when houses are better ventilated.

These data support the hypothesis that exposure of asthmatic children to passive cigarette smoke leads to increased severity of the disease. Whether this is an independent inflammatory action of cigarette smoke (in which case increased prevalence of asthma associated with maternal smoking should be, but probably is not, seen), a simple bronchospastic effect of cigarette smoke, a pharmacologic effect of some component of cigarette smoke, eg, nicotine, or an adjuvant effect of cigarette smoke on some other inflammatory trigger such as inhaled allergens, is not clear.

The therapeutic corollary of these data is important and self-evident.

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Pulmonary Infections in the Immunocompromised Host
Perspective on Procedures

The clinical challenge to sculpture empiric therapy and prolong survival for immunocompromised patients remains a dilemma. The three basic choices, observation alone, to start or broaden empiric therapy, or pursue invasive diagnostic procedures, are clear but difficult options. It is not surprising that Robin and Burke chose "Lung Biopsy in Immunosuppressed Patients" as an initial topic for risk-benefit analysis in Chest. With a major change in therapy or prolonged survival as an endpoint, open lung biopsy (OLB) risk does exceed benefit for most of these patients. For this reason, many institutions have limited the use of OLB and focused on improving alternate means to clarify pulmonary pathology.

Rosenow and colleagues have presented characteristic behavior patterns for various pathogens in many variable subsets of immunocompromised host. Although all meet a broad definition of immunocompromise, there are substantial differences in approach and analysis of risk for patients with solid tumor malignancies, leukemia, collagen vascular disease, acquired immunodeficiency syndrome (AIDS), and the expanding field of organ transplantation. Many factors must be analyzed by the team of physicians involved in caring for these patients. The onset and relation to treatment for the infiltrate, the focal or diffuse pattern, and rate of deterioration or improvement remain critical elements in choosing the pulmonary procedure. The pulmonologist is expected to decide which procedure, single or in combination, offers the best alternative for dealing with uncertainty in these high risk patients.

Saïto and co-workers, in this issue (see page 745), discuss bronchoalveolar lavage (BAL) in patients with acute leukemia. The authors describe the science of BAL without overstating the contribution that the art of BAL contributes in this setting. This art involves the clinical judgment exercised and treatment changes originated in these patients by the procedure. If other
team members are reluctant to accept any procedure as "negative for pathogens" and unwilling to sculpture therapy based on these results in clinical context, then that procedure can be judged only on positive predictive value.

As leukemia progresses and becomes refractory to treatment, the autopsy diagnosis is more often blood, edema, fibrosis, or the primary disease process rather than a specific infectious pathogen. Since OLB and autopsy do not provide a specific diagnosis in at least 20 percent of some subsets, including leukemia, we should not expect BAL and other less invasive procedures to have a high yield for a specific diagnosis. When BAL findings are individualized to each patient setting, they can be used to confirm diagnostic impressions earlier in the course of this subset.

The authors hold BAL to the strictest criteria for its contribution to diagnosis: autopsy confirmation of histology and culture within three weeks of the procedure. Their report is meticulous in describing their subset and important factors to consider in discerning the diagnostic yield from any pulmonary procedure. The pathologic behavior of Candida, which awaits the stress of combination therapy on the immune system and invades tissue an average of 19 days before death in leukemia, is reconfirmed. Since this fungus is often identified in other tissues (funduscopic examination) and cultures at this stage, lavage showing abundant yeast and pseudohyphae is useful confirmatory evidence of invasive candidiasis. Colonization seems a remote issue in this particular setting.

On the other hand, the data of Saito et al cast doubt on previous reports of efficacy for BAL in diagnosis of invasive aspergillosis. It has been suggested that washings, lavage, or a single sheathed catheter isolate may be enough evidence to confirm pulmonary infection with this organism. Aspergillus, like Candida, infects lung and causes alveolar hemorrhage. For this reason, early reports of positive washings with normal roentgenograms most likely represented colonization rather than invasion. The study of Saito et al refutes the suggestion that BAL can stand alone to distinguish colonization from invasion in many situations. If BAL is accepted as adequate for diagnosis without other supportive cultures, a low risk opportunity for definitive histology and culture by transbronchial lung biopsy (TBBX) or thin needle aspirate (TNA) may be lost.

When the available pulmonary procedure options are the topic at bedside rounds, risk benefit reported for each procedure in the immunocompromised host literature is of paramount importance. In any given situation, sputum, BAL, TBBX, or TNA may provide at least one pathogen to treat. When these procedures are negative for pathogens, an aggressive use of them in combination does provide adequate support for continued empiricism or observation despite the acknowledged limitations of sample size.

Prospective studies with stringent criteria for determination of diagnostic yield for any pulmonary procedure are difficult to design. These studies would clearly identify whether histology, autopsy, other cultures, or clinical outcome confirmed the pulmonary isolate. There are many situations for which the latter choice is appropriate, but these merit a separate category when diagnostic yield is presented. This same category should also be used to limit reporting nonspecific fibrosis by TBBX or OLB as a specific diagnosis. This finding may carry the same implication as negative for pathogens, but it does not represent the impact of identification of a treatable pathogen or condition.

