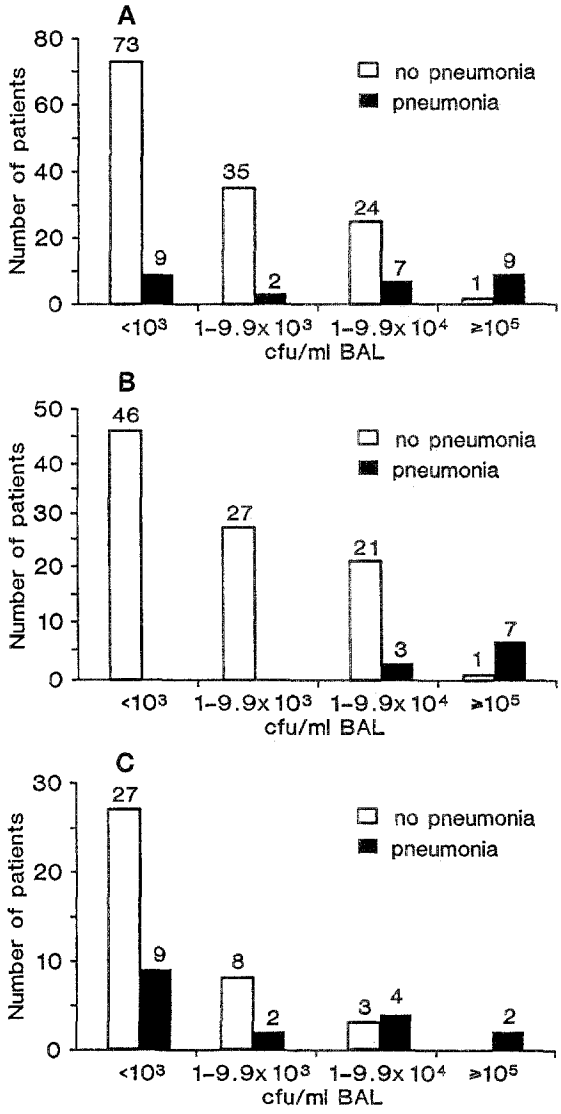

Figure 1 Distribution of the sum of cfu/ml BAL fluid in individual patients with and without bacterial pneumonia, considering **A** all patients, **B** patients not receiving antibiotics before BAL, and **C** patients treated with antibiotics at the time of BAL

Cl, 98–100%). In contrast, compared to the patients not pretreated with antibiotics, the sensitivity was significantly reduced to 12% (2/17; CI, 8–39%; $P=0.0037$) in patients receiving antibiotics at the time of BAL. Lowering the cut-off point in this patient group to 10^4 cfu/ml BAL fluid increased the sensitivity to 35% (6/17; CI, 26–67%; NS, $P=0.22$) but decreased the specificity from 100% (38/38; CI, 100–100%) to 92% (35/38; CI 88–100%; NS, $P=0.24$).

When a BI of ≥ 5 was taken as a diagnostic criterion for bacterial pneumonia, two further true-positive results were obtained (sensitivity 41%; CI, 31–66%; $P=0.77$ compared to the sensitivity of the absolute number of organisms at a cut-off point of 10^5 cfu/ml BAL fluid). The use of the BI, however, resulted in 16 additional false-positive diagnoses. Therefore, specifici-

Table 1 Characteristics of patients without bacterial pneumonia exhibiting a bacterial index of ≥5

