Investigative Bronchoscopy in Subjects with Asthma and Other Obstructive Pulmonary Diseases

Whether and When

The feasibility and utility of investigative bronchoscopy and airway instrumentation in asthma and other obstructive pulmonary diseases have been well documented. Bronchoalveolar lavage, segmental lavage, mucosal biopsies, endobronchial brushing and biopsies, and instrumentation of the tracheobronchial tree have been used to measure physiologic function of the airways, evaluate inflammatory mediators and cells in lavage fluid, assess the effects of bronchial challenge, and study the morphology of accessible intrapulmonary airways. Clearly, these techniques can be safely performed in subjects with mild to moderate asthma as long as appropriate precautions are exercised.

Since the research potential for airway endoscopy and instrumentation is enormous, ensuring the wide investigative use of these procedures, it is imperative that care be taken to ensure the safety of the subjects participating in such procedures. A workshop held in Columbia, Maryland, on November 19 and 20, 1990, brought together a number of American and European scientists with relevant hands-on experience. The participants assessed various safety and procedural issues and recommended a number of guidelines for the use of investigative bronchoscopy in subjects with asthma and other obstructive airway diseases.

The overriding guideline, of course, is that the safety of the subject is of paramount importance and cannot be jeopardized for the sake of obtaining scientific data. Other recommendations made by this group relate to patient choice, considerations regarding pre-and postprocedure monitoring, and potential hazards. Subjects who (1) are acutely ill, (2) are sensitive to local anesthetics or other medications used in the endoscopy procedure, (3) exhibit extreme bronchial hyperresponsiveness with severe airflow obstruction and/or (4) have coexisting cardiovascular diseases are not recommended as candidates for investigative bronchoscopy, nor are subjects with an uncorrected bleeding diathesis if endobronchial biopsy or brushing is planned. Subjects considered to be at high risk from the procedures are those with an FEV₁ less than 60 percent of predicted and those who have coexisting cardiopulmonary disease. In general, the greater the degree of bronchial responsiveness and/or the more severe the airflow obstruction at the time of bronchoscopy, the greater the risk of precipitating acute severe bronchospasm. In our current state of knowledge, fiberoptic bronchoscopy is not recommended for subjects with extreme bronchial hyperresponsiveness and severe airflow obstruction.

Age alone is not considered to be a factor for excluding any subject from participating in investigative bronchoscopic procedures. However, when the patient is over 60 years of age, other precautions are warranted. While there is a small but significant experience with investigative bronchoscopy in infants and children, specific recommendations cannot be made at this time for the use of bronchoscopic procedures in this age group.

All procedures should be performed by an experienced bronchoscopist with facilities available for the management of medical emergencies. If bronchoscopy is to be performed on a patient with a high level of bronchial responsiveness, the bronchoscopist must be prepared to terminate the procedure and treat the subject with bronchodilators if bronchospasm occurs. A route for injection of intravenous medication must be secured. The potential hazards include acute obstruction of the intrathoracic airways, laryngospasm, hypoxemia, apnea, drug reactions, airway perforation, fever, pulmonary infiltrates, and infection.

To minimize untoward events, it is recommended that prior to airway endoscopy the investigator obtain a complete medical history that includes information about the severity and activity of the subject's airway disease, current medications, and specific allergies, as well as an electrocardiogram and blood pressure recording. In addition, some objective assessment should be made of the subject's pulmonary function and gas exchange. During the procedure, arterial oxygen saturation, cardiac rhythm, and blood pressure should be monitored. After the procedure, the subject should be carefully monitored until his or her condition is back to baseline as measured by a return of the gag reflex and the absence of symptomatic airflow obstruction on pulmonary function testing. Postdischarge follow-up is strongly advised.

From a procedural standpoint, the techniques used in the literature to obtain tissue and fluid samples for study have varied so widely that no detailed scientific methodologic recommendations can be made. However, based upon the available data, there are some procedural limitations that should be observed. For
example, no more than 400 ml of fluid should be used during bronchoalveolar lavage. Brushes should be limited to two to four areas, and no more than six biopsy specimens from a combination of the main carina and one or more segmental or subsegmental carinæ should be taken during a single endoscopy procedure. There are no data on either the indications for or the safety of transbronnchial lung biopsies.

Bronchoscopy provides a valuable tool for the in situ investigation of airway physiology, biochemistry, and immunology in diseases such as asthma, cystic fibrosis, chronic bronchitis, bronchiectasis, and other chronic obstructive lung diseases. With use of this tool, it is possible to obtain fluids, cells, and tissue to investigate the morphologic, pathologic, molecular biologic, immunologic, biochemical, and neurobiologic factors that are important in understanding the pathogenesis, natural history, pathophysiology, and clinical features of these airway diseases. It also is feasible to examine the effects of acute and chronic therapeutic and pathologic interventions. In addition, airway endoscopy permits the development of new investigational procedures such as the insertion or implantation of surface sensors for the study of epithelial biochemistry, thermodynamics, biophysics, and defense mechanisms, as well as the definition and monitoring of biochemical and/or physiologic markers of disease.

Although the ability to use bronchoscopic techniques, while adhering to carefully designed guidelines, to sample lower respiratory tract secretions and cells, to measure physiologic function, and to correlate these findings with bronchial morphology in carefully characterized subjects provides a unique opportunity to investigate the pathophysiology of airway disease in man, it should be cautioned that obtaining valid scientific data from these procedures is difficult and complicated and requires extensive laboratory expertise. Furthermore, bronchoscopy and other forms of airway instrumentation are highly invasive and should be undertaken only after the investigator has developed the skills and resources to use these procedures, to make appropriate measurements and to evaluate the specimens accurately.

While no single workshop can possibly cover every aspect of an evolving procedure, these recommendations and guidelines provide a rational approach to current studies, as well as a basis for change as additional information becomes available.

Eugene R. Bleecker, M.D., F.C.C.P.
Baltimore;

Edward R. McFadden, Jr., M.D.,
Cleveland;

Suzanne S. Hurd, Ph.D.,
Robert A. Goldstein, M.D., Ph.D., F.C.C.P.; and
Jandhyala Sri Ram, Ph.D.,
Bethesda, Maryland

REFERENCES


Metered-dose Inhalers versus Hand-held Nebulizers
Some Answers and New Questions

Inhaled beta-agonist drugs are the mainstay of treatment of exacerbations of reversible airflow obstruction for several reasons: they provide rapid and potent bronchodilation and are associated with a low incidence of serious side effects, both compared with other classes of bronchodilators and compared with orally or parenterally administered beta-agonists. Generally, hand-held nebulizers have been most commonly employed in the hospital setting (emergency room patients and inpatients), while metered-dose inhalers (MDIs) have been primarily used in outpatients. Considerable evidence indicates that most