ments of the pathogenesis of asthma, but it may serve as a useful aid in some translational investigation.

Questions are stimulated by meaningful clinical observations. In part, this characteristic determines the value of a study. Good studies and good questions produce better understanding and better future studies.

Peter G. Tuteur, MD, FCCP
St. Louis, MO

Dr. Tuteur is Associate Professor of Medicine, and Director, Pulmonary Function Laboratory, Washington University School of Medicine.

Reproduction of this article is prohibited without written permission from the American College of Chest Physicians (e-mail: permissions@chestnet.org).

Correspondence to: Peter G. Tuteur, MD, FCCP, Pulmonary and Critical Care Division, Washington University School of Medicine, 660 South Euclid Ave, Campus Box 8052, St. Louis, MO 63110; e-mail: tuteurp@msnotes.wustl.edu

REFERENCES

Nosocomial Pneumonia

Therapy Is Just Not Good Enough

I will prevent disease whenever I can, for prevention is preferable to cure.

Modern version of the Hippocratic oath written in 1964 by Louis Lasagna

Treatment of nosocomial pneumonia remains a problem in the ICU in terms of morbidity, mortality—at least if pneumonia occurs after the fifth day of hospital admission—and costs. Rello and colleagues recently presented data on this issue, and calculated each episode of nosocomial pneumonia to cost the institution > $40,000 in mean hospital charges per patient. The authors concluded that strategies to prevent the occurrence of ventilator-associated pneumonia may not reduce mortality; they may yield other important benefits to patients, their families, and hospital systems. This may be—surely not intended by the authors—understood in a way that prevention of nosocomial pneumonia does not lead to a decrease in ICU mortality, whereas the authors most likely meant to emphasize that either their data do not support this assumption or the studies available today are unable to do so. All physicians are obliged to obey the Hippocratic oath, which not only demands to cure disease but to prevent it. Setting aside the percentage of nonintubated patients with nosocomial pneumonia, this is largely a problem of endotracheal intubation needed for mechanical ventilation. If patients are intubated for management reasons, such as in the preoperative setting or in emergency medicine, it is unquestionable that there are no alternatives to the endotracheal route. Selective digestive decontamination (SDD) is always mentioned as a preventive measure once the patient has been intubated, and there is a recent publication indicating an advantage in selected surgical patients. However, I am afraid that the SDD community has still not asked the correct questions. Since the systematic review by Nathens and Marshall, it has to be accepted that SDD reduces mortality in surgical patients, but the central question remains whether this is due to the complete regimen of SDD—including topical and parenteral antibiotics—or to the parenteral application alone. At present, I think that other measures of prevention deserve more attention and that leads us back to the pathophysiology of nosocomial pneumonia. The risk increases with each day of mechanical ventilation and doctors have to ask whether they did not miss the most suitable time point to extubate the patient. Since the studies by Esteban and colleagues, we know that structured approaches result in early extubation, presumably reducing the incidence of nosocomial pneumonia in those patients. I dare to hypothesize that many ICUs have not adopted standardized criteria for entering a weaning trial or an extubation protocol, and we are therefore a long way from doing the best to prevent nosocomial pneumonia. Avoiding endotracheal intubation is crucial to the prevention of nosocomial pneumonia, and noninvasive mechanical ventilation is a proven tool in patients with acute exacerbation of COPD, acute cardiogenic pulmonary edema, and at least a potential for pulmonary infections. In addition, noninvasive mechanical ventilation can also be successfully combined with a weaning protocol for selected patients, eg,
patients with COPD or patients who failed multiple conventional weaning trials.10,11 Noninvasive mechanical ventilation has matured to a stage where institutional problems outweigh technical ones, and establishing noninvasive mechanical ventilation has become a challenge to ICU personnel rather than to the individual doctor. Of course, noninvasive mechanical ventilation will not and should not replace endotracheal intubation in all cases, but the summary of all preventive measures will lead definitely to a lower incidence of nosocomial pneumonia in our ICUs.

Nevertheless, at a certain point nosocomial pneumonia will occur, and we have to face the problem of therapy. Many attempts have been made to structure this approach, and it is probably not only my perception that treatment guidelines are more often used in the ICUs around the world than the knowledge on prevention.12 Nevertheless, all guidelines take into account that initial therapy needs to be empiric because we are unable to identify the causative agent at the time when antimicrobial treatment needs to be initiated. There are reports emphasizing the importance of an effective initial therapy because successive changes in antibiotic regimens do not seem to affect mortality.13,14 Several risk factors have been identified to help guide this decision in clinical practice, and quite a few attempts to prove the applicability and effectiveness of such strategies were successful.15

Nosocomial infections due to methicillin-resistant *Staphylococcus aureus* (MRSA) deserve our special attention due to two important peculiarities. First, MRSA infections are closely monitored by the public because they are interpreted as an indicator for hygiene problems in the unit. Second, due to high colonization rates, MRSA should only be identified as the causative agent when, in addition to the defining resistance pattern, results of quantitative cultures of lower respiratory tract specimens indicate that this pathogen is likely to be causative.

