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REVIEW

Accuracy of diagnostic tools for the management of nosocomial respiratory infections in mechanically ventilated patients

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Accuracy of diagnostic tools for the management of nosocomial respiratory infections in mechanically ventilated patients. A. Torres.

ABSTRACT: This article reviews the medical literature concerning available diagnostic tools for managing nosocomial respiratory infections in mechanically ventilated patients. The first part deals with the reliability of the clinical criteria used in diagnosing nosocomial pneumonia in such patients and the accuracy of simple markers of pneumonia such as elastin fibres stain and antibody-coated bacteria. The second part reviews the presently available non-invasive and invasive methods for diagnosing pulmonary infections acquired during mechanical ventilation. With regard to invasive methods, protected specimen brush and bronchoalveolar lavage are extensively discussed in view of the different results in the literature. At the present time, these two methods seem to be the most accurate techniques available. The fact that bronchoalveolar lavage may combine the cytological examination and the quantitative culture of the sample obtained is noted. The role of percutaneous lung needle aspiration is also mentioned. Finally, histological diagnosis of pneumonia and pulmonary postmortem biopsy cultures are reviewed as "gold-standard" reference methods for investigation in this field. Future directions for further clinical research are addressed.

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In mechanically ventilated (MV) patients, pulmonary infections are common. The incidence of nosocomial pneumonia acquired during mechanical ventilation has not been well established and it ranges between 9–60% [1–7]. When a ventilator-associated pneumonia develops, the microbiological diagnosis of the pulmonary infection is crucial in order to provide an adequate antibiotic treatment and to avoid unnecessary chemotherapeutic regimens. Unfortunately, the clinical and bacteriological diagnosis of these pneumonias is difficult for a number of reasons. Firstly, common clinical symptoms and signs of pneumonia may be unreliable. A 30% rate of false-positives and false-negatives has been reported [4, 7]. Secondly, the upper airways of intubated patients are universally colonized by Gram-negative bacilli and other microorganisms [5]. This colonization leads to a contamination of simple methods of diagnosis such as endotracheal aspiration or fibreoptic bronchoaspirates. Finally, MV patients with pulmonary infections have often had previous antibiotic treatment; this decreases the specificity and the sensitivity of the different diagnostic methods employed [8]. In view of these difficulties, several non-invasive and invasive diagnostic techniques have been developed in recent years in order to improve diagnostic accuracy [8–12]. In the present article, we review the diagnostic value of the methods currently available for diagnosing nosocomial pulmonary infections in MV patients.

Clinical diagnosis

Several clinical criteria have been proposed to diagnose nosocomial pneumonia in MV patients. JOHANSON *et al.* [5] defined pneumonia when patients presented the following criteria: 1) fever; 2) leucocytosis; 3) purulent tracheobronchial secretions; and 4) the appearance of new and progressive infiltrates in the chest X-ray. Subsequently, CRAVEN *et al.* [6] added to these criteria the existence of a sputum Gram stain showing more than 25 leucocytes and fewer than 10 squamous epithelial cells per low-power field with recovery of a potential respiratory pathogen. Center for Disease Control (CDC) definitions for nosocomial pneumonia diagnosis [13] combine the use of clinical, radiographic and microbiological criteria. However, it is important to note that some of the clinical criteria

defined by the CDC are of little practical use, *e.g.* rales or dullness to percusion on physical examination of the chest, and are non-specific in mechanically ventilated patients.

Despite attempts at establishing dependable clinical criteria for diagnosing nosocomial pneumonia in MV patients, recent research has demonstrated lack of reliability. For example FAGON *et al.* [7] showed that neither fever nor leucocytosis (or leucopenia) were significantly more frequent in a group of MV patients with pneumonia when compared to MV patients without pulmonary infection. In addition, purulent endotracheal secretions present in MV patients, whilst possibly due to pneumonia, may instead by the consequence of purulent bronchitis. The appearance of new pulmonary infiltrates on the chest X-ray may be caused by other factors such as atelectasis, pulmonary oedema, pulmonary haemorrhage or pulmonary drug reactions. Other researchers [4, 7–9, 14] have all found a significant percentage of false-negative or false-positive results using clinical criteria. In a recent study FAGON *et al.* [7] analysed 16 clinical variables that may predict ventilator-associated pneumonia but could not find a combination distinguishing patients with bacterial pneumonia from those without.

