Smoking and Asthma*

Clinical and Radiologic Features, Lung Function, and Airway Inflammation

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Smoking may influence the type of airway inflammation observed in asthma and its response to therapy. More studies are needed on how smoking-induced changes in lung function/structure and airway inflammation may result in a change in clinical expression. We compared clinical, physiologic, radiologic, and airway inflammatory features of 22 smoking asthma patients (cigarette smoking history, 14.0 ± 7.6 pack-years [mean ± SD]) and 27 nonsmoking asthma patients. Mean age/duration of asthma of smoking and nonsmoking asthma patients were 31 years/14 years and 29 years/17 years, respectively. Quality of life, FEV₁, bronchodilator response, perception of bronchoconstriction, and methacholine responsiveness were similar in the two groups. Compared to nonsmoking asthma patients, smokers had more respiratory symptoms, a lower mean forced expiratory flow at 25 to 75% of FVC, FEV₁/FVC ratio, and lung diffusion capacity, and a higher functional residual capacity. Induced-sputum neutrophil and bronchial cell counts were higher and exhaled breath condensate pH was more acidic in smoking asthma patients. On high-resolution CT, airway and parenchymal abnormalities were more common in smoking asthma patients than in nonsmokers. In conclusion, compared with nonsmoking asthma patients, smoking asthma patients have features similar to what could be found in early stages of COPD.

Key words: asthma; COPD; exhaled breath condensate; high-resolution CT; induced sputum; lung diffusion capacity; pH; respiratory symptoms; smoking

Abbreviations: ACSS = Asthma Control Scoring System; ATS = American Thoracic Society; FEF₂₅₋₇₅% = forced expiratory flow at 25 to 75% of FVC; HRCT = high-resolution CT; HU = Hounsfield unit

Asthma is a common chronic inflammatory condition characterized by variable airway obstruction and hyperresponsiveness attributed to an underlying inflammatory process and bronchial structural changes.¹,² Smoking is surprisingly frequent in asthma patients, with a prevalence relatively close to that found in the general population.³,⁴ In addition to the numerous usual risks associated with cigarette smoke observed in patients without asthma, smoking asthma patients have increased asthma-related morbidity and severity and accelerated decline in pulmonary function.⁴–⁹ However, Wakefield et al¹⁰ showed that many asthmatic smokers believe that they are not personally at risk from smoking. Furthermore, smoking may change the perception of respiratory symptoms.¹¹ A negative relationship has been suggested between the duration and intensity of smoking and dyspnea intensity in asthma, but this remains to be further documented.¹²

Cigarette smoke may affect airway function in
different ways due to its toxic and proinflammatory effects.\textsuperscript{13} Nonasthmatic smokers frequently show signs of small-airways dysfunction, airway hyperresponsiveness, and a reduction of bronchodilator response.\textsuperscript{2,14–16} Smoking can also affect asthma and its response to treatment by influencing the underlying airway inflammatory process; increases in neutrophils have been described in this situation.\textsuperscript{17,18}

The influence of smoking on pulmonary function among asthma patients has not been studied as extensively as in nonsmokers, as smokers are generally excluded from studies. Furthermore, to our knowledge, no study has specifically looked at radiologic features of smoking asthma patients without an irreversible component of airway obstruction. We consequently need more data on the characteristics of smoking asthma patients in order to determine the possible mechanisms by which smoking increases the severity of asthma and may change airway function.

\section*{Materials and Methods}

\subsection*{Patients}

Eighteen- to 45-year-old, corticosteroid-naïve asthma patients were consecutively enrolled from the asthma clinics of Laval Hospital (Quebec City, Canada) and Sacré-Cœur Hospital (Montreal, Canada). Nonsmokers had not smoked in the last year and had a < 2 pack-year history of cigarette smoking; current smokers smoked > 10 cigarettes per day with > 5 pack-years of smoking. Smoking status was evaluated by self-report of study subjects. Patients had a medical history of asthma according to the criteria of the American Thoracic Society (ATS).\textsuperscript{19} All had a > 12\% increase in FEV\textsubscript{1} after salbutamol. FEV\textsubscript{1} had to be > 65\% of predicted and medication had to be stable for 3 months (including no asthma exacerbations) before entering the trial. No treatment for asthma was used except for short-acting \(\beta_2\)-agonists on demand. All patients provided an informed consent, and the study was approved by local Institutional Scientific and Ethics Committees.

