

Correspondence

THE ROLE OF HYPOVENTILATION AND VENTILATION-PERFUSION REDISTRIBUTION IN OXYGEN-INDUCED HYPERCAPNIA DURING ACUTE EXACERBATIONS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

To the Editor:

We read with great interest the article by Robinson and colleagues that appeared in the May 2000 issue of the Journal (1). In this article, the authors concluded that the major mechanism of hypercapnia in patients who retain CO₂ was a reduction in overall ventilation, as opposed to a redistribution of perfusion caused by the release of hypoxic pulmonary vasoconstriction (HPV).

The authors identified a group of patients as retainers if their PaCO₂ increased more than 3 mm Hg. This, however, makes the physiologic differences between retainers and nonretainers less clear. From a clinical standpoint, most physicians would not classify a patient whose PaCO₂ went from 43 mm Hg to 46 mm Hg as a retainer (subject 14).

Furthermore, the mean PaO₂ in the group of retainers was lower than that in the nonretainer group (54.5 versus 62.7 mm Hg, respectively) and neither group was particularly hypoxemic (1). This is in sharp contrast to the patients in the study by Aubier and colleagues, where the mean PaO₂ was 38 mm Hg (2). As HPV does not seem to play a physiologic role until PaO₂ is lower than 55–60 mm Hg (3), it is unlikely that there would be release of HPV in the nonretainer group, and only a mild release of HPV in the retainer group. Additionally, the Haldane effect, which as with HPV is more prominent at lower partial pressures of oxygen, may have contributed to hypercapnia, and deserves mention.

Robinson and colleagues also found that retainers had a significantly greater change in alveolar dead space while on oxygen as compared to nonretainers. Our interpretation of these data is that \dot{V}/\dot{Q} distribution changed due to a release of HPV in the retainer group, supporting the conclusions of Aubier and others (2, 4, 5). This effect may have been limited to the retainer group for the reasons outlined above. Finally, we were unclear as to why they concluded that the reduction in minute volume was *more* significant than changes in \dot{V}/\dot{Q} matching due to release of HPV, when neither of these variables was quantified as compared to the total change in PaCO₂.

This was the first study of its kind, and the authors should be commended on their techniques and innovative examination of a perplexing physiologic problem. However, we believe the categorization of their groups of responders and nonresponders, as well as their interpretations of the results, are subject to continued discussion and refinement.

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From the Authors:

We thank Drs. Feller-Kopman and Schwartzstein for their comments on our recent article (1).

The choice of a 3 mm Hg rise in PaCO₂ as hypercapnia was made with reference to the reproducibility of the electrode, as noted in the paper, so that a 3 mm Hg or greater rise could be regarded as real. We feel that this resulted in a reasonable separation of the patients, as the largest rise in CO₂ in the

“nonretainers” was 1.9 mm Hg and most actually had a fall in PaCO₂. Subject 14 did rise from a PaCO₂ in the normal range to 46 mm Hg, which would clinically be regarded as abnormal.

It is necessary to distinguish between the local P_{O₂} in the low \dot{V}_A/\dot{Q} regions of the lung, which would be well within the operating range for hypoxic pulmonary vasoconstriction (HPV) in our patients, and the final mixed PaO₂ which will be kept relatively high by the redistribution mechanism. In any case, a number of studies have shown that HPV is present even in patients with mild COPD and that it has an important role in preserving \dot{V}_A/\dot{Q} matching (2, 3). Release of HPV with oxygen administration would be expected to increase blood flow to low \dot{V}_A/\dot{Q} regions, manifest as an increase in log SD Q in our MIGET data, and this occurred *equally* in our CO₂ retainer (R) and nonretainer (NR) groups.

While there was some attendant increase in alveolar dead space with oxygen administration in the NR group, there was a larger and statistically significant increase in this dead space, and decrease in ventilation in the R group, which distinguished them from the NR patients. There may be another separate mechanism causing this larger increase in alveolar dead space in the R group, causally unrelated to the decrease in ventilation. However, we prefer the more economic hypothesis that the two are connected through an increase in alveolar P_{CO₂}.

