tion with PMNL. Additionally, direct binding of PSP/reg to PMNL derived from healthy volunteers was observed. Incubation of PMNL isolated from septic patients with PSP/reg did not show an effect over CD62L or CD11b cell surface levels. These data may suggest tolerance-like phenomena, although further investigations are required. One of the questions that remained unanswered in this work is what is the binding capacity of PSP/reg by sepsis-derived PMNL? In addition, it will be important to know if this unresponsiveness to PSP/reg or altered binding capacity are parameters that may be used as prognosis indexes. To assess the real relevance of PSP/reg as a sepsis marker will require further investigations. Furthermore, PSP/reg will be competing with new sepsis marker candidates such as peripheral endothelial progenitor cells (11), plasma Treg cells, CD25 levels (12), and B-type natriuretic peptide (13) to be crowned as the definitive sepsis marker.

Thus, finding the "perfect" sepsis marker has been one of the most elusive dreams in modern medicine. The list of potential sepsis markers increases day by day, and we still do not have a parameter or a group of them that can accurately and rapidly diagnose sepsis. Most of the current markers (clinical signs and laboratory measurements) are the product of the proinflammatory stage and therefore are nonspecific. Thus, if we can make a wish for the ideal sepsis marker, what would we ask for? Probably an important characteristic would be a parameter that is altered in all types of sepsis, independently of the agent causing the infection. This characteristic would eliminate "subpopulation of septic patients" and all the nightmares associated with conflicting data at the moment of evaluating a potential sepsis marker. Thus, it would be desirable to have a substance that reports early changes and can be detected in an easy and rapid way. Prognosis potential is also a characteristic that should be added to this wish list. PSP/reg seems to have a certain potential as a predictor of sepsis, although only time will tell if this protein fulfills the minimum requirements to be called a true sepsis marker.

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Predictive models: The angel is in the details*

Models for measuring severity of illness and predicting hospital mortality for patients in intensive care units (ICUs) are now in their third and fourth generation (1–3), and newer models have appeared recently (4, 5). This has come about as a result of the desire to assess ICU performance by comparing observed and predicted mortality (6, 7) and, at least in part, to the ability to capture data electronically. Large data sets containing numerous measurements on all patients have enabled the development of sophisticated predictive models. Simplicity, however, is not a hallmark of these systems. The leanest critical care hospital mortality model, Mortality Probability Model (MPM_0-III), still requires the collection of 17 data elements (3).

Statistical modeling in other acute care settings has lagged behind that in critical care. Recent attempts have been made to introduce predictive models outside of the ICU, most particularly in the area of rapid response teams/medical emergency teams (8). One example is the Modified Early Warning System (9), which was developed on 206 patients in a postoperative ward. This scoring system assigns "weights" to six physiologic measurements. The weights are summed and

*See also p. 1649.

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a cut-point >4 is used as an early warning signal. What is common among decision algorithms in rapid response teams/medical emergency teams is that they use triggers ("antecedents") and/or uncomplicated scoring algorithms to indicate possible patient deterioration. Here, simplicity is desirable, until such time as electronic data capture mechanisms permit the assimilation and multivariate analysis of high-dimensional data.

In this issue of *Critical Care Medicine*, Jones et al (10) examine how the Sequential Organ Failure Assessment (SOFA) score (11) measured while the patient is in the emergency department (ED), can predict hospital mortality for patients subsequently admitted to an ICU. The authors also gathered data for the SOFA score collected 72 hours postadmission as well as the difference between this value and the value recorded in the ED. These additional measurements may be useful variables for stratification in *post hoc* analyses, but as they are based on information collected after admission to the ICU, they cannot be used as a predictor for patients in the ED.

In addition to the SOFA score, the authors collected information on other physiologic measures while patients were in the ED: vital signs, oxygen saturation, Glasgow Coma Score, white blood cell count, and lactate concentration. These were all recorded prospectively on standardized forms. The patient population is narrowly focused in terms of case mix: 248 patients with severe sepsis who had resuscitation procedures initiated in the ED. This strategy is a wise one, given the difficulty of developing a model using what would be an otherwise heterogeneous population. Limiting the study to a single institution, however, means that the results reported by Jones et al must be considered exploratory.

The primary statistic chosen for determining the ability to predict hospital mortality was the area under the receiver operating characteristics curve (AU-ROC) (12). This is a measure of "discrimination," i.e., the ability to distinguish between patients who die vs. those who survive. The AU-ROC ranges from 0.50, which indicates that the prediction is no better than flipping a coin, to 1.00, which is a perfect predictor. All of the ICU predictive models cited above have AU-ROC values >0.80. Values lower than that are considered mediocre. Unfortunately, the AU-ROC to predict mortality using the SOFA score taken in the ED was only 0.75.

The authors compare this value with the AU-ROC generated by other variables they had collected, and found that none had higher AU-ROC values than the SOFA score. Given the additional physiologic variables that Jones et al collected, they might have considered a more sophisticated approach. They certainly could have constructed a pseudo–Modified Early Warning System instrument, which most likely would have increased their AU-ROC beyond 0.80.

The authors should be commended for assessing the value of the relatively simple SOFA score in the ED as a predictor of subsequent in-hospital mortality. But in their attempt to maintain simplicity, they gave away the opportunity to look at a metric that had high discrimination with little additional data capture burden. I agree with the authors that using ICU predictive models in the ED is at present not feasible. But, although simplicity can be alluring, it should not trump a comprehensive inclusion of enough variables to generate a precise yet timely prediction. When it comes to predicting outcomes, the angel is in the details.

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