\subsection*{Study Design}

At the first visit, a locally validated asthma-control questionnaire, the Asthma Control Scoring System (ACSS), and the Asthma Control Questionnaires were used to assess control in the last week.\textsuperscript{20,21} The Quality of Life questionnaire was administered, and a respiratory-symptom questionnaire evaluated their severity and type.\textsuperscript{22} A thoracic examination, allergy skin-prick tests, spirometry and bronchodilator response, pH measurements in exhaled air condensate, and sputum induction were performed. At the second visit, lung volumes and compliance measurements were obtained and a methacholine challenge was performed. At the third visit, high-resolution CT (HRCT) was performed.

\subsection*{Allergy Skin Tests}

Skin-prick tests were done with a battery of common airborne allergens. Atopy was defined as the presence of at least one positive (\(\geq 3\)-mm wheel) response to allergens.\textsuperscript{23}

\subsection*{Spirometry and Lung Volumes}

Spirometry was performed according to the ATS specifications\textsuperscript{24} using an ATS-approved spirogram and predicted values of Knudson et al.\textsuperscript{25} Lung volumes (body plethysmography), carbon monoxide diffusing capacity, and lung function were measured by standard methods.\textsuperscript{26} Smokers were asked not to smoke the morning of the visits, and this was checked by asking the patient before proceeding to the tests.

\subsection*{Methacholine Challenge and Perception of Bronchoconstriction}

Methacholine challenges were done according to the method described by Juniper et al.\textsuperscript{27} Inspiratory capacity was also measured at a 20\% fall in FEV\textsubscript{1}. Perception scores for breathlessness were obtained according to our previously described method on a scale from 0 to 10.\textsuperscript{28}

\subsection*{Induced-Sputum Analysis}

Sputum was induced using inhalations of increasing concentrations (3\%, 4\%, and 5\%) of hypertonic saline solution. Sputum was selected from the expectorate and was processed and examined for nonsquamous cell counts as previously described.\textsuperscript{29}

\subsection*{Exhaled Breath Condensate pH}

Exhaled breath condensate pH was measured using a modification of the technique proposed by Hunt.\textsuperscript{30} Patients breathed through a frozen sampling syringe for 1 min, and the resulting air condensate was recovered for analysis with an electronic pH meter.

\subsection*{Radiologic Studies}

The type and frequency of bronchial/parenchymal abnormalities and airway wall thickness on HRCT were determined according to an adaptation of our previously published method.\textsuperscript{31} All measurements were performed on GE Hi Speed CT/I or Phillips PQ 5000 (General Electric; Milwaukee, WI) scans. We used thin-section helical (spiral) CT to quantify airway dimensions and HRCT to evaluate lung parenchyma (Fig 1). Nonanagulated, 1-mm-thick slices were obtained at 10-mm increments through the lungs, first at suspended end-inspiratory volume and thereafter at the end of maximal inspiration. Scanning time was 1 s with 120 kilovolts and 200 mA. Images were recorded at a window width of 1,600 Hounsfield units (HU) and window length of –600 HU. The scans were interpreted without knowledge of the origin (smokers or nonsmokers) and by agreement between the two radiologists (G.C. and M.C.D.). Gas trapping was assessed by visual score according to Naidich et al.\textsuperscript{32} Emphysema was evaluated using a scale from 0 to 10.\textsuperscript{29} Perception scores for breathlessness were obtained according to our previously described method on a scale from 0 to 10.\textsuperscript{28}