Model calculations of the relative contributions to the rise in PaCO₂ in the R group revealed about 43% due to the increase in alveolar dead space, 46% due to the decrease in overall ventilation and the remaining 11% due to the Haldane effect (6%) and changes in cardiac output (5%).

In summary, we believe that our data are entirely consistent with those of Aubier (4) and others. However, the application of MIGET to this physiologic problem has allowed the further dissection of the above mechanisms. We conclude that the equal changes in log SD Q in the R and NR groups is evidence that release of HPV is not a distinguishing mechanism. Hypoventilation and a large increase in alveolar dead space are distinguishing mechanisms and they may be causally related.

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EFFECT OF UNPLANNED EXTUBATION ON OUTCOME OF MECHANICAL VENTILATION

To the Editor:

I read with interest the paper by Epstein and colleagues (1) regarding the outcome of unplanned extubation (UE). I have had a long-standing interest in this subject (2–5) and would like to comment on what I think is a skewed approach to the problem. Various studies have looked at different aspects of the problem, including predictors of UE, predictors of reintubation, outcome of UE, etc. Unfortunately, most of these studies have had relatively high rate of UE and this most basic aspect of UE is either not commented upon, or is viewed as an inevitable aspect of translaryngeal intubation. The current study had a UE rate of 11% per patient and 1.6% per intubated day. Another study also published in 2000 (6) also had UE rates of 11.4–17.1% per patient and 1.51–2.47% per intubated day. These high rates are found in much of the literature (1, 2). Compare this with the situation in Australia where, in 1998–1999, the Australian Council on Health Care standards re-

corded an UE rate of 119 incidents over 29,652 intubated days (0.4%) (5). Anecdotally, UE rates in the UK (3, 5) and Sweden (5) too are very low. Our experience is similar (2). Over 4 years (1994–1997) we recorded UE rates of 0.71% per patient and 0.39% per intubated day, respectively. This incidence was similar to that of 0.68% and 0.32% in the next two years (1998–1999). It is particularly instructive to read the experiences of medical and nursing personnel who have had the opportunity to work in different continents, as this clearly explains the marked difference in the UE rates (5). Unlike Epstein, who used physical restraints liberally in agitated patients, other ICUs that have recorded these low UE rates do not resort to physical restraint as a means of preventing UE. Does the physical restraint actually decrease UE, or does it worsen patient agitation and increase UE? The literature is equivocal.

Although the authors conclude that UE is not associated with increased mortality, they should note that in one particular study (7) the authors recorded 24 incidents of UE in 53 patients in which three incidents directly resulted in death. This gives a mortality of 5.7% directly as a consequence of UE. UE is a potentially fatal complication, and the best way to prevent any associated mortality is to ensure that the UE does not occur.

I believe that when viewing the problem of UE in the context of improving standards of critical care, statistical analysis regarding predictors of UE, predictors of reintubation, or predictors of mortality is not the way forward. Instead, each UE should be viewed as an individual incident, in an attempt at analyzing why such an incident was allowed to occur in the first place. Our experience showed that 50%–78% (2) of airway accidents were either completely or partly preventable. Focusing on individual incidents especially with respect to nursing supervision, adequate securing of the endotracheal tube, adequate sedation and appropriately early weaning is usually all that is required to keep UE rates below 0.5% per intubated day.

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From the Authors:

I agree with Dr. Kapadia that a skewed analysis of the unplanned extubation literature is not the best way to proceed. A review of the peer-reviewed literature clearly demonstrates that unplanned extubation is a frequent event when studying medical, general surgical, or multidisciplinary ICU patient populations (1). In these studies, with a minimum mean duration of mechanical ventilation of three days (range 3–11 days), 3 to 16% of patients experienced at least one episode of unplanned extubation. In contrast, Kapadia and colleagues, in an uncontrolled study, observed an extraordinarily low unplanned extubation rate among their ICU population, more than 75% of whom were cardiac surgery patients (2). Although the low rate was attributed to a specific prevention strategy, the authors failed to account for the impact of their unique case mix, with a mean duration of mechanical ventilation less than two days. Patients requiring such a short duration of ventilation are unlikely to have high severity of illness, require ICU procedures that have a tendency to lead to accidental extubation, or have the opportunity to experience self-extubation.