Patient no.	Age/ sex	Underlying condition(s); radiographic findings; diagnosis	Previous antibiotic therapy	Organisms cultured from BAL fluid (cfu/ml BAL fluid)	Bacterial index
1	39m[a]	HIV infection, acute bronchitis; normal chest radiograph; HIV-associated fever	no	viridans streptococci (2×10^4), *Candica albicans* (5×10^3)	8.0 (4.3)[b]
2	29m[a]	HIV infection, herpetic tracheobronchitis; normal chest radiograph	yes	normal oral flora[c] (1.8×10^4), *C. albicans* (2×10^3)	7.6 (4.3)[b]
3	36m	HIV infection, chronic bronchitis; normal chest radiograph; evaluation for suspected PCP negative	no	normal oral flora (6×10^3), *Haemophilus influenzae* (5×10^3), *C. albicans* (10^4)	11.5 (7.5)[b]
4	34m	asymptomatic; normal chest radiograph; evaluation for hilar lymphadenopathy unremarkable	no	*Streptococcus pneumoniae* 10^3), normal oral flora (10^3)	6.0
5	43f	HIV infection, chronic bronchitis; normal chest radiograph; evaluation for suspected PCP negative	no	viridans streptococci (2×10^3), *H. influenzae* (10^3)	6.3
6	35f	CMV infection after kidney transplantation; normal chest radiograph	no	*H. influenzae* (10^3), normal oral flora (2×10^4)	7.3
7	34m	pulmonary tuberculosis; only mild interstitial LUL changes on chest radiograph and CT scan	no	normal oral flora (1.4×10^4), *H. influenzae* (2×10^3)	7.4
8	29m	HIV and disseminated *Mycobacterium simiae* infection; subtle increased interstitial markings on chest radiograph; evaluation for suspected PCP negative	no	*Streptococcus pneumoniae* (4×10^4), *Staphylococcus aureus* (2×10^3), viridans streptococci (10^3)	10.9
9	52m	HIV infection, nonspecific interstitial pneumonitis; subtle increased interstitial markings on chest radiograph	no	*Staphyloccocus aureus* (1.4×10^4), normal oral flora (10^4)	8.1
10	67m	HIV infection, PCP; subtle increased interstitial markings on chest radiograph	no	*Staphylococcus aureus* (2×10^3), viridans streptococci (2×10^3)	6.6
11	38m	HIV infection, PCP; subtle increased interstitial markings on chest radiograph	no	*Streptococcus pneumoniae* (2.4×10^4), *Staphylococcus epidermidis* (3×10^3)	7.9
12	36m	HIV infection, PCP; subtle increased interstitial markings on chest radiograph	yes	*H. influenza* (10^3), normal oral flora (4×10^3)	6.6
13	35m	psoriasis vulgaris, chronic bronchitis; subtle chronic interstitial markings on chest radiograph	no	*Streptococcus pneumoniae* (5×10^3), *H. influenzae* (1.5×10^4)	7.9
14	20f	non-Hodgkin's lymphoma; bilateral interstitial infiltrates; suspected cytotoxic agent-induced pneumonitis, improvement after corticosteroid treatment	no	*Pseudomonas aeruginosa* (6×10^4), viridans streptococci (2.3×10^4)	9.2
15	18f[d]	severe renal failure after meningococcal sepsis, fluid overload; bilateral acinar shadows; improvement within 1 day, no antibiotic therapy	no	*Staphylococcus aureus* (1.2×10^3), *Xanthomonas maltophila* (1.2×10^3)	6.2
16	52m	asymptomatic chronically scarred LUL infiltrates; superinfection with *Mycobacterium xenopi*	no	viridans streptococci (7×10^4), *H. influenzae* (2×10^3), *Streptococcus pneumoniae* (1.1×10^4)	12.1
17	33m[e]	HIV infection, bronchitis; normal chest radiograph	no	*Streptococcus pneumoniae* (10^6)	6.0

[a] Patients with a bacterial index of <5, if *C. albicans* is not considered

[b] Values of bacterial index without consideration of *C. albicans* are shown in parentheses

[c] Normal oral flora defined as the growth of two or more of the following bacteria: viridans streptococci, *Neisseria* spp., coryneforms, coagulase-negative staphylococci

[d] Mechanically ventilated patient

[e] Patient with a bacterial index of ≥5 and an absolute number of cfu/ml BAL fluid of $\geq10^5$

CMV, cytomegalovirus; CT, computed tomography; HIV, human immunodeficiency virus; LUL, left upper lobe; PCP, *Pneumocystis carinii* pneumonia

ty was significantly reduced from 99 to 87% (116/133; CI, 83–94%; $P<0.0001$). The clinical data of the patients without pneumonia and with a BI of ≥5 are displayed in Table 1 (Table 1, patients 1–17).

The performance of the different diagnostic parameters is illustrated by the AUC of the ROC curve (Figure 2). Whereas the AUC for the BI was only 0.674, the AUC of the sum of the cfu/ml BAL fluid per patient reached 0.879. The AUC of the sum of cfu/ml BAL fluid including only patients without previous antibiotic treatment was 0.99.

