Cigarette Smoking, Airway Hyperresponsiveness, and Asthma

Asthma is a disease syndrome characterized by airway hyperresponsiveness to a number of ubiquitous bronchospastic triggering factors (pharmacologic, physical, etc). Asthma triggers can either be bronchospastic or inflammatory.1,2 Bronchospastic triggers (pharmacologic, exercise, cold air, hyperventilation, psychogenic, and possibly irritants) produce airways narrowing in proportion to the level of airway hyperresponsiveness, but do not enhance airway responsiveness; responses to these triggers can be considered "symptomatic" of asthma severity. By contrast, inflammatory triggers (allergen, occupational low molecular weight sensitizing chemicals, viral and Mycoplasma respiratory tract infections, ozone) induce or exacerbate asthma by causing enhancement of the airway hyperresponsiveness.

Cigarette smoke is one of the most common irritants which affects asthmatic patients. However, its role in the pathogenesis of asthma and airway hyperresponsiveness is not well defined. Cigarette smoke can cause acute reduction in airway caliber in man,3 and inflammation in animals.4 Its role as a possible inflammatory asthma trigger in man, assessed indirectly by enhancement in airway responsiveness, is uncertain. Controlled cross-sectional studies in smokers with normal lung function show enhanced airway responsiveness chiefly after many years of smoking;5,9 dose-response relationship is likely. Results are statistically significant but often of equivocal clinical significance. Enhanced airway hyperresponsiveness does not appear to be a feature of young or early smokers.5,7 By contrast, smokers with airflow obstruction have airway hyperresponsiveness which correlates strongly with the degree of obstruction10 and which shows some other differences from the airway hyperresponsiveness seen in asthma.11,12 Smokers with mild airway responsiveness can smoke up to eight cigarettes in rapid succession without acute enhancement of airway responsiveness.13 The relevance of these data to human asthma, however, may be minimal since studies dealing with active current cigarette smokers are, out of necessity, dealing with both a "selected" and "survivor" population. One animal study surprisingly showed reduced airway responsiveness to inhaled methacholine in six pack-year smoking baboons;14 a cross-sectional controlled study demonstrated similar findings in young cigarette smokers.7 Reduced airway responsiveness to aerosolized histamine in smoking dogs has been attributed to a protective effect of smoke-induced mucous hypersecretion; the reduced responsiveness was not evident when histamine was infused intravenously.15

Studies of both acute and chronic active smoking in asthmatic patients are difficult largely for the reasons that most asthmatic subjects choose not to smoke and that it is difficult to get non-smoking normal subjects, let alone non-smoking asthmatic patients, to participate in acute smoking studies. Some reports suggest asthma may develop or exacerbate paradoxically following smoking cessation.16

The effect of passive smoke is even more difficult to study and less well understood in asthmatic patients, despite the fact that many of our patients regard passive smoke as a major exacerbating factor. For this reason, attention has turned to examining the effect on children with or without asthma of parental smoking. In this regard, we are dealing with a captive population with limited control of their environment, ie, they are less highly selected than adult smokers or likely even less than adult passive smokers. Cross-sectional studies have consistently revealed a detrimental effect of parental smoking on lung function and/or asthma severity in children.17 Many of these studies have a common problem of possible unrecognized confounding variable(s), ie, an independent factor, such as lower socioeconomic status, could result in increased tendency to smoke and increased respiratory symptoms or asthma severity.17

In this issue (see page 701), the observations of Murray and Morrison on the effects of maternal smoking on asthma severity in 240 consecutive, referred asthmatic children are presented. Impressive differences in asthma severity and airway hyperresponsiveness to histamine were observed to be associated with in-home maternal smoking. Two factors support the hypothesis that passive cigarette smoke, rather than a confounding variable, caused the increased asthma severity. The first is the demonstration of a dose-response relationship between mother's in-home smoking and objective measures of asthma severity. The second is the demonstration that the relationship between maternal smoking and asthma severity is not present during the summer months
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.

Saito 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