After controlling for APACHE II, comorbid conditions, age, sex, and indication for mechanical ventilation in a medical ICU, we demonstrated that unplanned extubation resulted in a prolonged duration of mechanical ventilation, ICU stay and hospital stay and increased the need for postacute care among survivors (3). Our results highlight the need to focus on prevention of unplanned extubation among mechanically ventilated populations frequently encountered by ICU practitioners. One possible way of reducing the incidence of unplanned extubation is to apply “adequate” chemical sedation (2). Unfortunately there is accumulating evidence that aggressive sedation poli-

cies can lead to prolonged duration of mechanical ventilation, ICU and hospital stay and need for tracheostomy (4–6). Therefore, before advocating specific prevention strategies, investigators should conduct properly controlled studies in the ICU populations at highest risk for unplanned extubation.

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BIOLOGIC VARIABILITY IN MECHANICAL VENTILATION IN A CANINE OLEIC ACID LUNG INJURY MODEL

To the Editor:

We read with interest the article by Nam and colleagues that finds no advantage with biologic variability in mechanical ventilation in a canine oleic acid lung injury model (1). We have developed biologically variable ventilation (BVV) and have published a series of articles (2–5) showing its efficacy in experimental models—therefore, we have analyzed the article by Nam and colleagues and would like to report the following:

1. *Statistical analysis.* Nam and colleagues report no difference in Pa_{O_2} between groups in their study. Using longitudinal analysis (an ambiguous description in methodology) they report the p value for Pa_{O_2} between groups as 0.77. In their study, at 240 min, mean Pa_{O_2} is 79% greater with BVV. In our work we showed a Pa_{O_2} difference of 87%, favoring BVV at 240 min. We have examined their raw data as presented in their Figure 5 time course of Pa_{O_2} for the nine individual animals in each of the CV and BV groups. When analyzed using the same statistical approach as in our publications—a split plot ANOVA with repeated measures—we show a statistical significance for Pa_{O_2} between groups over time for their data. The group \times time interaction is $p = 0.0125$. At 240 min, by least squares means test to examine for effect of time for Pa_{O_2} between groups, $p = 0.0031$. Even with a Bonferroni's adjustment this difference would be significant. Thus, a benefit for oxygenation is seen with BVV in the study by Nam and coworkers when the statistical analysis is done as described in our studies. The approach to statistical analysis represents the fundamental difference in interpretation between our findings and those reported by Nam and colleagues. However, other important differences between the two studies are present to account for the negative findings by Nam and colleagues and include:
 2. *Differences in severity of ARDS.* The canine model by Nam and coworkers was associated with a total mortality of 33% versus 0% in our porcine model. It is highly questionable that valid conclusions can be made from animals so sick that end Pa_{O_2} is below normal venous O_2 in 5/10 animals reported in their Table 5.
 3. *Misinterpretation of stochastic resonance model.* Nam and colleagues have erroneously interpreted the work of Suki and colleagues—work that may offer an explanation for the efficacy of BVV(6). The model by Suki and coworkers assumes two populations of alveoli—one population aerated and the other collapsed. They do not base their model on P_{flex} as suggested by Nam and colleagues. An important part of the model by Suki and colleagues is that an optimal variability or noise occurs with stochastic resonance. The noise associated with variable f in our study was 11.5% (coefficient of variation) and in the study by Nam and colleagues it was 24%. Increased noise can decrease the optimal signal-to-noise ratio with stochastic resonance, and the 100% higher noise in the study by Nam and colleagues may be too great in this situation to maximize benefit.

In conclusion, the work by Nam and coworkers is seriously flawed with methodologic and interpretative errors. A more carefully designed study is necessary to independently prove or disprove the efficacy of BVV—in fact our analysis of Nam and colleagues' data for Pa_O₂ indicates that they have, in fact, shown efficacy for BVV. If, as we suggest, efficacy for BVV has been shown, the experiment performed by Nam and colleagues is a strong endorsement for the robustness of BVV, given the marked differences from our initial study.