Some authors even include the colony counts of fungal species in their calculations [8, 9]. However, this might not have a sound basis, since there is no evidence of the diagnostic utility of quantitative fungal cultures. There were two patients in our group (Table 1, patients 1 and

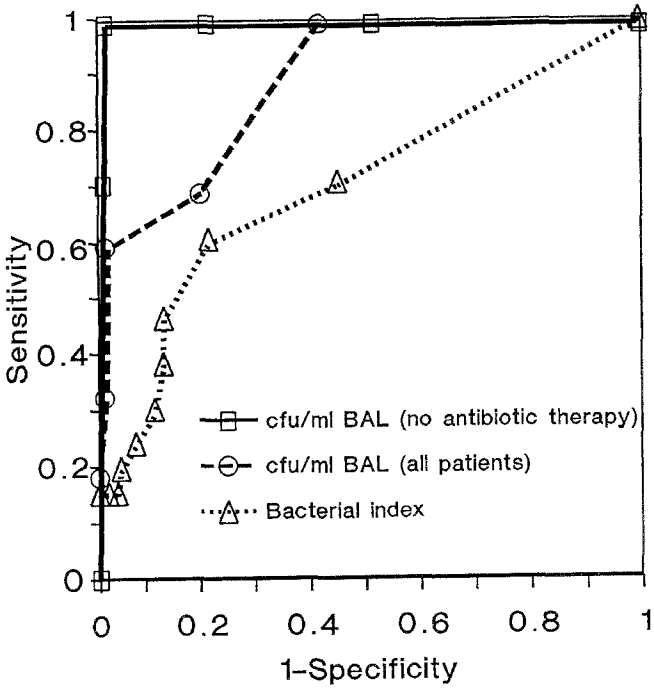

Figure 2 Receiver operating characteristic (ROC) curve for the bacterial index (AUC=0.674) for the sum of cfu/ml BAL fluid, including all patients (AUC=0.879) and considering only patients not treated with antibiotics at the time of BAL (AUC=0.99)

2) in whom the BI was lower than 5 when the fungal colony counts were not included. However, even by excluding these two cases, the specificity of a BI of ≥ 5 remained low at 89% (118/133; CI, 85–96%).

Discussion

The principal finding of this study is that using the BI at a cut-off of ≥ 5 in an unselected patient group with a relatively low prevalence of pneumonia (16.4%) results in an inacceptably low specificity for the diagnosis of bacterial pneumonia. Using the concept of the BI, which is calculated by adding up the $\log_{10}$ of the concentrations of the individual organisms per milliliter of BAL specimen (i.e., multiplying the numbers of colony-forming units of individual organisms per milliliter of BAL specimen), resulted in 17 false-positive results in patients who decisively did not suffer from bacterial pneumonia (Table 1). All these patients except case 17 (*Streptococcus pneumoniae,* 10^6 cfu/ml BAL fluid) would never have been diagnosed as having pneumonia if the absolute number of organisms at a cut-off of 10^5 cfu/ml BAL fluid had been used. Hence, by applying the BI methodology, the superb specificity of BAL for the diagnosis of bacterial pneumonia was significantly reduced from 99–87% ($P<0.0001$). The very low power of diagnostic discrimination of the BI is illustrated by the small AUC in the ROC analysis (Figure 2).

The BI was introduced by Johanson et al. [6], who used it in a baboon model of nosocomial pneumonia. They demonstrated a very good correlation of the BI of BAL fluid compared to the BI of quantitative lung tissue cultures. The BI was created with the attempt to let species present only in small numbers contribute to an estimation of the lungs' bacterial burden, especially during prolonged mechanical ventilation [6]. The hypothesis behind the BI was that the presence of multiple species in low concentrations indicated a marked impairment in host defenses, a hypothesis that is still unproven and basically untested. However, the study of Johanson et al. [6] became a landmark paper leading to a widespread use of quantitative bacterial cultures of BAL fluid for the diagnosis of bacterial nosocomial pneumonia [10, 15, 22]. Unfortunately, the BI was used rather uncritically by some subsequent authors [8, 9], while others relied on the absolute count of cfu/ml BAL fluid per single microorganism or the sum of cfu/ml per BAL specimen at the cut-off point of 10^5 as an indicator for pneumonia [4, 5, 10, 15, 16].