Helical scanning was performed at 140 kilovolts, 210 mA, 5-mm collimation, and pitch of 1.7:1. Approximately 3 cm of the lung was scanned. A targeted reconstruction in this area was performed with a field of view of 10 cm to obtain 1-mm-thick images centered on the apical segmental branches of the right upper lobe. Images were reviewed at a window length of –450 HU and window width of 1,200 HU.\textsuperscript{36} Regions of interest were traced manually with a computer mouse at the external perimeter and the internal perimeter of the bronchus. Lumenal area and total airway area in millimeters squared were calculated automatically. Total airway area minus lumenal area represents wall area.
Data were expressed using mean ± SD or median for continuous variables or as percentage for categorical data. Analysis of categorical variables was performed using the Fisher Exact Test. According to the distribution of continuous data, Student $t$ test or Wilcoxon rank-sum test were used to compare groups. The normality assumption was verified with the Shapiro-Wilk test and the Brown and Forsythe variation of Levene test statistic was used to verify the homogeneity of variances. The results were considered significant with $p$ values $<0.05$. Data were analyzed using a statistical software package (SAS v8.2; SAS Institute; Cary, NC). The minimal important difference for the Quality of Life questionnaire used had been estimated to be 0.522 and was considered to be an approximate 15% change for the Asthma Control Questionnaires.37

**Results**

**Patient Characteristics**

Forty-nine patients, 22 smokers and 27 nonsmokers, completed the study (Table 1). The two groups of patients were similar in regard to age and time since diagnosis (Table 1). They included 24 women (11 nonsmokers and 13 smokers) and 25 men (16 nonsmokers and 9 smokers) aged 20 to 44 years (mean, 30 ± 7 years). Smoking history, as expressed by the number of mean pack-years, was 14.0 ± 7.6 pack-years (range, 5 to 32 pack-years). Twenty-five nonsmokers (93%) and 18 smokers (82%) were atopic.

**Asthma Control**

From the ACSS questionnaire, the mean global asthma control scores, expressed as a percentage of optimal value according to the ACSS for the last week, were similar in smoking asthmatics and nonsmokers: 77.1% ± 11.2 vs 80.2% ± 12.9, respectively ($p > 0.05$). Mean clinical score, however, was significantly better in nonsmokers, with a value of 77.7% ± 15.4 for the smokers and 85.7% ± 10.7 for nonsmokers ($p < 0.05$). The two other components of the control score—physiologic and inflammatory (the latter expressed by sputum eosinophil count in percentage)—were similar between groups, with respective values of 82.7% ± 20.7 and 69.5% ± 22.5 for the smokers and 83.0% ± 19.0 and 69.1% ± 27.4 for nonsmokers (both $p > 0.05$).

The Asthma Control Questionnaire21 results were also similar between the study group and nonsmokers: 1.5 ± 0.6 vs 1.1 ± 0.8, respectively ($p > 0.05$). There was no significant difference in the mean number of emergency department visits in the last year between the smoking group and nonsmokers: 0.36 ± 0.9 visits vs 0.04 ± 0.2 visits ($p > 0.05$). The number of treatments with prednisone in the last year was similar in smokers and nonsmokers: 0.14 ± 0.5 vs 0.15 ± 0.6, respectively ($p > 0.05$). There was no statistical difference in the number of days of work or school absenteeism due to asthma in the last year between the two groups (smokers and nonsmokers): 0.55 ± 1.5 days and 0.11 ± 0.4 days ($p > 0.05$). With regard to the respiratory symptom questionnaire, smoking asthma patients had more respiratory symptoms than nonsmokers: 6.02 ± 5.6 vs 1.97 ± 2.2 ($p < 0.05$).
Inspiratory capacity following 20% fall in FEV₁ on methacholine

Response

Pulmonary Function Tests and Bronchodilator Response

The comparative pulmonary function tests for the two groups are detailed in Table 2. The mean resting prebronchodilator FEV₁ and FVC were similar in the two groups. The mean bronchodilator response, expressed as improvement in FEV₁ (percentage of predicted) was similar in the two groups: 15.2 ± 4.7% vs 14.9 ± 8.1% (p > 0.05). Forced expiratory flow at 25 to 75% of FVC (FEF₂₅–₇₅%) was lower in smokers. The mean resting and post-methacholine-induced inspiratory capacity at a 20% fall in FEV₁ were similar in the two groups.