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From the Authors:

Dr. Mutch and associates question our statistical methods (3), and their analysis of our data finds a significant benefit of BV on Pa_O₂. However, it is unclear whether they account for the data missing at later time points due to mortality. In contrast, we utilized longitudinal analysis, which is both well documented (1) and implemented in major statistical packages including Stata, SAS, and S-plus. This analysis includes all data from all animals, accounting for both temporal trends and correlations between measurements within each animal. The mean values at later time points are strongly influenced by the absence of data from the animals that died from hypoxemia, as well as the high Pa_O₂ in two BV outliers. Indeed, a simple inspection of Figure 5 shows no qualitative difference between the groups, with the exception of these two BV animals.

With regard to the differing severity of the oleic acid models, our initial postinjury Pa_O₂ was virtually identical to that in the original report of Lefevre and colleagues (2). In our discussion, we speculated that the fact that we reported worse outcomes despite similar initial injuries could reflect a species difference, with dogs demonstrating a more progressive type of injury that is unresponsive to BV.

Finally, we have not misinterpreted the work of Suki and colleagues (4). The whole lung pressure–volume (P–V) curve is the summation of P–V curves of all alveoli. This is simplified in the Suki and coworkers model to two groups, aerated units and collapsed but recruitable units. In this model, the equivalent of “Pflex” is determined by the opening pressure of the collapsed unit curve, and peak inspiratory pressures must be distributed about this value to benefit from stochastic resonance. We discuss in detail the differences in the “variability” between the studies. In an attempt to use a relevant “biological” variation, our respiratory pattern was recorded from an awake, spontaneously breathing dog. It had a coefficient of variation of 24%. We cannot speculate as to how much variability is optimal. We maintain, however, that there is no theoretical need for a “biological” source of variation. Perhaps as Suki and colleagues suggest, a breathing pattern with gaussian or other distribution with a different coefficient of variation might be more effective.

In summary, we agree with Dr. Mutch and colleagues that further study is necessary to independently prove or disprove the efficacy of BVV. However, our carefully done study is not, as they suggest, a “strong endorsement for the robustness of BVV.”

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COMPLICATIONS OF EVALUATING NODULES

To the Editor:

In the Clinical Commentary on the solitary pulmonary nodule (1), the authors quote an incidence of death from transbronchial biopsy of 0.24% and from resection, 3–7%. The former number is based on survey data 25 years old (2), and the latter on data collected nearly 40 years ago (3). Many patients would be dissuaded from definitive diagnosis and treatment if such numbers were quoted when obtaining informed consent. I do not believe they reflect more current outcomes, and are certainly not consistent with my personal experience. In the survey of transbronchial biopsies, most deaths were due to hemorrhage in patients with hemostatic disorders and do not apply to the general population of patients presenting with solitary pulmonary nodules.

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- Ost D, Fein A. Evaluation and management of the solitary pulmonary nodule. *Am J Respir Crit Care Med* 2000;162:782–787.
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From the Authors:

We appreciate Dr. Frank's comments about our article (1) and concur that patients need up-to-date information on potential complications. We suggest that the conservative statistics quoted in our article reflect current literature and experience. Contemporary mortality statistics reported by the Video Assisted Thoracic Surgery Study Group Data, based on 1,820 patients, indicated a mortality of 2.5% (2). Indications for VATS in this series included 865 nodules or masses with 24% eventually undergoing conversion to thoracotomy and further resection, usually lobectomy. Gambhir and colleagues, when reviewing the data for a decision analysis on solitary pulmonary nodules, used a baseline mortality for VATS of 2.5% with a range of 0.0–9.0% (3). For open thoracotomy, a mortality of 4.0% for curative surgery and 0.5% for exploratory surgery alone was used. A 30-d mortality ranging from 2.5% to 11% for pneumonectomy was recently reported (4).

The utility of bronchoscopy for the diagnosis of solitary pulmonary nodules is difficult to assess since most nodules are too small and peripheral to permit a high bronchoscopic yield. Most surveys do not distinguish bronchoscopy with transbronchial biopsy (TBB) from routine bronchoscopy. However, in two retrospective surveys conducted in 1977 and 1986 involving over 6,000 transbronchial biopsies, the mortality rates were 0.1% and 0.2% (5, 6). The mortality rate for TBB will clearly vary by center, volume, and population. We agree with Dr. Frank that flexible bronchoscopy is a procedure with a low complication rate, but there is insufficient data to conclude that contemporary morbidity and mortality complication rates are significantly lower than reported in the literature.

