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EDITORIAL

Tobacco smoke: old foe more important for asthma than commonly appreciated?

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Today, we are facing a worldwide epidemic of asthma, which is probably attributed to a number of factors associated with changes in environment and lifestyle. While the major driving factors behind the increase in asthma morbidity are current issues of much debate, tobacco smoking is a more clearly defined aetiological factor behind chronic conditions, such as cardiovascular disease and chronic obstructive pulmonary disease (COPD). Tobacco smoke is known to contain many thousands of different compounds that affect cell function in carcinogenic or irritative ways [1, 2]. Asthma is, as we currently see it, an inflammatory airways disease with activation of a multitude of a structural cellular elements, as well as mobile cells of the immune defence. It is widely appreciated that the asthmatic airways become hyperresponsive to a vast range of irritants, which may enhance the airway inflammation, as well as the bronchial hyperresponsiveness (BHR).

Tobacco smoke appears to have the capacity to modify asthmatic airway inflammation and increase BHR [3]. In this issue of the *European Respiratory Journal*, we have the privilege of a review by THOMSON *et al*. [4], who point out the current mechanistic understanding of tobacco effects on asthmatic airways. The complex pathophysiological events are reported to include both heightened and suppressed inflammatory events. At present, the foundation for the pathophysiological understanding is somewhat limited and, here, we have an important research arena that should attract scientists. This becomes even more obvious with the reduced efficacy of the key asthma medication, in terms of inhaled corticosteroids in smoking asthmatics, whose airways deteriorate faster than their nonsmoking counterparts.

It is well known that the decline in lung function among smoking asthmatics is increased [5]. Among middle-aged smokers, an increase in BHR, associated with decline in lung function, is recognised. Also, among teenagers and young adults, the incidence of wheezing is increased among smokers [6]. However, when the question considers the influence of smoking on asthma development, the evidence is still mixed and controversial.

A range of different methods has been used to approach this question, with contradictory results. Generally, cross-sectional population studies have not found current smoking to be associated [7]. Instead, cross-sectional studies have often found ex-smoking to be associated with asthma [8]. However, a cross-sectional design leads to difficulties, and it is not possible to decide about cause or consequence. When it comes to case-referent studies based on prevalent cases and some prospective studies, an association between ever-smoking and asthma has been found in several studies [9, 10].

In the current issue of the journal, PIIPARI *et al*. [11] present a population-based incident case-control study, which was designed to prospectively include all new asthma cases in the region studied. The authors were able to claim clearly increased odds ratios for the risk of developing asthma in current and ex-smokers compared with never-smokers. The risk increased up to 14 cigarettes per day. Before this study, only a limited number of investigators had gone through the process of performing longitudinal studies on the effects of smoking on asthma development in adults. Some of these have showed current smoking to be a risk factor for incident asthma [12, 13]. In most of these studies, a weakness is that the diagnosis of asthma has been based on questionnaire data, *i.e.* reported by the subjects under study that they have asthma diagnosed by a physician. However, in one of the prospective population studies advocating an association between current smoking and incident asthma, the asthma diagnosis was verified by methacholine tests [14], and these results [15, 16] point to the same conclusion as the results from the study by PIIPARI *et al* [11]. Thus, use of methods is crucial when exploring the relationship between current smoking and the development of asthma. Classification of disease is another critical aspect. There has been a tendency to classify respiratory disease as chronic bronchitis or COPD once the subjects under study are smokers, while nonsmokers have been more prone to be labelled with asthma [15]. Cross-sectional studies with prevalent cases of disease lead to difficulties, while prospective population studies have better possibilities to answer that question, though the results from prospective studies also still tend to be conflicting [16].

An interesting aspect in the present study by PIIPARI *et al.* [11] is that it contrasted with most other studies in the field, by using a population-based incident case-control study design. In cooperation with physicians at all healthcare centres in the Tampere region in Finland, new cases of asthma were included. The investigators had taken precautions to include all new cases, as based on the physician′s diagnosis, together with asthmatic symptoms and reversible airways obstruction. Another important and, perhaps, most beneficial aspect was the addition of randomly selected control subjects from the same region.