According to our findings, the concept of the BI, calculated by adding up the $\log_{10}$ cfu/ml BAL fluid of the individual microbial species per patient, thus multiplying the number of cfu/ml of different organisms, has no sound microbiological basis. In such a way, the presence of very low concentrations of several different colonizing bacteria in an individual patient might lead to a BI of >5. In particular, this may occur in immunosuppressed patients (such as in 12 of our study group, Table 1). Why the lungs of these patients contain quite high bacterial burdens is of great interest and should be studied further. Although our series included mainly nonventilated patients, we believe that our findings also apply to intubated and mechanically ventilated patients. Since two-thirds of our patients were immunocompromised, it is not intelligible why the diagnostic criteria for bacterial pneumonia, i.e. the amount of bacterial burden in the lung to cause invasive infection, should not apply to patients with other types of host defense impairment, such as mechanical ventilation in an ICU setting.

We are well aware that our study lacks a gold standard for the diagnosis of bacterial pneumonia. However, while the clinical diagnosis of bacterial pneumonia remains unreliable, especially in cases of nosocomial pneumonia [1, 23], we are confident that none of the 17 patients listed in Table 1 had bacterial pneumonia. In most cases the chest radiograph was normal or showed only slightly increased interstitial markings, and in all cases another diagnosis could be established. It was not our intention to demonstrate the value of BAL for the diagnosis of pneumonia but to prove the low specificity, i.e. the high number of false-positive results, using the methodology of the BI. Therefore, we decided to study a consecutive heterogenous series of patients with a low prevalence of pneumonia, including ventilated and

nonventilated as well as immunocompromised and immunocompetent patients.

Our findings of a low specificity of the BI are supported by a recent paper investigating 27 mechanically ventilated patients without clinical or radiographic evidence of pulmonary infection [24]. Analyzing the BAL data by means of the BI at a cut-off of 6 gave 23% false-positive results. The authors suggest that a BI of 8 would be the best threshold to get a low percentage of false-positive results. This value is far higher than the BI cut-off of 5 or greater used by most other authors [8, 9].

In contrast to the BI, the use of the absolute number of cfu/ml BAL fluid of the individual organisms at the cut-off point of 10^5 was highly specific (99%) for the diagnosis of bacterial pneumonia. On the other hand, the relatively low sensitivity (33%) of the cfu/ml BAL fluid was mainly due to a high rate of patients receiving antimicrobial therapy prior to bronchoscopy. This is a major problem in the use of quantitative cultures in clinical practice and has been addressed by others [22]. Considering merely the cases not treated with antibiotics prior to BAL, the sensitivity for the diagnosis of bacterial pneumonia increased to 70%, which is comparable to the findings of other studies [16]. This is also clearly demonstrated by the large increase of the AUC in the ROC analysis (Figure 2). As mentioned above, however, it must be remembered that this study was not designed to assess the value of BAL for the diagnosis of bacterial pneumonia, and that there was no gold standard test to prove the true-positive rate, i.e. the sensitivity of the BAL cultures.

In conclusion, we have shown that the use of the BI as a diagnostic parameter for bacterial pneumonia results in an unacceptably low specificity. Thus, the concept of the BI is not applicable to clinical practice. Quantitative bacterial cultures of BAL fluid, however, may be a valuable tool for the diagnosis of bacterial pneumonia when the absolute amount of colony-forming units of individual species per milliliter of BAL fluid is used at a cut-off point of 10^5, especially when patients without prior antibiotics are considered.

Acknowledgement The authors are indebted to the Zurich Lung Association, Zurich, Switzerland, for their support of the study.