Some reports continue to present diagnostic yield by consolidation of many different subsets. Since differences in pathogen isolation between subsets and risk-benefit analysis for procedures among subsets is now well defined in the literature, it is surprising that this practice has not been abandoned. For example, including Pneumocystis carinii isolation by BAL or TBBX in patients with AIDS can falsely raise expectations for a true-positive isolate by these procedures in other subsets. Even in a patient with AIDS, BAL is seldom reliable as the sole diagnostic source when the clinician suspects pathogens or processes other than Pneumocystis carinii.

It has also been suggested that BAL may diagnose hemorrhage in the immunosuppressed host; however, bleeding accompanies many infectious agents and other processes. Hemorrhage can be safely assumed to be the sole cause for pulmonary infiltrates only when hemosiderin-laden macrophages predominate in the lavage, pulmonary edema has been excluded, therapy is not altered, and the alveolar disease clears rapidly (one to three days).

All of the pulmonary procedures are complementary and can be used in an additive fashion, since each is relatively safe at some point in the treatment course. Those patients without increased risk for bleeding should be approached aggressively for lung tissue (TBBX or TNA) for histology and culture. As research on the efficacy of lavage effluent analysis continues, some consistency between those effluents and lung parenchymal findings will need to be identified. With the accumulated experience reported in the immunocompromised host literature, enthusiasm for additive benefit from OLB has waned. We must exercise caution before re-directing such enthusiasm to the diagnostic power of BAL in that same literature.

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Mortality and Sleep Apnea
The Trouble with Looking Backward

Recently, two retrospective studies have addressed the issue of mortality in patients with sleep apnea syndrome (SAS). Their appearance in this journal has provided the readers of Chest with seemingly contrasting impressions on the natural history of this disorder; this merits further comment. A study by Gonzalez-Rothi and coworkers1 spanning the years of 1978-1986 compared the five-year mortality of 91 patients with documented SAS with that of 35 control patients of similar age and body habitus who had normal sleep tracings. Complete follow-up was obtained on all patients in this study which included deaths, causes, time, and circumstances of death, as well as morbidity variables. Although SAS patients in this study had significant sleep-disordered breathing (mean apnea-hypopnea indices of 42), their five-year mortality, as assessed by Kaplan-Meier life table analysis, was no different than that of the control subjects. Moreover, none of the SAS patients died during sleep. Although SAS patients had more vehicular mishaps than control subjects, none died as a result of a motor vehicle accident. The authors concluded that their findings did not support (either statistically or by simple numerical trend) the hypothesis that SAS patients have increased mortality, or for that matter, that they are at increased risk of dying during sleep. The findings thus leave the reader to either concur with the authors’ conclusions or to consider the possibility of a “type 2” statistical error (insufficient numbers to detect statistically significant differences in mortality between the two groups) in their analysis.

An earlier study by He and coworkers,1 spanning the same eight-year period, included male patients over age 15 with documented SAS.2 Of an initial group of 706 patients studied, follow-up information was obtained in only 385 patients (55 percent of the total sample), and it was from the latter proportion of the group upon which the data analyses were based. The results of multiple life table analyses of combinations of subgroups by these investigators showed that SAS patients with apnea indices greater than 20 who were younger than 50 years old had a higher mortality than patients with apnea indices less than 20. An increased mortality rate that could be directly related to the magnitude of the sleep apnea index was not present in the subgroup of patients over age 50, however. Patients with SAS who were treated with either tracheostomy or nasal CPAP (but not uvulopalatopharyngoplasty) in this study had significantly better overall survival than untreated patients, irrespective of pre-therapy apnea index.

The findings by He and coworkers, thus, leave the reader to conclude that if sleep apnea is present and untreated, then the greater the number of sleep disordered breathing events one has, the more likely one is to die—provided one is older than 15 and younger than 50 years of age. The reader would then be pressed to ask “But, to die of what?” and further, “Why die of SAS if one is younger than if one is older,” when SAS is epidemiologically more prevalent in middle aged, and older men? To satisfy the reader’s concept of direct causality between the severity of sleep apnea and increased mortality, a pathophysiologically plausible explanation for this relationship should be able to withstand a testable hypothesis: if people with SAS have recurrent nocturnal hypoxemia, episodic pulmonary hypertension, and associated cardiac arrhythmias, then they should die during sleep. A corollary to that hypothesis is that since SAS is more prevalent in older men, who are also more likely to suffer from underlying cardiac and respiratory disease, if one is older and one has more severe apnea, then one should have an increased chance of mortality. The reader is then left wondering why more older men with higher apnea indices in the study by He and coworkers did not die. By neither providing causes/circumstances of death, nor comparisons of mortality between SAS patients and a control population of patients without SAS, any inferences to be made from this study regarding causality and the natural history of SAS are therefore posed with potential shortcomings.

As an explanation of the findings of He et al of increased mortality in the younger SAS patients, it might also be tempting for the reader to hypothesize that many of their patients might have been Pickwickian, since this disorder (which is also associated with sleep-disordered breathing and apneas) tends to manifest earlier in life and is well known to be associated with high mortality.68 Were this the case, a different