Two important conclusions ensue from these investigations. Firstly, clinical criteria fail to accurately diagnose pulmonary infection in MV patients, since ventilator-associated pneumonia may be easily misdiagnosed or overdiagnosed. Secondly, it is necessary to find a simple marker that will facilitate the diagnosis of ventilator-associated pneumonia, especially in adult respiratory distress syndrome (ARDS) patients. The low reliability of clinical criteria in detecting pneumonias during mechanical ventilation has necessitated the investigation and utilization of invasive and non-invasive techniques for the diagnosis of these pulmonary infections in ventilated patients.

Non-invasive techniques

Although aspiration through the endotracheal tube or tracheostomy is the simplest non-invasive technique for obtaining pulmonary secretions for microbiological culture, its usefulness in diagnosing nosocomial pneumonias in MV patients has yet to be firmly established. Two reports from our group [10, 11] comparing qualitative cultures of endotracheal aspirates to quantitative cultures of protected specimen brush (PSB) and bronchoalveolar lavage (BAL) samples concluded that endotracheal aspiration was non-specific (specificity 20–30%) in diagnosing ventilator-associated pneumonia. Some studies are consistent with these findings [12, 15], although others have reported different results. For instance, KASIAN *et al.* [16] showed that endotracheal aspiration samples taken immediately after intubation were useful in 11 out of 14 children with a pulmonary infection. GREIL *et al.* and BRUN-BUISSON [17, 18], using protected and distal aspirate sampling, have had satisfactory results in diagnosing ventilator-associated pneumonias. BAIGELMAN *et al.* [19] found no advantages in culturing PSB samples over routine tracheal suctioning cultures.

Few studies investigating the diagnostic value of endotracheal aspirates using quantitative cultures have been carried out. In addition the results of these studies have been quite inconsistent. BORDERON *et al.* [20] found no agreement between quantitative cultures of endotracheal aspirates and quantitative cultures of lung biopsies taken immediately after death (taking 10^7 colony forming units (CFU)·ml^{-1} as cut-off point). In a more recent study PAPAZIAN *et al.* [21], comparing blind distal bronchial sampling to PSB quantitative cultures, found an excellent agreement between both techniques (the cut-off point for both methods was estimated at 10^4 CFU·ml^{-1}). Our group [22] found no correlation between quantitative cultures of endotracheal aspiration (taking 10^3 CFU·ml^{-1} as a cut-off point) and quantitative cultures of PSB and BAL. However, a preliminary study [23] involving 16 patients with definite pneumonia, having undergone previous antibiotic treatment, and 23 control MV patients without pneumonia, suggests that quantitative cultures (using 10^5 CFU·ml^{-1} as cut-off point) of endotracheal aspirates may have a similar diagnostic accuracy to that of PSB and BAL.

The large discrepancies in the reported results may be due to several factors: 1) heterogeneity among populations studied; 2) differences among the criteria of pneumonia used; 3) lack of reliable control groups; and 4) effects of previous antibiotic therapy. For these reasons, we believe that further studies comparing endotracheal aspirate cultures to "gold standard" techniques such as pulmonary biopsy are needed to determine the usefulness of endotracheal aspirate cultures for the microbiological diagnosis of nosocomial pneumonia in MV patients.

Recently, there has been much concern about finding accurate makers of pneumonia. SALATA *et al.* [24] prospectively investigated 51 intubated patients with sequential examinations of tracheal aspirates for graded Gram stains, quantitative cultures and elastin fibres. Higher grade Gram stain for polymorphonuclear cells and bacteria was seen in patients with pneumonia, but a significant degree of overlap was present. Quantitative tracheal aspirate colony counts were also greater in patients with pulmonary infection and correlated with the Gram stain grading. A colony count $\geq 10^5$ CFU·ml^{-1} was seen in the majority of patients with pneumonia, but also in 40% of patients without pulmonary infection. The presence of elastin fibres (stained with KOH, see fig. 1) in the endotracheal aspirate was highly specific for the presence of necrotizing pneumonia. The technique was not very sensitive (52%) but very specific (the positive predictive value was 100%). Interestingly, the existence of elastin fibres preceded the roentgenographic appearance of pulmonary infiltrates by two days. Despite these apparently good results, the specificity of elastin

fibres for diagnosis of necrotizing pneumonia in patients with ARDS is much lower [25] and there is no further information about this technique.