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THE PROBLEM OF DOSE-RESPONSE AND THERAPEUTIC RATIO OF INHALED STEROIDS

To the Editor:

I read with interest the article by Nielsen and Dahl comparing the therapeutic ratio of dry powder inhaled (DPI) fluticasone propionate and budesonide (1). The study involved giving patients with mild to moderate asthma up to 3200 µg daily of budesonide—twice the maximal recommended dose for severe persistent asthma. Each dose was administered for two weeks, and if a longer period had been given, the steep part of the dose–response curve for bronchial hyperresponsiveness would have been seen at much lower doses. Furthermore, the actual slope might have been steeper with longer treatment, which would alter the potency ratio.

Baseline PD₂₀ with budesonide (259 µg) and fluticasone (271 µg), would indicate a mild degree of hyperresponsiveness and, consequently, little room for improvement. This is highlighted by only a 0.11 doubling dose improvement between baseline versus budesonide 800 µg and 0.38 doubling doses versus budesonide 1600 µg. To put this into perspective, in a previous study of mild to moderate asthmatics, methacholine PD₂₀ was measured at baseline (PD₂₀ = 18 µg), with a subsequent 1.7 doubling dose shift after budesonide 800 µg for 3 weeks and 2.7 doubling doses after 1600 µg for 3 weeks (2). This suggests that their potency ratio was probably influenced by the rather shallow slope of the dose–response curve with both drugs.

One would have predicted that the relative potency between fluticasone and budesonide DPI would be closer to unity since the twofold difference in glucocorticoid potency between fluticasone and budesonide is likely to be offset by the twofold greater respirable dose between the DPI's (3). For example, in asthmatic children receiving budesonide and fluticasone DPI, there was no difference in the lowest effective maintenance dose or in urinary cortisol excretion (4).

The slopes for suppression of 24-h uncorrected urinary cortisol were markedly different, and so it is not possible to make a proper estimate of relative potency. Also, one would have to cast doubt on the validity of the uncorrected urinary cortisol data, as it is more conventional to correct for urinary creatinine excretion. The findings of Nielsen and Dahl for cortisol suppression are not consistent with other data from asthmatic patients, were steady-state dosing with fluticasone 2000 µg daily and budesonide 1600 µg daily produced 34% versus 16% suppression of the 20-h area under curve plasma cortisol profile (5). Finally, in a meta-analysis of 21 studies evaluating urinary cortisol, the slope for fluticasone was 4.3-fold ($p < 0.001$) steeper than for budesonide (6).

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To the Editor:

The article by Nielsen and Dahl (1) concludes that fluticasone has a higher therapeutic ratio than budesonide. On the basis of the data presented, this conclusion appears unlikely.

As an efficacy measure, bronchial hyperresponsiveness was used, which is less suitable because of its marked time-dependency. Full effects of inhaled steroids are not reached within two weeks as used by the authors, rather several months are needed (2). In addition, the rate of improvement may differ between different doses (3) and by that also between different steroids. Such factors make the design selected by Nielsen and Dahl unsuitable for potency comparisons.

Furthermore, using cumulative dose response, comparing doses that are not equal on a microgram-to-microgram basis creates a bias in favor of the lower doses. An initial low dose may result in substantial improvement, whereas subsequent higher doses result in relatively small further improvements. This underscores the need to work on the same part of the dose–response curve for the two drugs.

In regard to the systemic effects, Nielsen and Dahl claim lower cortisol suppression with fluticasone. The authors acknowledge that their finding is in contrast to several other studies, and this could have been further substantiated by the inclusion of a systematic review and meta-analysis from 1999 comprising 21 dose–response studies on inhaled steroids using urinary cortisol as measure. This analysis consistently showed less cortisol suppression for budesonide than for fluticasone (4).