The pattern of distribution of lung volumes was different in smokers, who had a higher mean functional residual capacity (p < 0.05) [Table 2]. Lung diffusion capacity was lower in smoking asthma patients, while airway resistance was not. Finally, 16 smoking and 20 nonsmoking patients underwent a measure of pulmonary compliance and maximal transpulmonary pressure. Smokers had a lower compliance (p < 0.05) and a similar maximal transpulmonary pressure (p > 0.05) than nonsmokers.

Asthma Quality of Life Questionnaire

The mean global score was similar in smokers and nonsmokers: 5.47 ± 0.8 vs 5.58 ± 1.0, respectively (p > 0.05). With regard to the various domains, there were no significant differences in regard to symptoms: 4.72 ± 1.2 vs 5.10 ± 1.0 (p > 0.05); activities, 5.78 ± 1.0 vs 5.87 ± 1.2 (p > 0.05); emotions, 5.85 ± 1.4 vs 5.52 ± 1.7 (p > 0.05); or environment, 5.49 ± 1.2 vs 5.47 ± 1.3 (p > 0.05), respectively.

Airway Responsiveness and Perception of Bronchoconstriction

The degree of airway hyperresponsiveness did not differ between the groups. Perception scores at 20% fall in FEV₁ during methacholine-induced bronchoconstriction were not different in smokers (2.53 ± 1.84) and nonsmokers (2.19 ± 1.07) [p > 0.05].

Airway Inflammation

The number and percentage of cells found in induced sputum are reported in Table 3. Median (range) total sputum cell counts, absolute sputum eosinophil, macrophage, and lymphocyte counts were similar in smokers and nonsmokers. In contrast, median (range) absolute sputum neutrophil counts were significantly higher in smokers than nonsmokers (p < 0.05). A higher proportion of bronchial cells was found in induced sputum of smokers (p < 0.05). Exhaled air condensate pH was lower in smokers (p < 0.05) [Table 3].

HRCT Findings

The main findings are summarized in Table 4. Smokers had more frequent airway and parenchymal abnormalities, but the main finding was a reduced airway lumen area in smokers (p = 0.02). When airway lumen area was corrected for height or sex, this difference was still significant (p > 0.05). This was due to the presence of smaller airways and not an increased airway wall thickness.

Table 2—Pulmonary Function Test Results*

<table>
<thead>
<tr>
<th>Variables</th>
<th>Smokers</th>
<th>Nonsmokers</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV₁, % predicted</td>
<td>87.0 ± 13.3</td>
<td>89.3 ± 13.7</td>
</tr>
<tr>
<td>FVC, % predicted</td>
<td>106.3 ± 17.9</td>
<td>100.2 ± 12.6</td>
</tr>
<tr>
<td>FEV₁/FVC ratio, absolute value</td>
<td>70.4 ± 9.0†</td>
<td>76.0 ± 8.2†</td>
</tr>
<tr>
<td>FEF₂₅–₇₅%, % predicted</td>
<td>55.2 ± 14.5†</td>
<td>70.3 ± 19.9†</td>
</tr>
<tr>
<td>Total lung capacity, % predicted</td>
<td>102.8 ± 13.9</td>
<td>97.5 ± 11.0</td>
</tr>
<tr>
<td>Functional residual capacity, % predicted</td>
<td>105.6 ± 15.6†</td>
<td>92.7 ± 12.0†</td>
</tr>
<tr>
<td>Residual volume, % predicted</td>
<td>111.1 ± 29.8</td>
<td>97.8 ± 23.8</td>
</tr>
<tr>
<td>Diffusion capacity for carbon monoxide, % predicted</td>
<td>90.5 ± 11.4†</td>
<td>90.3 ± 15.1†</td>
</tr>
<tr>
<td>Diffusion coefficient, % predicted</td>
<td>93.1 ± 12.4†</td>
<td>106.0 ± 16.3†</td>
</tr>
<tr>
<td>Airway resistance, % predicted</td>
<td>205.2 ± 56.0†</td>
<td>154.8 ± 52.0†</td>
</tr>
<tr>
<td>Inspiratory capacity, % predicted</td>
<td>97.6 ± 19.3</td>
<td>98.0 ± 19.5</td>
</tr>
<tr>
<td>Inspiratory capacity following 20% fall in FEV₁ on methacholine test, % predicted</td>
<td>78.2 ± 15.0</td>
<td>77.2 ± 13.9</td>
</tr>
<tr>
<td>Compliance, L/cm H₂O</td>
<td>0.19 ± 0.06†</td>
<td>0.25 ± 0.12†</td>
</tr>
<tr>
<td>Maximal transpulmonary pressure, cm H₂O</td>
<td>32.0 ± 20.7</td>
<td>44.0 ± 27.9</td>
</tr>
<tr>
<td>Geometric mean provocative concentration of methacholine causing a 20% fall in FEV₁ (confidence interval), mg/mL</td>
<td>1.09 (−0.54 to 0.73)</td>
<td>1.26 (−0.33 to 0.79)</td>
</tr>
</tbody>
</table>

