Diagnosis of pneumonia in the critically ill patient: Is it time to abandon bronchoscopy?*

Many infectious and noninfectious diseases may compromise the pulmonary distal airways in the immunocompromised patient and present with clinical and radiologic findings consistent with acute pneumonia. This broad clinical picture labeled "pneumonia" may be caused by an array of diverse mechanisms and etiologies including but not limited to: exudates in bacterial pneumonias, transudates in pulmonary edema, blood in posthematopoietic stem cell transplantation (HSCT) and vasculititis, malignant cells in lung cancer, granulation tissue in organizing pneumonias, and lipoproteinaceous material in alveolar proteinosis. This remarkable range of potential etiologies presenting as "pneumonia" in the immunocompromised patient is compounded by the fact that these patients frequently present with atypical (or lack of) clinical and radiologic findings. These obstacles may lead to substantial delays in both diagnosis and therapy (1–6).

To decrease the time to diagnosis of pneumonia, as well as to increase the precision of diagnosis, the clinician needs to put in perspective a very detailed patient history, which includes: underlying disease (affects predominantly T cell, B cell, or both); type of chemotherapy (intensity and duration); total length of immunosuppression based on the underlying disease and last chemotherapy administration; type of allograft, whether lung-heart, lungs, small bowel, liver, pancreas, kidney-pancreas, or kidney (each allograft is associated with different risks for infections and rejections); and type of HSCT (allogeneic, auto, nonmyeloablative). Each of these factors taken from the patient's history is invaluable to the pursuit of an accurate etiologic diagnosis of patients with pneumonia. As a case in point, a classic challenging clinical scenario is seen in the patient who received a lung allograft and presents to intensive care with a presumptive diagnosis of pneumonia in the first few weeks post-transplantation. This patient's differential diagnosis includes: bacterial pneumonia, fungal pneumonia, cytomegalovirus pneumonia, pulmonary edema, pulmonary embolism, pulmonary hemorrhage, allograft rejection, acute respiratory distress syndrome, and hypersensitivity drug reactions (3, 6). Another important clinical example pertains to the diagnosis of diffuse alveolar hemorrhage, which is rarely seen in situations other than acute leukemia and post-HSCT (4).

These tremendous diagnostic challenges are documented in HSCT patients by the study of Dr. Sharma and colleagues (4), which demonstrated that 72% of the pulmonary complications were not diagnosed antemortem. In another immunocompromised population, the solid organ transplant patients, pneumonias remain among the most common causes of death (6). Therefore, how can we improve the early diagnosis of pneumonia in the immunocompromised critically ill patient? The diagnostic tools we have currently available are often divided into noninvasive and invasive techniques. The noninvasive tools are comprised of Gram stain, culture, special stains, enzyme-linked immunosorbent assay, polymerase chain reaction of sputum and/or blood, antigenemia (e.g., *Cryptococcus*, *Aspergillus*, *Histoplasma*, *Cytomegalovirus*), antigenuria (e.g., *Leigionella*, pneumococcus, *Cryptococcus*, *Histoplasma*), and serology for infectious agents. The invasive tools are comprised mainly of the collection of bronchoalveolar lavage (BAL) with or without transbronchial biopsy by fiberoptic bronchoscopy, computed tomography–guided lung biopsy, and open-lung biopsy (2, 7, 8). Intuitively, the invasive tools would provide fewer false-positive results as a consequence of higher specificity. Nonetheless, a systematic review and meta-analysis (9), as well as a more recent large randomized clinical trial (10), have failed to demonstrate survival benefits from invasive techniques when compared with noninvasive ones in a mixed (mostly immunocompetent) patient population. To our knowledge, no large randomized trial comparing invasive and noninvasive tools has been completed solely in immunocompromised patients up to this date.