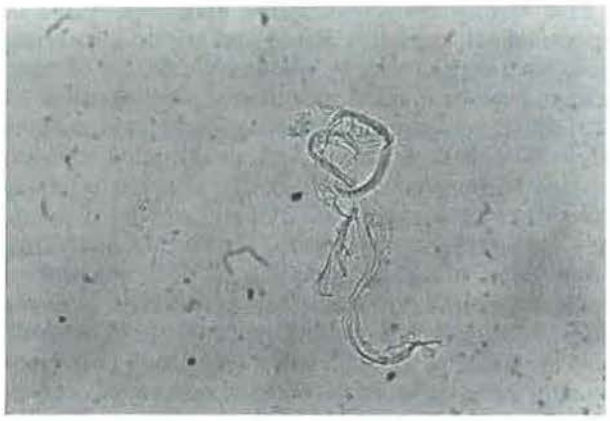

Fig. 1. – Elastin fibres seen in a KOH preparation of endotracheal aspirate sample at an original magnification ×400. (Courtesy of Dr J. Puig de la Bellacasa).

According to a study by WINTERBAUER [26] the technique of antibody-coated bacteria has a sensitivity of 73% and a specificity of 98% in the diagnosis of bacterial pneumonia. A clear advantage of this technique is its ability to detect the infection even when quantitative bacterial counts are low due to previous antibiotic therapy. In a study of tracheal aspirates in intubated patients, WUNDERIK *et al.* [27] found a sensitivity of 54% and a specificity of 100%. In our experience [28] this technique has an important percentage of false-positive results (30%) when compared to PSB in MV patients.

Blood cultures are theoretically a "gold standard technique". Unfortunately, the sensitivity is low (around 20%) [29] and the specificity may not be very high in MV patients who may have several primary sources of bacteraemia [30].

Invasive techniques

The theoretically low specificity of the cultures of simple endotracheal aspirates and other non-invasive methods have promoted the search for invasive methods to diagnose pulmonary infections in intubated and non-intubated patients. Unlike non-invasive methods, invasive methods permit direct access, thereby facilitating the collection of bronchial and parenchymal tissue and bronchial secretions for sampling.

In intubated patients the bronchoscope has to go through the endotracheal tube and obviously this can easily contaminate the inner channel. To avoid contamination, WINTERBAUER *et al.* [31] designed a non-protected brushing system with a sterile, single-sheeted, disposable bronchial cytology brush. Quantitative cultures were performed. Twenty nine of the 33 patients with pneumonia had a count above 4×10^3 CFU·ml^{-1}. None of the control group had a count above 3.4×10^3 CFU·ml^{-1}.

Protected specimen brush

In order to avoid contamination of oropharyngeal flora, WIMBERLEY *et al.* [32] developed a PSB system (fig. 2). *In vitro* [32] and *in vivo* studies [33–43] have demonstrated that PSB is a highly sensitive and specific method for diagnosing pneumonias in non-intubated patients when quantitative cultures were performed, taking the cut-off point to distinguished colonization from infection at 10^3 CFU·ml^{-1}. Only HALPERIN *et al.* [44] have found a low specificity of PSB in healthy volunteers infected by rhinovirus. However, these results may be due to an improper PSB sampling methodology.

The PSB technique has some limitations due to its complexity. Liquid lidocaine cannot be used and a high dose of nebulized lidocaine has to be administered (10–15 ml of 4% solution) (only in non-intubated patients). Another limitation is that PSB samples have to be microbiologically processed using quantitative methods. This represents a considerable personnel and material cost for this method. PSB cost itself is relatively high (around 4$ in Spain) and must be taken into account. The remaining requirements for PSB use are summarized in table 1 (adapted from MEDURI [45]).

