First, it is surprising that significant differences in the evaluated outcomes are found in studies with such small sample sizes (<70 patients per study in all studies). Second, all the studies except the trial by Trevisan et al were carried out in respiratory units admitting mostly patients with COPD. This is not the rule in most ICUs. Third, the control groups (invasive weaning) in these studies do not reflect current clinical practice. For instance, in the study most favorable to NIPPV, outcomes in patients assigned to invasive weaning were: rate of nosocomial pneumonia, 59%; rate of reintubation, 21%; need for tracheostomy, 59%; and ICU mortality, 41%. To try to compare those data with the real world, we have searched in the databases of two international studies on mechanical ventilation. In these databases, we have selected patients with COPD who required mechanical ventilation for >3 days and had a duration of weaning >3 days. This patient population would be similar to that in the study by Ferrer et al. From a total cohort of 10,151 patients who were mechanically ventilated, we found 160 patients meeting the above-mentioned criteria. The outcomes of this cohort were: rate of nosocomial pneumonia, 7%; rate of reintubation, 21%; need for tracheostomy, 9%; and ICU mortality, 10% (data not previously published). Last, the withdrawal of the endotracheal tube for patients failing a spontaneous breathing trial could raise ethical issues.

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End-of-Life Treatment and Antibiotic Resistance Data Raise Questions

To the Editor:

I read with interest the recent article in CHEST by Levin and colleagues (September 2010), which reported that only a limitation-of-therapy order in ICU patients was independently associated with acquisition of resistant organisms, whereas other factors such as antibiotic days, ICU length of stay prior to isolation of a resistant organism, antibiotic therapy prior to ICU admission, and so forth were not. However, the data reported and the study design raise some questions.

First, the authors included two ICUs in their study: an Israeli 12-bed ICU from July 2005 to January 2006 and a Canadian 20-bed ICU from January 2003 to December 2003. In 2007, Levin and colleagues2 published data about the same Canadian ICU (Sunnybrook Health Sciences Centre, Toronto, ON) during the same period of time and on almost the same number of patients (338 and 337, respectively). Differences in the data published (quinolone-resistant bacteria) are summarized in Table 1.

Second, also in 2007, Levin et al published data on the same Israeli medical-surgical ICU, describing transmission of Acinetobacter baumannii due to the contamination of portable radiographs. One might speculate whether the high amount of A. baumannii isolates present (94 within 6 months in the Israeli ICU vs only eight within 12 months in the Canadian ICU) was also because of a prolonged outbreak.

Third, in 450 patients, 64% unique pathogens were isolated, with a maximum of 331 being resistant. Twenty-seven patients were excluded because they were infected or colonized at admission, and 82 were grouped as having a resistant pathogen, meaning that on average, a patient harbored four resistant pathogens, which seems fairly high.

Fourth, it remains unclear why data from incomparable ICUs (with respect to their attitude toward limitation of therapy, general resistance situation, amount of antibiotics used, etc) are combined to perform a logistic regression analysis (which requires homogeneity) to find predictors for the isolation of resistant pathogens. Why was this not done separately for each ICU?

Finally, the authors concluded that nonwithdrawal of therapy leads to increased use of antibiotics and consecutively to a higher prevalence of resistant pathogens. However, another explanation might be that no more or less microbiologic sampling was done in different ICUs.

Table 1—Differences in Data Published on Canadian ICU

<table>
<thead>
<tr>
<th>Organism</th>
<th>Quinolone-Resistant/Total Number of Isolates</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>20101</td>
</tr>
<tr>
<td></td>
<td>20072</td>
</tr>
<tr>
<td>Enterobacter</td>
<td>4/28</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>12/43</td>
</tr>
<tr>
<td>Klebsiella species</td>
<td>0/17</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>37/63</td>
</tr>
<tr>
<td>Acinetobacter baumannii</td>
<td>2/8</td>
</tr>
</tbody>
</table>

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patients after withdrawal of therapy, and thus, no more pathogens could be found.

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Response

To the Editor:

We are complimented by Dr Meyers’ interest in our publications1,2,3 and appreciate her comments. Dr Meyer comments on differences in isolate counts in our various publications. Careful examination of the methodology of the articles reveals that the Infection Control Hospital Epidemiology article included isolates resistant only to ciprofloxacin, whereas the CHEST article included isolates resistant to all fluoroquinolones.

Unique isolates were defined as patient-, site-, and resistance-pattern-specific, meaning that a patient who was heavily colonized with Pseudomonas aeruginosa, for example, could harbor isolates in the surgical wound, sputum, urine, blood, and surveillance cultures (five isolates in this example of only one bacterial species). Further, even a single change in antibiotic sensitivity could double the number of unique isolates. This may have somewhat artificially inflated the number of resistant isolates reported.

For these reasons, counting isolates has significant limitations, and thus, the current research focused on patient acquisition of resistant bacteria, regardless of the site or the number of isolates involved. Considering patient acquisition of resistant organisms is, in our opinion, more clinically relevant and robust. When considered in this way, the number of patients acquiring ciprofloxacin-resistant bacteria in the Infection Control Hospital Epidemiology and CHEST reports is identical. Indeed, isolate distribution was included in the current study only to illustrate the huge differences in the load of resistant bacteria that existed between the Jerusalem and Toronto ICUs.

The high number of Acinetobacter baumannii isolates in Jerusalem may well have resulted from a very prolonged outbreak. However, we would suggest that the conditions in the Jerusalem ICU (whether related to end-of-life care decisions or not) contributed to the maintenance of the outbreak and further justified the comparison of the two ICUs.

As reported in the “Discussion” section of the article, combining the two populations (from Jerusalem and Toronto) is problematic. Although it is true that the populations are not identical, there is much in common between them. Further, performing separate regression analyses is limited because in the Toronto environment of low prevalence of resistant bacteria, few patients will acquire these bacteria, regardless of any other care consideration.

Regarding the fifth point, this is our hypothesis. Patients usually die within hours of withdrawal of therapy, so clearly there is limited opportunity for additional microbiologic studies or administration of antibiotics. In contrast, patients who die without withdrawal of therapy are obviously severely ill, are at high risk of infection, and receive more antibiotics. They are also present in the ICU for longer periods of time and can therefore act as a reservoir for resistant bacteria for the rest of the ICU.

To discover whether there really is a connection between end-of-life care and the acquisition of resistant bacteria will require a multicenter prospective study. We are currently planning such a study, to be performed during the coming winter under the aegis of the European Society of Intensive Care, and would welcome Dr Meyers’ support and participation.

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