

LETTERS TO THE EDITOR

Nosocomial pneumonia during mechanical ventilation

We read with interest the editorial by Dr Brun-Buisson published in the November issue (1995;50:1128-30). Since part of our work was alluded to in several parts of the text, we feel it necessary to reply to avoid confusion to the readers interested in the field of the diagnosis of ventilator-associated pneumonia (VAP). Firstly, Dr Brun-Buisson stated that, in one of our papers,¹ we concluded that lung histological and microbiological findings on immediate necropsy biopsy samples are inadequate "gold standards" in patients receiving antibiotics. Actually, our conclusion was that quantitative cultures of immediate necropsy biopsies are not a good gold standard since they cannot discriminate the histological absence or presence of pneumonia (page 331, first paragraph, reference 2). Our recommendations for future studies were to use the histopathology of necropsy pulmonary biopsies as a gold standard, comparing patients with and without antibiotics and considering different time intervals of treatment (page 331, second paragraph, reference 2). The results of this study¹ have been confirmed by others²⁻⁴ and only the recent work by Chastre *et al*⁵ disagrees with most of the necropsy studies performed upon humans. However, one can argue, as the author did, that our results and those of others could be biased by the presence of prior antibiotic treatment which is, on the other hand, a frequent and real situation when managing mechanically ventilated patients who develop VAP. For that reason, we repeated our necroscopic study using a human model of multiple bilateral bronchus sampling with an average of 16 biopsy specimens per patient.⁶ This time we also included patients free from antibiotics (at least 48 hours before dying), and compared these with patients who received antibiotics. The results were exactly the same as those of our previous work, irrespective of the presence or absence of antibiotics. Furthermore, when classifying pneumonia into four different evolution categories, quantitative cultures of lung biopsy specimens could not discriminate between the presence or absence of pneumonia. In view of this work and that of previous authors,¹⁻⁴ we believe that histology (with positive or negative cultures) is the only acceptable gold standard of VAP. Obviously, experienced pathologists have to differentiate initial periods of VAP from initial periods of diffuse alveolar damage when using necroscopic histology to validate diagnostic techniques for pneumonia.

In another part of the editorial Dr Brun-Buisson refers to the inaccuracy of quantitative cultures of endotracheal aspirates to diagnose VAP. This is a controversial issue in the literature. However, at least five studies⁷⁻¹¹ support quantitative cultures of endotracheal aspirates for the diagnosis of VAP. One of

these studies⁴ has been performed in a post mortem human model. We think that a sampling method which omits bronchoscopic techniques should be taken into account for the routine management of patients with VAP.

We agree with Dr Brun-Buisson that the best way to study the specificity of diagnostic methods in the context of VAP is in patients without pneumonia as we have done previously.¹² Dr Brun-Buisson suggested technical problems in our paper concerning oral contamination since high counts of non-pathogenic oropharyngeal organisms were reported. Although no explicit reference was made to the type of technical problems, these can be due to sampling or to oral contamination. With regard to sampling, and since diagnosis of VAP with bronchoscopic techniques is not an issue for amateurs, one experienced member of staff with a particular interest in the field (AT) personally performed most of the techniques for that study which removes the possibility of sampling errors. With regard to oral contamination, our study¹² shows that only two of 12 (16%) microorganisms isolated from protected specimen brush samples in counts of $\geq 10^3$ cfu/ml were non-pathogenic oropharyngeal flora. In bronchoalveolar lavage samples all but one isolate (10^4 cfu/ml) did not correspond to oropharyngeal flora. When carefully analysed, our results indicate that oral contamination was not a major problem in that study. Furthermore, a study of identical design concerning the specificity of the techniques¹³ confirmed our results in mechanically ventilated patients without suspected pneumonia. On the other hand, this study fits very well with the concept that mechanically ventilated patients frequently have colonised distal airways. Our necroscopic studies have confirmed this finding.^{1,6}

We hope that our comments will help the reader to better understand the editorial comment by Dr Brun-Buisson.