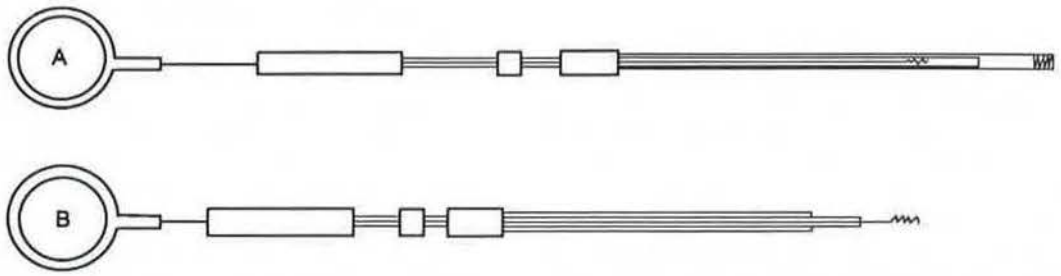

Fig. 2. – A. Schematic diagram of the protected specimen brush. (Reprinted by permission of publishers Doyma Ed, Barcelona). B. Protected specimen brush prepared for sampling after removing the polyethyleneglycol plug.

PSB diagnostic accuracy has been checked in MV animal models [46, 47] as well as in humans [1, 8, 10, 11, 48–51]. HIGUCHI *et al.* [47] evaluated the usefulness of PSB in a primate model of oleic acid-induced acute diffuse lung injury with nosocomial pneumonia. The authors found that PSB had a 70% sensitivity

and 90% specificity. Similar results were obtained by MOSER *et al.* [46] when they compared PSB to transthoracic needle aspiration and transbronchial biopsy in a ventilated canine model of *Streptocccus pneumoniae* pneumonia. It should be pointed out, however, that the animal subjects in these two studies had not received previous antibiotic treatment, thus, the results have to be interpreted accordingly. Two of the studies performed in humans [49, 51] were evaluated without quantitative cultures, a prerequisite for an accurate interpretation of PSB results, and it is difficult to compare them with the remaining studies. CHASTRE *et al.* [8] studied the diagnostic accuracy of PSB in MV patients who died in an intensive care unit [8]. The researchers performed a PSB of the anterior segment of the left lower lobe, shortly after death. This same segment was then removed, quantitatively cultured and histologically processed. These authors confirmed 10^3 CFU·ml^{-1} as the cut-off point to distinguish colonization from infection. In patients who had undergone previous antibiotic therapy the specificity of PSB cultures using the said cut-off point was 42%. The same group evaluated the PSB in a group of 147 MV patients suspected of having pneumonia [1]. They demonstrated a high negative predictive value of PSB and a 75% positive predictive value using the cut-off point of 10^3 CFU·ml^{-1}. BAUGHMAN *et al.* [50] performed a bilateral PSB in MV patients and found concentrations greater than 10^3 CFU·ml^{-1} in areas with pneumonia. In PSB samples from unaffected areas microorganism consistently grew in concentrations below the cut-off point.

Table 1. – Methodology of protected specimen brush (PSB) sampling in intubated or tracheostomized patients

1. Sedation and administration of short acting paralytic agent.
2. Avoid the injection of lidocaine.
3. Avoid the suction of bronchial secretions through the fibreoptic bronchoscope channel.
4. The bronchoscope has to be positioned close the segmental area corresponding with chest X-ray infiltrates.
5. Advance the PSB 3 cm out of the distal tip of the bronchoscope.
6. Push the inner cannula of the PSB to eject the polyethyleneglycol plug into the airways.
7. Wedge the brush in the subsegmental area.
8. Retract the brush into the inner cannula, the inner cannula into the outer cannula and remove the PSB from the bronchoscope.
9. Once the PSB is out of the bronchoscope, the distal portion of the inner cannula has to be wiped with a 70% alcohol solution.
10. The brush has to be advanced and cut with sterile scissors into a sterile solution containing 1 ml of ringer-lactate.
11. The tube with the PSB and ringer-lactate needs to be submitted immediately to the microbiology laboratory for quantitative bacteriological processing.

(adapted from MEDURI [45]).