Collection of information on present and past smoking is known to be a difficult issue, but was managed in a reasonable fashion. The investigators advocate that since the study was introduced as an investigation of environmental factors in general, with smoking-related questions being only a part of the questionnaire, a major recall bias would not be likely.

An important strength of the study is the fact that there is a physiological verification of the diagnosis of asthma. The way it has been done can, of course, be discussed and questioned. Though reversible, some subjects may have COPD, which may overestimate the risk. However, the validity of the

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diagnosis is far more consistent than a diagnosis based on self-administrated questionnaires. The data analyses and presentation is also very clear.

Apart from the well-known association between tobacco smoking and chronic obstructive pulmonary disease, the PIIPARI *et al*. [11] study, with its design aspects, suggests smoking to be an underestimated contributing factor to asthma development. The review paper by THOMSON *et al*. [4] further strengthens the argument that smoking produces adverse effects in the airways of asthmatic individuals. Together, these papers add additional strength to the argument that people with heredity for, or already established asthma would have an even stronger reason to avoid tobacco smoke. It also further encourages anti-tobacco activities at all different levels in healthcare and society.

References

1. Curtin GM, Hanausek M, Walaszek Z, Mosberg AT, Slaga TJ. Short-term *in vitro* and *in vivo* analyses for assessing the tumor-promoting potentials of cigarette smoke condensates. *Toxicol Sci* 2004; 81: 14–25.
2. Kirkham PA, Spooner G, Ffoulkes-Jones C, Calvez R. Cigarette smoke triggers macrophage adhesion and activation: role of lipid peroxidation products and scavenger receptor. *Free Radic Biol Med* 2003; 35: 697–710.
3. Nadel JA, Comroe JH. Acute effects of inhalation of cigarette smoke on airway conductance. *J Appl Physiol* 1961; 16: 713–716.
4. Thomson NC, Chaudhuri R, Livingston E. Asthma and cigarette smoking. *Eur Respir J* 2004; 24: 822–833.
5. Lange P, Parner J, Vestbo J, *et al.* A 15-years follow-up study of ventilation function in adults with asthma. *New Engl J Med* 1998; 339: 1194–1200.
6. Strachan DP, Butland BK, Anderson HR. Incidence and prognosis of wheezing illness from early childhood to age 33 in a national British cohort. *BMJ* 1996; 312: 1195–1199.
7. Senthilselvan A, Chen Y, Dosman JA. Predictors of asthma and wheezing in adults. *Am Rev Respir Dis* 1993; 148: 667–670.
8. Lebowitz MD. Smoking habits and changes in smoking habits as they relate to chronic conditions and respiratory symptoms. *Am J Epidemiol* 1977; 105: 534–543.
9. Flodin U, Jönsson P, Ziegler J, Axelsson O. An epidemiologic study of bronchial asthma and smoking. *Epidemiology* 1995; 6: 503–505.
10. Vesterinen E, Pekkanen J, Koskenvuo M. Prospective study of asthma in relation to smoking habits among 14729 adults. *Thorax* 1988; 43: 534–539.
11. Piipari R, Jaakkola JJK, Jaakkola N, Jaakkola MS. Smoking and asthma in adults. *Eur Respir J* 2004; 24: 734–739.
12. Larsson L. Incidence of asthma in Swedish teenagers: relation to sex and smoking habits. *Thorax* 1995; 50: 260–264.
13. Torén K, Hermansson BA. Incidence-rate of adult onset asthma in relation to age, sex, atopy and smoking. A Swedish population-based study of 15813 adults. *Int J Tuberc Lung Dis* 1999; 3: 192–197.
14. Lundbäck B, Rönmark E, Jönsson E, Larsson K, Sandström T. Incidence of physician-diagnosed asthma in adults: a real incidence or a result of increased awareness? Report from the Obstructive Lung Disease in Northern Sweden Studies. *Respir Med* 2001; 95: 685–692.
15. Burrows B, Lebowitz MD, Barbee RA, Cline MG. Findings before diagnoses of asthma among the elderly in a longitudinal study of a general population sample. *J Allergy Clin Immunol* 1991; 88: 870–877.
16. Godfredsen NS, Lange P, Prescott E, Osler M, Vestbo J. Changes in smoking habits and risk of asthma: a longitudinal population based study. *Eur Respir J* 2001; 18: 549–554.