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- 1 Torres A, El-Ebiary M, Padró L, Gonzalez J, Puig de la Bellacasa J, Ramirez J, *et al*. Validation of different techniques for the diagnosis of ventilator-associated pneumonia. Comparison with immediate postmortem pulmonary biopsy. *Am J Respir Crit Care Med* 1994;149:324-31.
- 2 Rouby JJ, Martin de Lassale E, Poete P, Nicolas MH, Bodin L, Jarlier V, *et al*. Nosocomial bronchopneumonia in the critically ill: histologic and bacteriologic aspects. *Am Rev Respir Dis* 1992;146:1059-66.
- 3 Marquette CH, Copin MC, Wallet F, Neviere R, Saulnier F, Mathieu D, *et al*. Diagnostic tests for pneumonia in ventilated patients: prospective evaluation of diagnostic accuracy using histology as a diagnostic gold standard. *Am J Respir Crit Care Med* 1995;151:1878-8.
- 4 Papazian L, Thomas P, Garbe L, Guignon I, Thirion X, Charrel J, *et al*. Bronchoscopic or blind sampling techniques for the diagnosis of ventilator-associated pneumonia. *Am J Respir Crit Care Med* 1995;152:1982-91.
- 5 Chastre J, Fagon JY, Bornet-Lesco M, Calvat S, Dombert MC, Al Khani R, *et al*. Evaluation of bronchoscopic techniques for the diagnosis of nosocomial pneumonia. *Am J Respir Crit Care Med* 1995;152:231-40.
- 6 Fàbregas N, Torres A, El-Ebiary M, Ramirez J, Hernández C, González J, *et al*. Histopathological and microbiological aspects of ventilator-associated pneumonia. *Anesthesiology* 1996;84:260-71.
- 7 Marquette CH, Georges H, Wallet F, Ramon P, Saulnier F, Neviere R, *et al*. Diagnostic efficiency of endotracheal aspirates with quan-

titative bacterial cultures in intubated patients with suspected pneumonia. Comparison with the protected specimen brush. *Am Rev Respir Dis* 1993;148:138-44.

- 8 El-Ebiary M, Torres A, Gonzalez J, Puig de la Bellacasa J, Garcia C, Jimenez de Anta MT, *et al*. Quantitative cultures of endotracheal aspirates for the diagnosis of ventilator-associated pneumonia. *Am Rev Respir Dis* 1993;148:1552-7.
- 9 Middleton R, Broughton WA, Kirkpatrick MB. Comparison of four methods for assessing airway bacteriology in intubated mechanically ventilated patients. *Am J Med Sci* 1992;304:239-45.
- 10 Papazian L, Martin C, Albanese J, Saux P, Charrel J, Gouin F. Comparison of two methods of bacteriologic sampling of the lower respiratory tract: a study in ventilated patients with nosocomial bronchopneumonia. *Crit Care Med* 1989;17:461-4.
- 11 Papazian L, Martin C, Meric B, Dumon JF, Gouin F. A reappraisal of blind bronchial sampling in the microbiologic sampling diagnosis of nosocomial bronchopneumonia. A comparative study in ventilated patients. *Chest* 1993;106:236-42.
- 12 Torres A, Martos A, Puig de la Bellacasa J, Ferrer M, El-Ebiary M, Gonzalez J, *et al*. Specificity of endotracheal aspiration, protected specimen brush and bronchoalveolar lavage in mechanically ventilated patients. *Am Rev Respir Dis* 1993;147:952-7.
- 13 Rodriguez de Castro F, Solé J, Elcuaz R. Quantitative cultures of protected brush specimens and bronchoalveolar lavage in ventilated patients without suspected pneumonia. *Am J Respir Crit Care Med* 1994;149:320-3.

AUTHOR'S REPLY I agree with Torres and colleagues that lung pathology, when examined by experienced pathologists, should be considered as the test least subject to bias for determining the presence or absence of pneumonia. The purpose of my editorial was to highlight problems that arise when this test is applied to patients who have received mechanical ventilation for some time, often have associated lung disease and have received multiple antibiotics, and eventually have died at an unknown time delay from prior or ongoing pulmonary infection. In this context, lung pathology appears to be especially difficult to use when attempting to assess the diagnostic value of various sampling techniques of respiratory secretions, which implies relating cultures of these samples to lung pathology and tissue cultures. Conflicting studies continue to be published in this area, and I believe it is useful to stress potential problems in the analysis and interpretation of such studies.