The explanations provided by the authors for their divergent results on cortisol suppression are that most of the other studies were performed in healthy volunteers and were of short duration, from 3.5–7 d. However, the majority of cortisol assessment studies have been performed in asthmatic patients (4). The suggestion that time may change the relation in regards to cortisol suppression between the two drugs implies that this shift should have taken place during the second week of their study. Nielsen and Dahl provide no data to support this hypothesis, which overall seems highly unlikely, especially as the patients were treated with inhaled steroids for at least one month before entering the study, according to the inclusion criteria.

Careful down-titration of doses, measurement of lung function, and recording of asthma symptoms, show that budesonide via Turbuhaler and fluticasone via Diskhaler are clinically equipotent (5). On the systemic side, fluticasone exerts a higher cortisol suppression than any other inhaled corticosteroid (4), which most probably is explained by the marked systemic accumulation of the drug (5).

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From the Authors:

We thank Drs. Edsbäcker and Lipworth for their interest in our article (1). We note with interest that the authors do not offer any major new criticism of our study that we had not already considered and self-critiqued in the discussion of our article (including the duration of treatment and the applicability of the outcome measures chosen). We appreciate that our data are inconsistent with the proportion of the literature to which Drs. Edsbäcker and Lipworth both refer and, indeed, we discussed many of the original articles that contributed to the meta-analysis that they mention (2) in our discussion. The studies that show fluticasone propionate to have a greater effect on cortisol levels than budesonide are those conducted in healthy volunteers or in patients with very mild asthma receiving high corticosteroid doses. Moreover, the meta-analysis (2), treatment with fluticasone propionate in adult asthmatics was considered in only five of 21 studies, including 56 individuals in all. This seems a quite fragile basis for the categorical statement on comparative bioavailability made by Dr. Edsbäcker. It is now well-established that the systemic bioavailability of fluticasone propionate is at least 2-fold higher in healthy volunteers than in patients with asthma of the appropriate severity for the dose (3–5). Indeed, the results of our double-blind, placebo-controlled study are entirely consistent with the remainder of the literature that Drs. Edsbäcker and Lipworth do not mention, in which fluticasone propionate and budesonide are given to patients with asthma at therapeutically appropriate doses (see 6 for meta-analysis).

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FEV₆ AS A SURROGATE FOR FVC: AUTHORS SHOULD HAVE INCLUDED ROC-CURVE ANALYSES

To the Editor:

We have read with interest Swanney and colleagues' recent article (1) on forced expiratory volume in 6 seconds (FEV₆) as an acceptable surrogate for forced vital capacity (FVC). Simplifying pulmonary diagnosis has positive implications both clinically and in population-based epidemiological studies. However, we are concerned with a possible deficiency in the development of a simplified measure of FVC. The issue of cutpoint selection is important in the evaluation of a diagnostic test, where a continuous variable has been dichotomized. In this case, we are concerned with FEV after a certain time. The traditional approach to the selection of a cutpoint is the evaluation of a receiver operating characteristic curve (2, 3). The selection of a cutpoint of 6 seconds is practical but somewhat arbitrary. It is possible that a cutpoint of 3, 4, 5, or 7 seconds (FEV₃, FEV₄, FEV₅, FEV₇) yields more information. Forced expiratory volume at arbitrary time points should be available with little modification of existing spirometry software. For reference values, the spirometric curves from NHANES III were digitized (4), facilitating the same analysis, and hence could be made available. Additionally, 33% of spirometries were technically inadequate. The authors state that n = 65 (40%) of these had "normal lung function." Presumably, these should have been included in the analysis. Furthermore, a cutpoint of less than 6 seconds may increase the proportion of acceptable spirometries. We hope that the promise of a simplified

and adequate measure of FVC will be further strengthened if the present and future investigators incorporate this perspective.

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1. Swanney MP, Jensen RL, Crichton DA, Beckert LE, Cardno LA, Crapo RO. FEV₆ is an acceptable surrogate for FVC in the spirometric diagnosis of airway obstruction and restriction. *Am J Respir Crit Care Med* 2000;162:917–919.
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4. Hankinson JL, Odencrantz JR, Fedan KB. Spirometric reference values from a sample of the general U.S. population. *Am J Respir Crit Care Med* 1999;15:179–187.