Linezolid is the first licensed member of the oxazolidinone class of antibiotics, with activity against almost all Gram-positive pathogens including MRSA.16 For ICU specialists, it is therefore an alternative to vancomycin, especially because its excellent tissue penetration and spectrum of side effects were expected to translate into clinical advantages. However, studies on nosocomial pneumonia—powered to test for equivalence of treatments—failed to also show a clinically meaningful advantage of this drug in comparison to vancomycin. Rubinstein and colleagues15 randomized 396 patients to either linezolid or vancomycin each plus aztreonam for 7 to 21 days and saw no difference in clinical and microbiological outcomes. These results remained unchanged when the design of this study was continued with additional 623 patients.15 Stevens and associates19 reached similar conclusions after randomizing 460 patients with nosocomial infections to a comparable drug regimen.

It is therefore difficult to understand that in this issue of CHEST (see page 1789), Wunderink and coworkers present results indicating a clinical superiority of linezolid in patients with nosocomial MRSA pneumonia. How did that happen, and why is it still worth reporting? Wunderink and coworkers combined the databases of the two publications17,18 with identical study designs now including 1,019 cases with nosocomial pneumonia, a procedure generally not too attractive in scientific research. They consequently analyzed three sets of patients: the intent-to-treat population (n = 1,019), the population with documented *S aureus* infection (339 of 1,019 patients, 33%), and the MRSA subset (160 of 1,019 patients, 16%). Significant differences in favor of the linezolid group in terms of mortality and clinical cure rates were shown for the MRSA subset only. This effect, however, was probably due to the fact that all patients were treated empirically with linezolid or vancomycin from the day of the diagnosis of infection. This left 859 of 1,019 patients (84%) who would have done without linezolid or would have done better without vancomycin, which is not the optimal therapeutic approach to non-MRSA Gram-positive pneumonia.

The important message of this article, however, must be that there is probably a way to reduce the mortality in MRSA pneumonia, but we need to identify these patients better. The authors comment on the currently available concepts for the identification of episodes of nosocomial MRSA pneumonia, but there is more work to do. Prospective studies trying to evaluate the benefits of
linezolid in MRSA pneumonia could for example include molecular methods established for MRSA screening,20 to at least exclude non-MRSA patients within a few hours. This approach bears the potential to substantially reduce the number of patients receiving overtreatment. The study by Wunderink and coworkers does reveal a small advantage in selected patients if linezolid is included into empiric antibiotic therapy of nosocomial pneumonia, but each intensivist could probably make a much larger difference if he or she would be constantly reminded of his or her Hippocratic oath and be asked: What did you do to prevent it?

Torsten T. Bauer, MD
Bochum, Germany

Dr. Bauer is lecturer of Internal Medicine at the Ruhr-University of Bochum, and senior physician in the Department of Pneumology, Allergology, Sleep Medicine and Respiratory Support. Dr. Bauer is also chair of the group of “Respiratory Infections and Sepsis in the ICU” of the European Respiratory Society, and vice-chair of the group of “Respiratory Infections and Tuberculosis” of the German Respiratory Society. Dr. Bauer has received honoraria for lectures from AstraZeneca, Aventis, Bayer Vital, GSK, MSD, Pharmacia, and Pfizer. Reproduction of this article is prohibited without written permission from the American College of Chest Physicians (e-mail: permissions@chestnet.org).

Correspondence to: Torsten T. Bauer, MD, Medical Clinic III, Bergmannsheil-Clinic of the Ruhr-University, Buerkle-de-la-Camp Platz 1, D-44780 Bochum, Germany; e-mail: torsten.bauer@RUHR-UNI-Bochum.DE

REFERENCES


Cardiogenic Shock
What Has Changed?

The oft-repeated adage that we have gained the ability to keep critically ill patients alive longer is valid for the complication of cardiogenic shock. So the next question is, has the disease state changed in the last 40 years? The breathtaking advances in cardiology that have focused on reperfusion of the myocardium after an infarct are supplemented by intensive care to preserve the myocardium. The exhaustive review by Hollenberg and colleagues estimated the incidence of cardiogenic shock at 5 to 10% after myocardial infarction, a value that has