I have no reservation on the technical skills of Torres and coworkers to perform bronchoscopy. The problem I see with some studies that use lung pathology¹⁻⁶ is that their results are contradictory to some well accepted principles – for example, that pulmonary infection (as one would expect from any bacterial infection) is associated with substantial growth (in the range of 10^{3-6} cfu/g) from lung tissue,^{4,5} and that tracheal aspiration is a relatively sensitive diagnostic test for pneumonia but a non-specific one during prolonged tracheal intubation⁷⁻⁹ because of frequent colonisation of the upper and even the lower airways. Clearly, the finding of pathological aspects "typical of pneumonia" associated with no or insignificant growth from lung specimen cultures as reported by Torres *et al* and others^{1,2} raises questions. Obviously, there are problems with either the interpretation of lung pathology (timing of samplings, prior lung history) or the cultures of the specimens (prior antibiotics, efficiency of lung defences), or both, if we are talking about bacterial pneumonia. In this context it is difficult to interpret correlations between

lung pathology and cultures of respiratory secretions.

Numerous studies have been performed in this area in recent years in an attempt to clarify the diagnostic approach to the so-called "ventilator-associated pneumonia". It would be unfortunate if such efforts were wasted simply because of misinterpretation. The practical issue for physicians who care for patients on mechanical ventilation is to learn how much they can rely on the sampling technique(s) they routinely use when pulmonary infection is suspected. Taken together, the studies by Torres *et al* and others simply suggest that tracheal aspirates are just as good as other more "sophisticated" techniques using quantitative cultures and/or protected specimens, with or without bronchoscopy. I have already mentioned the potential impact of this approach on antibiotic usage in intensive care units and its consequences. But are we 25 years behind with diagnostic techniques of pulmonary infection?

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- 1 Torres A, El Ebiary M, Padro L, Gonzales J, de la Bellacasa JP, Ramirez J, *et al*. Validation of different techniques for the diagnosis of ventilator-associated pneumonia. Comparison with immediate post-mortem biopsy. *Am J Respir Crit Care Med* 1994;149:324-31.
- 2 Rouby JJ, Martin de Lassale E, Poete P, Nicolas MH, Bodin L, Jarlier V, *et al*. Nosocomial bronchopneumonia in the critically ill: histologic and bacteriologic aspects. *Am Rev Respir Dis* 1992;146:1059-66.
- 3 Marquette CH, Copin MC, Wallet F, Nevriere R, Saulnier F, Mathieu D, *et al*. Diagnostic tests for pneumonia in ventilated patients: prospective evaluation of diagnostic accuracy using histology as a diagnostic gold standard. *Am J Respir Crit Care Med* 1995;151:1878-88.
- 4 Chastre J, Viau F, Brun P, Pierre J, Dauge MC, Bouchama A, *et al*. Prospective evaluation of the protected specimen brush for the diagnosis of pulmonary infections in ventilated patients. *Am Rev Respir Dis* 1984;130:924-9.
- 5 Johanson WG, Seidenfeld JJ, Gomez P, De Los Santos R, Coalson JJ. Bacteriologic diagnosis of nosocomial pneumonia following prolonged mechanical ventilation. *Am Rev Respir Dis* 1988;137:259-64.
- 6 Hill JD, Ratliff JL, Parrott JCW, Lamy M, Fallat RJ, Koeniger E, *et al*. Pulmonary pathology in acute respiratory insufficiency: lung biopsy as a diagnostic tool. *J Thorac Cardiovasc Surg* 1976;71:64-71.
- 7 Johanson WG, Pierce AK, Sanford JP, Thomas GD. Nosocomial respiratory tract infection with gram-negative bacilli. The significance of colonization of the respiratory tract. *Ann Intern Med* 1972;77:701-6.

Silica exposure and risk of lung cancer

The objective review by Weill and McDonald (January 1996;51:97-102) of the role of silica exposure and the risk of lung cancer was long overdue and thoroughly needed. The authors endorse, albeit to a limited extent, the study by Checkoway *et al* of diatomite workers,¹ but in doing so they do not mention a most important observation that casts doubt on the alleged excess risk of lung cancer in the diatomite cohort. Thus, the overall SMR for lung cancer was 1.43, a figure which supports a mildly increased risk. Lacking a smoking history and in an effort to control the con-

founding effects of smoking, the authors calculated the SMRs for other cigarette smoke "induced" cancers – namely, those of the larynx, bladder, kidney, and oesophagus – and found no increase. While all of these cancers are related to cigarette smoking to some extent, the association is much more tenuous than it is for lung cancer. Other factors, in particular alcohol and diet, also have a significant effect. In contrast, the SMR for emphysema for the diatomite workers was 180, indicating a greater risk of dying from emphysema than from lung cancer. The cause and effect relationship between cigarette smoking and emphysema is as compelling, if not more so, than it is between lung cancer and smoking. Moreover, there is virtually no cause of disabling emphysema leading to death other than cigarette smoking.