Because bronchoscopy is not always available in an intensive care setting, it is useful to have non-bronchoscopic methods available for guiding PSB sampling in MV patients. ZUCKER *et al.* [52] studied the blind use of PSB in intubated patients. Using PSB cultures obtained in this way, these authors had an 81% success rate in making decisions concerning antibiotic selection. Our group [10] found a similar diagnostic value using a blindly guided Mètras catheter (fig. 3) (a type of catheter used for bronchography) when compared to PSB *via* fibreoptic bronchoscopy. The proper placement of the Métras catheter was confirmed in the majority of cases. Other investigators have had similar success in using this technique [53]. The Mètras catheter can also be guided fluoroscopically, if needed, as it has radiopaque tip. MARQUETTE *et al.* [48] compared the PSB to a single standard biopsy brush occluded with an agar plug. *In vitro* and *in vivo* studies produced similar results comparing the two systems. Recently, a new device [54] has been designed to blindly obtain secretions from a bronchial segment. This new system has an everting through-lumen balloon that provides sterile access to lower airways. Although commercially available, its reliability has yet to be proved.

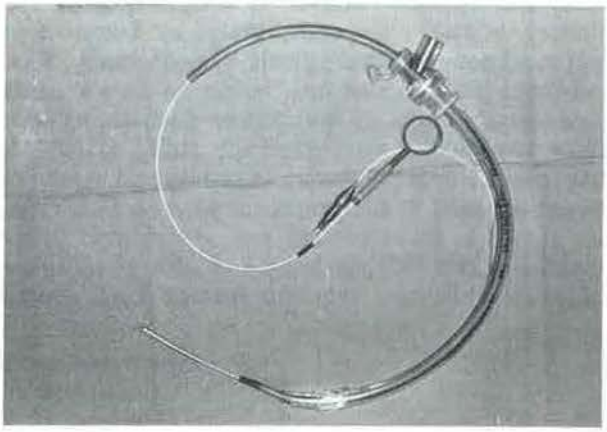

Fig. 3. – Protected specimen brush inside the inner channel of a Métras catheter. The Métras catheter has a radiopaque tip that can direct the protected specimen brush using a fluoroscopic system.

In light of the literature concerning PSB, we conclude that this technique is a reliable method for diagnosing nosocomial pneumonias in MV patients. At the fifth "Conférence de Consensus en Réanimation et Médicine d'urgence" it was agreed that PSB, using 10^3 CFU·ml^{-1} as a threshold, was the most reliable method to diagnose ventilator-associated pneumonias [55]. However, in our opinion several questions remain to be answered. It seems clear that a negative PSB either rules out a pneumonia or is the consequence of an appropriate antibiotic therapy [1, 8]. The problem emerges with the false-positive results that may be the consequence of a prior antibiotic therapy or the bacterial contamination of lower airways in some patients [56, 57]. Our group [58] studying MV

patients without pulmonary infection who had been treated with antibiotics found a low PSB specificity (50%) using 10^3 CFU·ml^{-1} as the cut-off point. The specificity reached 100% when the cut-off point was raised to 10^5 CFU·ml^{-1}. In the intensive care setting the majority of patients receive or have received antibiotic therapy when they develop pneumonia. Thus, with antibiotic treatment, one must keep the possibility of false-positive cultures in mind since antibiotics may promote colonization of lower airways.

Complications of PSB which are very uncommon (<1%) include haemoptysis, haemorrhage and barotrauma. Severe haemoptysis has been described in the presence of bleeding disorders [10].

Bronchoalveolar lavage

Bronchoalveolar lavage (BAL) is a well-known bronchoscopic technique used to evaluate pulmonary interstitial diseases as well as to diagnose pulmonary infiltrates in immunocompromised patients [59–61]. It was generally believed that specimens retrieved by lavage had the same problem as fibreoptic bronchoaspirates, *i.e.* the contamination of the oropharynx and upper airways from bacterial flora. However, the utility of Gram stain and semiquantitative cultures of the fluid retrieved by BAL to diagnose respiratory infections was demonstrated by THORPE *et al.* [62] in 92 non-intubated patients. Concomitantly, KAHN and JONES [63] reported their results on the use of the quantitative cultures of BAL in non-intubated patients. These two studies established the utility of BAL to diagnose bacterial pulmonary infections and agree that the cut-off point to distinguish colonization from infection should be set at 10^5 CFU·ml^{-1}. In addition, in one of these studies [63] the finding of ≤1% of squamous epithelial cells was required for the BAL sample retrieved specificity. The specificity of BAL (using quantitative cultures) has also been well established in non-intubated patients [43] but there is still little clinical experience. Recently PANG *et al.* [42] compared the bacteriology of bronchiectasis using PSB and BAL, obtaining similar results (the cut-off point of BAL 10^4 CFU·ml^{-1}).