References

1. Andrews CP, Coalson JJ, Smith JD, Johanson WG: Diagnosis of nosocomial pneumonia in acute, diffuse lung injury. Chest (1981) 80:254–258
2. Haas H, Morris JF, Samson S, Kilbourn JP, Kim PJ: Bacterial flora of the respiratory tract in chronic bronchitis: comparison of transtracheal, fiberbronchoscopic, and oropharyngeal sampling methods. American Review of Respiratory Diseases (1977) 116:41–47
3. Bartlett JG: Diagnostic accuracy of transtracheal aspiration: bacteriologic studies. American Review of Respiratory Diseases (1977) 115:777–782
4. Kahn FW, Jones JM: Diagnosing bacterial respiratory infection by bronchoalveolar lavage. Journal of Infectious Diseases (1987) 155:862–869
5. Thorpe JE, Baughman RP, Frame PT, Wesseler TA, Staneck JL: Bronchoalveolar lavage for diagnosing acute bacterial pneumonia. Journal of Infectious Diseases (1987) 155:855–861
6. Johanson WG, Seidenfeld JJ, Gomez P, de los Santos R, Coalson JJ: Bacteriologic diagnosis of nosocomial pneumonia following prolonged mechanical ventilation. American Review of Respiratory Diseases (1988) 137:259–264
7. Xaubet A, Torres A, Marco F, de la Bellacasa JP, Faus R, Augusti-Vidal A: Pulmonary infiltrates in immunocompromised patients. Diagnostic value of telescoping plugged catheter and bronchoalveolar lavage. Chest (1989) 95:130–135
8. Gaussorgues P, Piperno D, Bachmann P, Boyer F, Jean G, Gérard M, Léger P, Robert D: Comparison of nonbronchoscopic bronchoalveolar lavage to open lung biopsy for the bacteriologic diagnosis of pulmonary infections in mechanically ventilated patients. Intensive Care Medicine (1989) 15:94–98
9. Pugin J, Auckenthaler R, Mili N, Janssens JP, Lew D, Suter PM: Diagnosis of ventilator-associated pneumonia by bacteriologic analysis of bronchoscopic and nonbronchoscopic "blind" bronchoalveolar lavage. American Review of Respiratory Diseases (1991) 143:1121–1129
10. Meduri GU, Beals DH, Maijub AG, Baselski V: Protected bronchoalveolar lavage. A new bronchoscopic technique to retrieve uncontaminated distal airway secretions. American Review of Respiratory Diseases (1991) 143:855–864
11. Speich R, Wüst J, Hess T, Kayser FH, Russi EW: Prospective evaluation of a semiquantitative dip slide method compared with quantitative bacterial cultures of BAL fluid. Chest (1996) 109:1423–1429
12. Chastre J, Fagon JY, Bornet Lecso M, Calvat S, Dombret MC, al Khani R, Basset F, Gibert C: Evaluation of bronchoscopic techniques for the diagnosis of nosocomial pneumonia. American Journal of Respiratory and Critical Care Medicine (1995) 152:231–240
13. Faling LJ: New advances in diagnosing nosocomial pneumonia in intubated patients. Part I. American Review of Respiratory Diseases (1988) 137:253–255
14. Johanson WG: Ventilator-associated pneumonia. Light at the end of the tunnel? Chest (1990) 97:1026–1027
15. Meduri GU, Baselski V: The role of bronchoalveolar lavage in diagnosing nonopportunistic bacterial pneumonia. Chest (1991) 100:179–190
16. Meduri GU: Diagnosis and differential diagnosis of ventilator-associated pneumonia. Clinics in Chest Medicine (1995) 16:61–93
17. Torres A: Accuracy of diagnostic tools for the management of nosocomial respiratory infections in mechanically ventilated patients. European Respiratory Journal (1991) 4:1010–1019
18. Baselski VS, El-Torky M, Coalson JJ, Griffin JP: The standardization of criteria for processing and interpreting laboratory specimens in patients with suspected ventilator-associated pneumonia. Chest (1992) 102, Supplement 1:571–579
19. Baron EJ, Weissfeld AS, Fuselier PA, Brenner DJ: Classification and identification of bacteria. In: Murray PR, Baron EJ, Pfaller MA, Tenover FC, Yolken RH (eds). Manual of clinical microbiology. American Society for Microbiology, Washington, DC (1995) pp 249–264
20. Simon RS: Confidence intervals for reporting results of clinical trials. Annals of Internal Medicine (1986) 105:429–435
21. Hanley JA, McNeil BJ: The meaning and use of the area under a receiver operating characteristic (ROC) curve. Radiology (1982) 143:29–36

22. Meduri GU, Chastre J: The standardization of bronchoscopic techniques for ventilator-associated pneumonia. Chest (1992) 102, Supplement 1:557–564
23. Fagon JY, Chastre J, Hance AJ, Guiguet M, Trouillet JL, Domart Y, Pierre J, Gibert C: Detection of lung infection in ventilated patients: use of protected specimen brush and quantitative culture techniques in 147 patients. American Review of Respiratory Diseases (1988) 138:110–116
24. Torres A, Martos A, de la Bellacasa JP, Ferrer M, El-Ebiary M, González J, Gené A, Rodríguez-Roisin R: Specificity of endotracheal aspiration, protected specimen brush, and bronchoalveolar lavage in mechanically ventilated patients. American Review of Respiratory Diseases (1993) 147:952–957