Weill and McDonald correctly cast doubt on studies that rely on subjects selected from silicosis registries or from registers of those who have been compensated. One of the papers referred to is that of Ng *et al* who studied subjects with silicosis in Singapore.² The paper stated that over 90% of their cohort were smokers, compared with 60% of the general population. It is difficult to understand how so many studies that rely on silicosis registries and their like find their way into print. The question as to whether exposure to silica per se or silicosis is associated with an increased rate of lung cancer cannot be answered by statistical manipulation of defective data; statistics obviously have a role to play but, as Bradford Hill pointed out many years ago, only in conjunction with other criteria, the most important of which is biological plausibility.

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- 1 Checkoway H, Heyer NJ, Demers PA, Breslow NE. Mortality among workers in the diatomaceous earth industry. *Br J Ind Med* 1993;50:586-97.
- 2 Ng TP, Chan SL, Lee J. Mortality of a cohort of men in a silicosis register: further evidence of an association with lung cancer. *Am J Ind Med* 1990;17:163-71.

BOOK REVIEW

Tobacco and Health. Scientific editors: Sir Richard Doll and Sir John Crofton. (Pp 227; £45.00). London: Royal Society of Medicine Press Ltd, 1996. 1 85315 272 2.

This book, edited by two of the most eminent men in the field, is composed of 17 chapters by current contributors in the area of smoking and health.

The chapters on price and consumption of tobacco by Townsend, on tobacco and the developing world by Mackay and Crofton, and on children and smoking: the family circle by Charlton are particularly pertinent and well written. Epidemiology and mortality are presented in two clear, easily digested chapters by Wald, Peto and co-authors. Sir

Richard Doll deals with cancers weakly related to smoking. Authors from the Bart's group spell out the harm from passive smoking and evidence of its effects on the respiratory and cardiovascular systems as well as during pregnancy.

The chapters by Reid on tobacco control, Chapman on advertising, and Pollock on the tobacco industry make stimulating, informative reading and are complemented by accounts of the current legal position of tobacco and of the industry's tactics.

There are informative chapters on smokeless tobacco, the history of tobacco substitutes, and the moves to reduce tar and nicotine levels. Baron provides a balanced discussion of the putative beneficial effects of nicotine and cigarette smoking, and a chapter is devoted to women as a vulnerable target group. The overview of cessation by Foulds is a competent account delivered from the viewpoint of a psychologist in the field, but perhaps more space could have been given to work and progress with patients.

This readable book is up to date, comprehensive, and well referenced. It is likely to be of interest to a wider audience than just medics, paramedics, public health experts, psychologists, and students who wish to be well informed. I recommend it not just to interested individuals, hospital and university libraries, but also to the general public. – IAC

NOTICES

International Lung Sounds Association

The 21st International Conference on Lung Sounds will be held in Chester, UK on 4-6 September 1996. For further information please contact Raymond L H Murphy Jr, Faulkner Hospital, 1153 Centre Street, Boston, MA 02130, USA (Telephone: 617 522-5800, x 1968; Fax: 617 522-4156) or John Earis, Liverpool Medical Institution, 114 Mount Pleasant, Liverpool L3 5SR, UK (Telephone: 151 709 9125; Fax: 151 707 2810). Internet address: HTTP://WWW.UMANITOBA.CA/FACULTIES/MEDICINE/PEDIATRICS AND CHILD HEALTH/ILSA/

4th International Congress on the Immune Consequences of Trauma, Shock and Sepsis

The 4th International Congress on the Immune Consequences of Trauma, Shock and Sepsis – Mechanisms and Therapeutic Approaches will be held in Munich on 4-8 March 1997. The deadline for abstracts is 30 October 1996. For further information contact Prof Dr med E Faist, Ludwig-Maximilians-University Munich, Klinikum Grosshadern, Dept. of Surgery, Marchioninistrasse 15, 81377 Munich, Germany. Phone: 49-89-7095-3441/2461. Fax: 49-89-7095-2460. E-mail: faist@gch.med.uni-muenchen.de.