The use of BAL in MV patients is much more controversial. JOHANSON *et al.* [64, 65] studied the cultures of tracheal aspirates, BAL, PSB, direct lung aspirates and the histology and microbiology of lung biopsy in 35 baboons after 7–10 days of intubation and mechanical ventilation. The majority of animals were treated with prophylactic intravenous or topical regimens. These authors found that quantitative cultures and bacterial indices of BAL samples showed an excellent correlation with the bacterial concentrations and bacterial indices of the cultures of lung tissue. The bacterial index was obtained as the sum of the logarithmic concentrations of individual bacterial species. BAL showed a slightly lower specificity than PSB but it was clearly more sensitive. CHASTRE *et al.* [66] were the first to compare BAL to PSB in MV humans. They concluded that quantitative cultures of BAL had little value in identifying patients with pulmonary infection. However, the finding of more than 25% of intracellular organisms in cells recovered by BAL was a 100% specific marker of pneumonia in MV patients. The same authors [67] later established the cut-off point of intracellular microorganisms to distinguish pneumonia at 5–7% (sensitivity 86%, specificity 96%). Recently, our group [11] compared the utility of BAL and PSB in 34 non-immunosuppressed MV patients suspected of having bacteria pneumonia. Quantitative cultures of BAL showed a good correlation with quantitative PSB cultures. Moreover, bacterial indices of BAL cultures were significantly correlated to bacterial indices of PSB cultures (fig. 4).

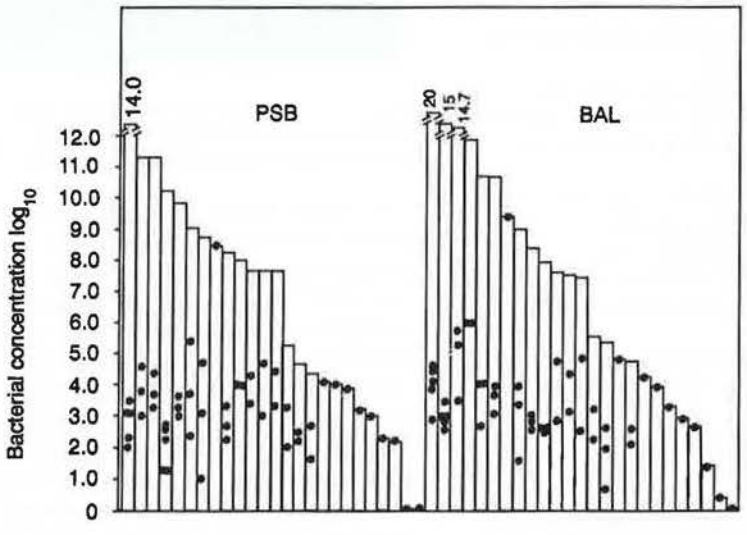

Fig. 4. – (taken from [11]). Bacterial concentrations (in $\log_{10}$ CFU·ml^{-1}) and bacterial indices of individual microorganisms obtained from the cultures of protected specimen brushes (PSB) and bronchoalveolar lavages (BAL) in 25 patients with nosocomial pneumonia acquired during mechanical ventilation. ▭: bacterial index: ●: individual organisms.

The diagnostic accuracy of BAL and PSB was similar (cut-off points for both techniques 10^3 CFU·ml^{-1}) (BAL: sensitivity 59%, specificity 71%, PSB: sensitivity 59%, specificity 86%). GUERRA and BAUGHMAN [68] studied the efficacy and safety of BAL in 60 MV patients. They found a sensitivity of 60%. BAL cultures obtained from control group patients were always below 10^4 CFU·ml^{-1}. Other authors have proposed bronchoscopic [69] and non-bronchoscopic [70, 71] protected BAL for the diagnosis of pulmonary infections in MV patients. GAUSSORGUES *et al.* [70] used a Swan-Ganz catheter to perform BAL. They compared the quantitative cultures of BAL obtained by this procedure to the quantitative cultures obtained by pulmonary biopsy. In nine cases with histologically proven pneumonia, BAL correlated with biopsy cultures. A protected system to perform BAL using a double telescoping plugged catheter has recently been evaluated in MV patients [71]. The sensitivity of this technique in diagnosing pulmonary infections was 80%, whereas the specificity was 66%. MEDURI *et al.* [72] published, in abstract form, the effectiveness of BAL sampling through a protected transbronchoscopic balloon-tipped catheter. Using a threshold of 10^4 CFU·ml^{-1}, protected BAL was considered an effective tool for diagnosing pneumonia in MV patients. PSB results offered a worse diagnostic value. In table 2 the diagnostic value of BAL results obtained by different authors is shown.

