There is considerable interest in routinely identifying these patients in clinical practice. Indeed, the results of the study by Menéndez et al. [1], as pointed out by the accompanying comment [2], shed additional light on the dimly lit question of how long to administer treatment for CAP or hospital-acquired pneumonia [3–5].

Although we agree with the novelty and clinical usefulness of this analysis, we feel that the primary concerns for clinicians in the care of patients with CAP are still mortality and the risk of complications and not the time to clinical stability or the duration of treatment. In this regard, it is debatable whether patients who die should be excluded from an evaluation of clinical stability, as was done in the study by Menéndez et al. [1]. In fact, 80 deceased patients (5.6% of the sample) were excluded from the analysis, even though they would have represented 39.2% of patients whose condition failed to respond to the initial treatment and 21% of patients with complications, if we consider death a complication of CAP. Thus, the exclusion of these patients might have significantly affected the results of the study. In addition, from a clinical point of view, this exclusion is not acceptable, because the risk of death is one of the outcomes of CAP we would like to identify and try to prevent in our daily practice.

In an ongoing prospective evaluation of patients with CAP admitted to our general respiratory unit, among the first 60 consecutive patients whose condition was scored by the pneumonia severity index (PSI) [6] at admission to the unit, the 30-day mortality rate was 13%. The age of patients at the time of death was significantly higher than the age of survivors (83.1 years vs. 61.0 years; P <.0017, by Mann-Whitney U test), and mortality only occurred in patients with PSI class IV disease (21% of patients) and PSI class V disease (50% of patients). In these groups of patients, age was the most important factor that could predict an unfavorable outcome (P = .0006, by a logistic model fit), since 38% of patients aged ≥76 years died. In addition, the median length of hospital stay, which could represent an indirect measure of time to stabilization, was greater for patients whose age was greater than the upper limit of the 95% CI (median hospital stay, 12 days), compared with the length of stay for patients whose age was within or less than the 95% CI (median hospital stay, 10.5 days). Thus, it is surprising that Menéndez et al. [1] did not correct and/or control for the influence of age on the time required to reach clinical stability, nor did they consider death as an additional measure of treatment failure.

In conclusion, in addition to attempting to better understand the predictive clinical parameters that define the natural course of CAP in specific patients, we should not lose our focus on the identification and treatment of patients at risk of death or at risk of developing complications, who are often elderly patients.

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References

Reply to De Maria et al.

Sr—We appreciate the interest and comments of De Maria et al. [1] regarding our article about clinical stability and community-acquired pneumonia (CAP) [2]. We agree with them that mortality is the most important outcome when we are faced with a patient with CAP. In fact, the first question we ask ourselves at the moment that CAP is diagnosed is: What is the probability that my patient will survive this episode? This is our main concern, and to answer this critical question there is a great deal of evidence available, which has been evaluated in meta-analyses and in observational studies with univariate and multivariate analyses. In the past decade, prognostic scales have been developed to identify the initial severity of CAP and to stratify groups of patients with different risks of death (e.g., the risk classes of Fine [3] and CURB-65 scores [4]). In a prior study by our group, with the same cohort of patients, we verified that mortality was adjusted to the risk classes of Fine and that mortality dramatically increased if there was treatment failure. Our first contribution to the topic of mortality and CAP was to identify risk factors for treatment failure in relation to the patient, the type of treatment, and the initial disease severity [5].

In the second study [2], we aimed to...
answer what we think is the second question we must ask: If the patient survives, how long will it take for the patient to reach clinical stability? This question is most important in estimating the duration of hospitalization and, possibly, in deciding the duration of antibiotic treatment. Most patients who die during hospitalization for CAP do not reach clinical stability or, if they do reach it, they lose it later because of complications. The probability that a severe complication will appear after stability is reached is <1% [6]; we also found that the probability of death after stability is reached is <1%. Given this information, we believe that inclusion of the patients who died without ever reaching clinical stability or who died after reaching clinical stability and later losing it would not add information in the prediction of clinical stability in survivors. Estimation of the duration of hospitalization or the number of days from admission to death was not our aim either.

Clinical stability has not been studied as thoroughly as mortality has been, and this because of, among other factors, the lack of a widely accepted definition of clinical stability for patients with CAP. Halm et al. [6] propose an interesting and useful definition that uses 5 clinical parameters widely accepted by clinicians. In the study, Halm et al. [6] showed that a greater initial severity of CAP, as measured by the risk classes of Fine, is associated with a greater number of days needed to reach clinical stability. In our study [2], we also found that the number of days needed to reach stability correlated with the initial severity but not with the patient’s age (in an analysis of patients aged >65 years). That is why we decided not to include age as a factor in our statistical multivariate analysis to predict clinical stability, whereas we included other factors, such as presence of a comorbid condition and the type of treatment received. We believe that, besides mortality, other important issues, such as the response to treatment and clinical stability, merit attention to increase our knowledge about CAP.

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References

Appropriate Antimicrobial Therapy for Community-Acquired Methicillin-Resistant Staphylococcus aureus Carrying the Panton-Valentine Leukocidin Genes

SIR—We have reviewed with great interest the article by Francis et al. [1], which describes 4 cases of pneumonia due to community-acquired methicillin-resistant Staphylococcus aureus (CA-MRSA) carrying the Panton-Valentine leukocidin (PVL) genes. Although the discovery of this virulence factor is of interest from a research perspective, it is uncertain what impact the discovery may have on the determination of appropriate antibiotic therapy for CA-MRSA. These questions remain: should we routinely test for the presence of the PVL genes in severe cases of CA-MRSA, and, if so, would the presence of this gene alter decisions about antimicrobial management of the infection?

In an attempt to answer the questions posed, we searched the literature to identify and evaluate other case reports about pneumonia due to PVL-secreting CA-MRSA (table 1) [2–4]. Of the 25 cases reviewed, we determined, on the basis of the susceptibility profile of the S. aureus isolates that were cultured, that patients in 20 of the cases received appropriate antimicrobial therapy. Despite receipt of “appropriate” therapy, 14 of the 20 patients died within days after admission to a hospital. It is interesting that, of the patients who died while receiving appropriate therapy, not one had any underlying disorders, indicating that this organism is, in fact, a highly virulent pathogen. The question remains whether vancomycin, because of its pharmacodynamic properties, would serve as appropriate empirical therapy for this patient population.

It is well documented that the penetration of vancomycin in lung tissue is poor because the drug is a highly polar compound with increased molecular weight [5]. Therefore, vancomycin at a standard dosage of 1000 mg intravenous every 12 h cannot maintain a concentration above the MIC90 of MRSA (i.e., 4 µg/mL) in the lung epithelium of a patient with normal renal function [5]. Additionally, <20% of the plasma concentration is actually found in the epithelial lining fluid (ELF), leading to findings that at least 40% of patients who are treated with vancomycin do not achieve adequate concentrations [6]. We postulate that patients who received appropriate therapy with vancomycin for the treatment of CA-MRSA pneumonia may not have received a high enough dose to penetrate their already necrotic lung tissue and to overcome the large inocula of...