percent decrease in resistance in an airway in which the wall area was 45 percent. Since an increase in airway wall thickness is one of the pathogenetic mechanisms that leads to the decrease in maximal expiratory flow in patients who have COPD, it would be expected that those patients with more severe baseline airflow obstruction would have thicker airway walls. Thus, another explanation for the relationship between starting FEV₁ and bronchodilator response is equal smooth muscle relaxation irrespective of starting FEV₁, but a greater effect of the relaxation in those with the most inflamed and thickened airway walls.

A similar mechanism may explain the exaggerated airway narrowing that develops in patients who have COPD in response to inhaled pharmacologic agents that stimulate smooth muscle contraction. A 30 percent muscle shortening in an airway in which the airway wall contributes 20 percent of the total area within the smooth muscle layer will result in a 600 percent increase in resistance, while the same amount of smooth muscle shortening will increase the resistance to 1,300 percent of baseline in an airway in which the wall area makes up 30 percent of the total area.

These calculations show that changes in measures of resistance and maximal flow are not linearly related to changes in airway smooth muscle length. Similarly, changes in smooth muscle length, even if precisely known, would not allow an extrapolated conclusion about changes in smooth muscle activation. The degree to which smooth muscle will shorten when stimulated is influenced by the magnitude of the stimulus, the length of the muscle relative to optimal length, and the load that the muscle must overcome to shorten. There is evidence that smooth muscle in vivo does not contract isometrically or isotonically but instead shortens under increasing tension provided by elastic afterloads. The elastic loads are related to the cartilage in the large airways and to the lung elastic recoil in the intraparenchymal bronchi and bronchioles. If there is a decrease in cartilage and/or lung elasticity, then the load on the contracting smooth muscle is less, and a given degree of muscle activation will produce more shortening and airway narrowing. Since a loss of cartilage and lung elasticity are features of the development of COPD, this has direct relevance to the results reported by Gross and colleagues. As they in fact suggest, it is possible that the greater bronchodilatation in patients with more severe obstruction is due to a greater effect on airway caliber of a given amount of cholinergic tone rather than to a greater amount of tone.

Whatever the explanation for the interesting findings of Gross et al, it is clear that one cannot equate the magnitude of change in a measure of airflow resistance or maximal expiratory flow to a change in smooth muscle length or excitatory state. Pulmonary physiologists and pharmacologists have for years fallen into the trap of analyzing the in vitro dose-response curve as if it were an in vivo smooth muscle preparation. An appreciation of the complex mechanical factors that link smooth muscle activation or relaxation with the resultant changes in airway diameter and flow rates suggest that it would be prudent to extrapolate cautiously.

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REFERENCES

Lidocaine Topical Anesthesia for Flexible Bronchoscopy

Since its introduction into the United States almost 20 years ago, flexible bronchoscopy has arguably become the invasive procedure most frequently performed by chest physicians. The ready acceptance of this procedure is probably based not only on its high diagnostic utility, but also on its low complication rate. Complications of flexible bronchoscopy can generally be divided into complications of the bronchoscopic examination and biopsy procedures (for example, hypoxemia, airway obstruction, bleeding, pneumothorax) and adverse effects of medications used before and during the bronchoscopic procedure. In fact, adverse reactions to medications probably account for at least half of the serious morbidity and the rare mortality associated with flexible bronchoscopy. Although mild systemic sedation with drugs such as midazolam or meperidine is commonly employed for flexible bronchoscopy, the procedure can be performed in selected patients without any systemic sedative pre-medication. However, both pre-treatment with atropine to decrease secretions and prevent...
vasovagal reactions and adequate topical airway anesthesia are generally considered essential for satisfactory bronchoscopy. Currently, lidocaine is the topical anesthetic of choice for bronchoscopic procedures. Three pertinent issues related to lidocaine anesthesia for flexible bronchoscopy are: (1) effectiveness of lidocaine in inducing airway anesthesia, (2) potential effects of lidocaine "contamination" of bronchoscopic specimens, and (3) the safety of lidocaine administration.

Extensive clinical experience would indicate that lidocaine is an effective topical anesthetic for bronchoscopy and studies have documented the effectiveness of lidocaine for inducing airway anesthesia. Lidocaine can be delivered to the upper airways by spraying via an atomizer, by ultrasonic or jet nebulization, and by the use of lidocaine as a jelly or viscous solution. Anesthesia of the lower airways is generally induced via injection of lidocaine through the bronchoscope channel. Interestingly, systemic administration of lidocaine can also induce some degree of airway anesthesia. The duration of airway anesthesia induced by topical lidocaine is approximately 20-40 minutes and in our experience, inhalation of lidocaine aerosol can achieve airway anesthesia down to the level of the mid-trachea.

Lidocaine is present in many bronchoscopic specimens and therefore might alter the results of in vitro studies on these specimens, especially microbiologic studies. Although lidocaine (even without preservative) can inhibit the growth of aerobic and anaerobic bacteria, fungi, and mycobacteria in vitro, the concentrations of lidocaine measured in bronchoalveolar lavage (BAL) fluid and protected brush catheter specimens are generally well below the reported minimal inhibitory concentrations for these organisms. Lidocaine can also impair the metabolic function of alveolar macrophages and other immunocompetent cells when studied in vitro. But again, the concentrations of lidocaine measured in BAL fluid have generally been lower than the levels of lidocaine required to have significant effects on these cells when studied in vitro.