PSB. The fifth "Conférence de Consensus en Réanimation and Médecine d'urgence" held in Paris in 1989 had not yet recommended the use of quantitative cultures of BAL to diagnose ventilator-associated pneumonia [55], but at that time there was less information available about this technique. The contradictory results between some studies should encourage more research comparing BAL to a "gold standard" technique such as postmortem pulmonary biopsy.

Percutaneous lung needle aspiration

The diagnostic value of percutaneous lung needle aspiration (PLNA) using ultra-thin needles (25 gauge) is similar to that of PSB [73]. To our knowledge there are no references comparing PLNA to BAL. PLNA has been classically contraindicated in patients undergoing mechanical ventilation because of the risk of barotrauma and, in fact, there are no references using this procedure in humans during artificial ventilatory support. In non-mechanically ventilated patients the rate of pneumothorax is 8% [73]. The rate of this complication in patients undergoing ventilatory support is unknown. BERGER and ARANGO [12] performed this technique in 11 critically ill patients but they did not mention whether patients were MV. Apparently the sensitivity of PLNA in this study was 100%. MOSER *et al.* [46] investigated the diagnostic value of PLNA in a MV model of *Streptococcus pneumoniae* pneumonia. They found a sensitivity of 100% and a specificity of 88%. We [74] studied the diagnostic accuracy of

Table 2. – Bronchoalveolar lavage diagnostic accuracy in nosocomial pneumonias acquired during mechanical ventilation

Author [Ref.]	n	Sens. %	Spec. %	Cut-off CFU·ml^{-1}	Antb.	*Via*	Ref. test
JOHANSON *et al.* 1988 [64]	19 (baboons)	74	87	NS	Yes	FB	Pulmonary biopsy
GAUSSORGUES *et al.* 1988 [70]	13	93	89	NS	NS	Cuffed catheter	Pulmonary biopsy
CHASTRE *et al.* 1988 [66]	21	NS	69	10^4	No	FB	PSB quantitative cultures
TORRES *et al.* 1989 [11]	25	72	71	10^3	Yes	FB	PSB quantitative cultures
GUERRA *et al.* 1990 [68]	60	60	100	10^4	NS	FB	NS
ROUBY *et al.* 1990 [71]	59	80	66	NS	Yes	Double protected catheter	Pulmonary biopsy

Sens. – sensitivity; Spec. – specificity; Antb. – prior antibiotic therapy; FB – fibreoptic bronchoscope; PSB – protected specimen brush; NS: not specified.

In view of the studies mentioned above, BAL seems to be an alternative to PSB for diagnosing pulmonary infections in MV patients, although clinically it seems that the specificity is slightly worse than that of

PLNA (using a 22 gauge needle) in seven critically ill MV patients with pneumonia in whom a PSB did not give a microbiological diagnosis. The sensitivity obtained was 37.5%, keeping in mind that these patients had been treated with antibiotics. Nevertheless, PLNA results were crucial for the outcome of these patients. PLNA during mechanical ventilation is probably less dangerous than had been believed, particularly when using thin needles (22–25 gauge). The new generation of ventilators are able to suspend respiratory cycles momentarily in paralysed patients. Furthermore, extensive consolidations avoid an easy introduction of air into pleural space. Thus, we recommend the use of PLNA in MV patients with extensive and severe pneumonia either when other diagnostic procedures, such as PSB or BAL have not been able to identify the microbiological cause of the pneumonia or when there is no favourable clinical response despite the antibiotic treatment against the microorganisms previously isolated in cultures of the samples retrieved by these techniques (PSB or BAL).