In this edition of *Critical Care Medicine*, Dr. Azoulay and colleagues (11) evaluated diagnostic bronchoscopy in hematology and oncology patients with acute respiratory failure in a large prospective observational study performed in 15 French intensive care units. The study assessed 148 cancer patients with hypoxemic acute respiratory failure. They compared the invasive (BAL) and noninvasive strategies and concluded that, in critically ill cancer patients, the BAL was not more effective than noninvasive techniques, and, in addition, led to more respiratory status deterioration (and mechanical ventilation). The strengths of this study consist of the prospective design, the selection of cases and controls from the same institutions, and the use of a concurrent standard of care without interference into clinical decisions by the intensive care physician. The weaknesses of this study are the following: a) statistically significant imbalance of baseline characteristics in nine of 11 measured factors, a substantial imbalance likely related to a selection bias (the invasive arm included significantly higher risk [e.g., allogeneic HSCT] and sicker patients [e.g., hypoxemia] than the noninvasive arm); b) lack of description of other major factors impacting the severity of illness, such as Logistic Organ Dysfunction scores in each strategy group, proportion of patients undergoing noninvasive positive pressure ventilation or mechanical ventilation just before the start of each diagnostic strategy, timing of antibiotics initiation in relation to the performance of each diagnostic strategy, blinded review of the adequacy of antibiotics in each group, and proportion of community-acquired and hospital-acquired pneumonias in each

*See also p. 100.

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group; and c) presence of informative censoring, which creates bias in the survival analyses for BAL performed vs. nonperformed (Fig. 3*A*) and BAL yielded a diagnosis vs. did not yield a diagnosis (Fig. 3*B*). Furthermore, the two survival analyses suffered from lack of statistical power, because an approximate 25% absolute reduction in death would need to have occurred with the current study sample size. This reduction evidently is not realistic.

In summary, we congratulate Dr. Azoulay and colleagues (11) for their major efforts to improve our understanding of the role of different techniques to diagnose pneumonia in the immunocompromised patient. We agree with the authors that noninvasive techniques may be as effective as invasive ones. However, we disagree with their conclusion that invasive BAL techniques lead to increased respiratory status deterioration based on their significant selection bias. We believe that an adequately powered and randomized clinical trial will circumvent the problems found in their study, and provide better guidance to which diagnostic technique brings the most benefits and the least harm to immunocompromised patients with acute pneumonia.

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Suicidal intention and self-immolation: What is the outcome?*

The article by Dr. Thombs and Bresnick (1) in this issue of *Critical Care Medicine* reveals a surprising finding from the American Burn Association National Burn Repository that shows no difference in mortality or length of stay in those patients whose injuries are self-inflicted compared with those with burns caused by accident. This relationship is elicited once both groups of patients have been matched according to a "propensity score" based on 19 predictor variables. This finding is in stark contrast to almost every other article written about this subject (2–9). However, no study has ever controlled for so many patient variables or included such a large number of patients. This is the first time that it has been shown that patients who are admitted with self-inflicted burns neither require a longer stay in intensive care nor experience an increased mortality rate.

Self-immolation has been recorded since the time of the Ancient Greeks when Heracles is said to have built his own funeral pyre (10) to free his body from the torment of the Tunic of Nessus. Throughout history, there have been references to self-immolation associated with different beliefs, such as ritual *Sati* in which a Hindu widow would throw herself onto the funeral pyre of her dead husband. The Charan and Rajput castes, living in Gujarat and Rajasthan, are famous for their bravery and their unflinching ability to carry out the act of self-immolation. During the great divide of the Russian Orthodox Church in the 1600s, there were reports of entire villages of "Old Believers" burning themselves to death in what was called a *fire baptism* (11). In more modern times, those carrying out self-immolation have often done so for personal and for political reasons, such as Thich Quang Duc, the Buddhist monk who set fire to himself on the roadside in Saigon in 1963 as a protest against the treatment endured by other Buddhist monks under the dictatorial rule of President Ngo Dinh Diem. In the last century, there were also several high profile self-immolators protesting against communist persecution, including the Czech student Jan Palach and Oscar Brüsewitz, a German priest who set fire to himself in a crowded market place. Protests against the U.S. government had rarely involved self-immolation until Kathy Change, in 1996 on campus at the University of Pennsylvania, and more recently, Malachi Ritscher, in 2006 on the Kennedy Expressway during the morning rush hour near downtown Chicago, caught the headlines.

Suicide is defined as "all cases of death resulting directly or indirectly from a positive or negative act of the victim himself, which he knows will produce this result" in the classic work *Suicide* (12), written by Émile Durkheim in 1897. In it,

***See also p. 118.**

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