From the Authors:

We thank Dr. Brøgger and colleagues for their comments on our study (1). Our paper was intended as a starting point for defining an optimal endpoint.

FEV₆ was not chosen at random. It is an acceptable end-of-test criterion in the American Thoracic Society guidelines. The commercial spirometer we used reported only FVC and FEV₆. In addition, we only have reference data for FVC and FEV₆ from the NHANES III study (2). We understand waveform data in the NHANES study were stored, but the data are not currently available to the public.

We are reassured that FEV₆ is a reasonable choice by the fact that it performs so well (3). Previous work, published only in abstract form, suggests the minimum variation in a FVC surrogate occurred at about 6 seconds of exhalation (4). Shorter times are less attractive because FEV₆ can be projected from much shorter times (abstract) and longer times would begin to defeat our goal of a simple, practical endpoint.

We look forward to other studies to assess the accuracy and clinical validity of this and other endpoints in clinical spirometry.

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ERRATUM: TREATMENT OF GRAM-POSITIVE NOSOCOMIAL PNEUMONIA: PROSPECTIVE RANDOMIZED COMPARISON OF QUINUPRISTIN/DALFOPRISTIN VERSUS VANCOMYCIN

To the Editor:

Since the publication of this paper, it has come to my attention that a number of numerical errors appeared, principally in the tables. None of these errors alters the conclusions of the paper or our confidence in them. However, we would be very grateful if the record could be set straight by the publication of an erratum giving the correct data.

The errors are as follows:

Table 2b: Six of the p values shown are incorrect; the right-hand column should read: 0.97, 0.74, 0.76, 0.55, 0.79, 0.59, 0.91, 0.74, 0.33, 0.38, 0.47, 0.01. The percentage of patients in the quinupristin/dalfopristin group on mechanical ventilation (row 9) should be 80.4, not 70.4.

Table 3: Several of the numbers in this table are incorrect. A corrected version of the table appears below.

TABLE 3. GRAM-POSITIVE PATHOGENS IDENTIFIED MOST FREQUENTLY (\geq 5% INCIDENCE) BY TREATMENT GROUP IN THE ALL-TREATED POPULATION WITH A BASELINE PATHOGEN AND IN THE BACTERIOLOGICALLY EVALUABLE POPULATIONS

Pathogen	Treatment Groups	
	Quinupristin/ Dalfopristin n (%)	Vancomycin n (%)
All-treated population with a baseline pathogen		
<i>Staphylococcus aureus</i>	68 (39.3)	69 (39.9)
<i>Streptococcus pneumoniae</i>	16 (9.2)	10 (5.8)
Bacteriologically evaluable population with only gram-positive pathogen		
<i>Staphylococcus aureus</i>	31 (75.6)	36 (65.5)
<i>Streptococcus pneumoniae</i>	3 (7.3)	2 (3.6)
<i>Streptococcus mitis</i>	3 (7.3)	2 (3.6)
<i>Streptococcus agalactiae</i>	0 (0.0)	3 (5.5)
Bacteriologically valuable population with gram-positive and gram-negative pathogens		
<i>Staphylococcus aureus</i>	20 (30.3)	17 (28.8)
<i>Streptococcus pneumoniae</i>	8 (12.1)	6 (10.2)

Table 6b: The clinical success rate for the all-treated population with a baseline pathogen, gram-positive only, quinupristin/dalfopristin group (row 4) should be 13/31, not 3/31. The clinical success rate for the all-treated population with a baseline pathogen, gram-negative only, quinupristin/dalfopristin group (row 5) should be 15/31 (48.4), not 5/31 (55.6). The clinical success rate for the all-treated population with a baseline pathogen, gram-negative only, vancomycin group (row 5) should be 15/27 (55.6), not 15/20 (75).

Table 7: The p value for the related adverse clinical events, nonvenous (line 3) should read < 0.01 , not 0.10.

In the METHODS section, page 754, right-hand column, paragraph 1, line 11 should be < 10 squamous epithelial cells, not > 10 squamous epithelial cells.

I would like to further underline our conclusion that in this study, quinupristin/dalfopristin was shown to be equivalent to vancomycin in the treatment of nosocomial pneumonia due to gram-positive pathogens.

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