Airway Secretion and Asthma

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Asthma is a disease of unknown cause that tends to affect predominantly the airways. Components of the asthmatic syndrome include acute and chronic bronchospasm and evidence of airway inflammation. Patients who die of asthma are often noted to have signs of severe airway abnormalities including plugging with mucus and thickening of the airway wall.

The airway is a dynamic organ and, besides conducting the flow of air, it contains a complex secretory apparatus and is obviously involved in lung defense. Because of the derangements seen in asthma, it is logical to suspect that measurement of airway clearance would be affected in the asthmatic syndrome. Using various techniques, investigators have measured clearance of secretions from the asthmatic lung and, consistent with the unknown nature of asthma, observations of airway clearance in this disease have been variable. Indeed, within a given group of asthmatic subjects, mucociliary clearance measurements have been defined as ‘normal’, ‘abnormal or reduced’ and finally ‘increased’ or faster than normal. It is likely that some of these differences are related to the technical aspects of measurement. While rigorous criteria for assessing the initial sites of deposition of radiolabeled particles and the techniques for analyzing retention curves have not been set, some observations probably reflect the disease process. We know that hospitalized asthmatic patients have markedly impaired clearance of retained aerosols from the lung [1]. With treatment, clearance can return towards normal but in chronic asthma many patients appear to have impaired clearance primarily from central airways [2]. A subset of asthmatics do appear to have mucociliary clearance that is more rapid than normal [3].

In the present issue of Respiration, Svartengren et al. [4] have measured mucociliary clearance using radiolabeled aerosols and a recently modified technique of ‘very slow inhalation’. Under these circumstances particles are thought not to deposit in the ‘central airways’ because of reduced forces of inertial impaction. They settle predominantly in airways thought by these authors to be distal bronchioles. In their asthmatic patients, these particles appear to be retained for a longer period of time than in normal subjects indicating that the ‘small airways’ of these patients were abnormal both in the resting state and after an induced bronchoconstriction.

The technique utilized by Svartengren et al. [4] has several advantages in that the collimated detectors are very sensitive and the amount of radioactivity necessary to label airway mucus is very low. The sensitivity of these detectors also enables prolonged observation over a longer period of time than that generally utilized by the γ camera. However, the technique does lack regional sensitivity. For example, we do not really know where these airways are. Future studies combining their technique with γ camera imaging may be helpful. While the clearance of radiolabeled aerosols from Svartengren’s patients was not different after allergen bronchoprovocation, it is possible that the sites of deposition were different. Following allergen inhalation even with reversal of the FEV₁, particles may have deposited more centrally. Local inflammatory effects might have impaired clearance, but a direct comparison with control airways was not possible. In spite of these limitations, the study does demonstrate that relatively asymptomatic asthmatic patients have abnormal clearance.
What is the importance of this and other studies of mucociliary clearance in our understanding and treatment of asthma? These studies are technically difficult, and often the results from one laboratory to another are discordant. However, many investigators feel that the future of asthma therapy lies in our understanding of the inflammatory process. Medications designed to affect airway inflammation are very difficult to assess in terms of dose/response. How can the response in asthma be evaluated if there is no immediate bronchodilation? Clinical trials often rely on diaries which record patients' symptoms. A unifying observation throughout most of the mucociliary clearance literature is that improvements in clinical asthma seem to be related to improvements in airway clearance. If so, then measurement of airway clearance may be a useful indicator of a medicine’s potential for therapeutic effectiveness. In the early stages of clinical trials, dose escalation studies can be carried out with airway clearance as a potential primary endpoint. The effects of a new drug on mucociliary clearance, possibly combined with an analysis of expectorated sputum and airway biopsies, would set the stage for the proper design of large-scale clinical trials.

References