Pulmonary biopsy

Pulmonary biopsy is not a technique to be taken into account for the diagnosis of ventilator-associated pneumonias since other less invasive methods are able to identify the responsible microorganisms with less risk [75, 76]. Nevertheless, histological and quantitative cultures of pulmonary biopsy taken immediately postmortem are considered "gold standard" methods for comparing other techniques, and for this reason are useful in clinical studies. The histological definition of pneumonia is considered when there is accumulation of polymorphonuclear leucocytes in alveoli and adjacent bronchi [77]. The majority of nosocomial pneumonias in MV patients are bronchopneumonias. The histological diagnosis of these bronchopneumonias is based on the presence of consolidation foci spread on the lungs. There are very few studies in humans that have used the histology of the pulmonary biopsy as a "gold standard" reference test [8, 9, 20, 70, 71]. Although these studies have to be considered the most reliable to investigate the diagnostic value of a particular technique, we must keep in mind the bronchopneumonic characteristics of the ventilator-associated pneumonias and the necessity of sampling several sites in all the pulmonary lobes when using pulmonary biopsy as a reference test. More studies using postmortem pulmonary biopsies and necropsy findings are necessary to definitely establish the diagnostic accuracy of the available methods for the diagnosis of pulmonary infections in MV patients.

Conclusion

The diagnosis of nosocomial pneumonias in MV patients is still a matter of controversy. Despite the important amount of information available on this subject, there are still several problems which require solution. It seems clear that clinical criteria are subject to an important percentage of error and that there are no absolutely reliable clinical markers of pneumonia. Other markers such as elastin fibres or antibody-coated bacteria need further clinical investigation. As for the different sampling methods available, PSB seems to have been the most thoroughly studied, although there is very little information about the modifications in its diagnostic value caused by prior antibiotic therapy. Taking into account the fact that the majority of ventilated patients are treated with antibiotics, we believe that the specificity of PSB in these cases is an issue which has yet to be adequately solved. There is also very little information about antibiotic changes induced by PSB results and whether the final outcome of patients is modified or not by using the information provided by this technique. BAL is a promising technique but more clinical studies are needed. Despite the need for further research, the finding of more than 5–7% of intracellular bacteria seems to be a specific marker of pneumonia. In a recent review performed at MacMaster University [78], the authors conclude that a randomized trial of PSB *versus* an empirical therapy with antibiotics is required. In contrast, the fifth "Conférence de Consensus en Réanimation et Médicine d'urgence" [55] recommended the use of the PSB (using a threshold of 10^3 CFU·ml^{-1}) and BAL sampling to search for intracellular microorganisms as the methods for diagnosing, and managing nosocomial pneumonias acquired during mechanical ventilation. Our personal view is that quantitative cultures of PSB and BAL are valid tools for diagnosing and managing nosocomial pneumonias in MV patients and their utilization depends on personal experience. Future efforts in investigation have to be directed towards valid and simple techniques of sampling lower airway secretions and also towards determining specific markers of parenchymal pulmonary infection.

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Précision des moyens diagnostiques utilisés pour l'approche des infections respiratoires nosocomiales chez les patients sous ventilation mécanique. A. Torres.

RÉSUMÉ: Il s'agit d'une revue de la littérature médicale concernant les techniques de diagnostic disponibles pour faire face aux infections respiratoires nosocomiales chez les patients soumis à une ventilation mécanique. La première partie concerne la valeur des critères cliniques utilisés pour le diagnostic des pneumonies nosocomiales chez ces patients, et la précision de marqueurs simples de la pneumonie, comme les colorations des fibres élastiques et des bactéries marquées par anticorps. La seconde partie fait la revue des méthodes actuellement disponibles, invasives ou non invasives, pour le diagnostic des infections pulmonaires acquises au cours de la ventilation mécanique. En ce qui concerne les méthodes invasives, la brosse protégée et le lavage broncho-alvéolaire font l'objet d'une large discussion, sur base de différents résultats de la littérature. Actuellement, ces deux méthodes s'avèrent les plus précises de celles qui sont disponibles. Le fait que le lavage broncho-alvéolaire permette de combiner l'examen cytologique et la culture quantitative de l'échantillon obtenu est souligné. Le rôle de la ponction transcutanée pulmonaire à l'aiguille est également mentionné. Finalement, le diagnostic histologique de pneumonie et les cultures de biopsies pulmonaires post-mortem sont considérés comme les "golden standards" pour les recherches dans ce domaine. Des orientations futures pour des recherches cliniques ultérieures sont également évoquées. *Eur Respir J., 1991, 4, 1010–1019.*