Adverse effects of lidocaine include hypersensitivity reactions, toxicity caused by excessive lidocaine blood levels, and bronchoconstrictor reactions to inhaled lidocaine aerosols. Hypersensitivity to lidocaine is well documented and can be catastrophic. Fortunately, hypersensitivity reactions to lidocaine are rare. Toxic blood levels of lidocaine can occur during bronchoscopy and result primarily from direct administration of lidocaine to the tracheobronchial mucosa. Inhalation of lidocaine aerosols results in only minimal drug absorption with very low measured blood levels. As documented by McAlpine and Thomson in this issue (see page 1012), inhalation of nebulized lidocaine can cause significant bronchoconstriction in patients with asthma. As the authors note, previous studies have documented bronchoconstrictor responses to inhaled lidocaine in patients with hyper-responsive airways disease, although this has not been a universal finding. Two of the findings of these authors of particular interest are the lack of correlation between lidocaine-induced bronchoconstriction and airway response to histamine, and the prevalence of significant bronchoconstrictor responses to lidocaine in their study population. The lack of statistical correlation between lidocaine-induced bronchoconstriction and histamine responsiveness may simply reflect the small sample size, and only one patient with what would generally be considered mild histamine responsiveness had a significant response to lidocaine inhalation. Also, although there is generally a correlation between airway responses to various nonspecific stimuli (for example histamine and methacholine), some authors have found poor correlation with other stimuli such as ultrasonically nebulized distilled water. In the three subjects studied with lidocaine both with and without preservative, there appeared to be no important effect of the preservative per se. Although the 25 percent prevalence of significant bronchoconstrictor responses to inhaled lidocaine in this study is within the range of that reported in previous studies, this is not our experience in over 2,400 bronchoscopic procedures performed in our laboratory. Indeed, we have not noted clinical exacerbation of asthma caused by lidocaine inhalation in any patient. This is probably because most bronchoscopists are less inclined to use the bronchoscope in patients with moderate or severe clinical asthma. In addition, we have routinely added a beta-agonist (metaproterenol or albuterol) to the lidocaine solution to be inhaled for all patients with any history of airway disease, and it seems likely that this practice will prevent most bronchoconstrictor reactions to the inhaled lidocaine.

Nevertheless, while lidocaine anesthesia of the airways for bronchoscopy is generally safe and effective, the article by McAlpine and Thomson reminds us that even routine procedures should be performed with care and forethought.

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References

The Concept of “Organizing Pneumonia”

Inflammation of distal lung structures (alveoli, alveolar ducts, and respiratory bronchioles)—i.e., pneumonia—may in some instances fail to resolve completely and result in varying degrees of organization and fibrosis. The site of this organizing process, however, for reasons that remain unclear, may be predominantly intraluminal with relative preservation of distal air space architecture, or predominantly interstitial, associated with significant architectural distortion. When organization is predominantly intraluminal, characteristic aggregates of proliferating granulation tissue (mainly concentric whorls of fibroblasts and myofibroblasts) are observed within alveoli and alveolar ducts (Masson bodies) as well as respiratory bronchioles. For decades this latter process has been known to occur as a chronic sequel of unresolved bacterial lobar and tuberculous pneumonia and continues to be referred to as organizing pneumonia. This type of organization has also been observed in such varied disorders as collagen vascular disease, “uremic” lung, “rheumatic” pneumonia, experimental paraquat toxicity, and focally in predominantly interstitial organizing disorders such as hypersensitivity pneumonitis, chronic eosinophilic pneumonia, and usual interstitial pneumonia (UIP), also called fibrosing alveolitis and idiopathic pulmonary fibrosis.

Several clinical reports of predominantly intraluminal organizing pneumonia (ILOP) of no known etiology but associated with collagen vascular disease in some patients have appeared since 1981. The terms organizing pneumonia-like process, relapsing organizing pneumonia, cryptogenic organizing pneumonia, and most recently, idiopathic bronchiolitis obliterans organizing pneumonia (BOOP) have been used to describe what appears to be a new nosologic entity. The pathology of this condition and its differentiation from usual interstitial pneumonia (UIP), although alveolar epithelial damage appears to be an early event in both processes, have also been well described. With respect to nomenclature, to avoid clinical diagnostic confusion, perhaps the aspects of “pneumonia” and “intraluminal organization” only should be stressed. Although bronchiolitis obliterans is also observed pathologically, the predominant clinical profile of idiopathic ILOP is that which results from distal lung structure consolidation rather than from more proximal small airway obstruction; i.e., idiopathic ILOP is mainly characterized by lateralizing radiographic “pneumonic” consolidations associated with ventilatory restriction, rather than a predominantly obstructive ventilatory defect associated with a “military” or “overdistention” radiographic pattern.