*Data are presented as mean ± SD unless otherwise indicated.†p < 0.05.
Table 3—Cell Analysis of Sputum Samples*

<table>
<thead>
<tr>
<th>Variables</th>
<th>Smokers</th>
<th>Nonsmokers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cell counts, /10⁶</td>
<td>0.49 (0.05–3.21)</td>
<td>0.30 (0.006–5.41)</td>
</tr>
<tr>
<td>Cell viability, %</td>
<td>77.4 ± 8.1</td>
<td>66.5 ± 13.3</td>
</tr>
<tr>
<td>Eosinophils, /10⁶</td>
<td>0.006 (0.0–0.16)</td>
<td>0.006 (0.0–0.5)</td>
</tr>
<tr>
<td>%</td>
<td>3.7 ± 7.5</td>
<td>6.7 ± 12.3</td>
</tr>
<tr>
<td>Neutrophils, /10⁶</td>
<td>0.14 (0.005–1.03)</td>
<td>0.03 (0.001–5.07)</td>
</tr>
<tr>
<td>%</td>
<td>36.1 ± 18.1</td>
<td>26.2 ± 23.8</td>
</tr>
<tr>
<td>Macrophages, /10⁶</td>
<td>0.14 (0.04–2.21)</td>
<td>0.17 (0.002–1.61)</td>
</tr>
<tr>
<td>%</td>
<td>56.6 ± 19.3</td>
<td>61.9 ± 25.2</td>
</tr>
<tr>
<td>Lymphocytes, /10⁶</td>
<td>0.004 (0.0–0.04)</td>
<td>0.002 (0.0–0.05)</td>
</tr>
<tr>
<td>%</td>
<td>1.0 ± 0.7</td>
<td>1.4 ± 1.3</td>
</tr>
<tr>
<td>Bronchial cells, /10⁶</td>
<td>0.01 (0.0–0.8)</td>
<td>0.002 (0.0–0.02)</td>
</tr>
<tr>
<td>%</td>
<td>2.6 ± 2.0</td>
<td>3.7 ± 5.2</td>
</tr>
<tr>
<td>pH</td>
<td>6.3 ± 0.5†</td>
<td>6.8 ± 0.5†</td>
</tr>
</tbody>
</table>

*Data are presented as median (range) or mean ± SD.
†p < 0.05.

Between-Parameter Correlations

There were no significant correlations between the number of pack-years and either clinical, physiologic, or inflammatory parameters. There was no correlation between baseline airway caliber and the number of sputum inflammatory cells such as eosinophils and neutrophils. Looking at gender differences, we found that male patients showed a correlation between the number of pack-years of cigarette and quality of life (p < 0.05).

Discussion

Our study provides both confirmatory and original data on the effect of smoking on asthmatic airways and on the relationships between clinical, physiologic, radiologic, and inflammatory features in this population. Compared to nonsmoking asthma patients, smokers had increased respiratory symptoms, lower mean expiratory flows and lung diffusion capacity, and increased lung hyperinflation and induced-sputum neutrophil and bronchial cell counts. Exhaled breath condensate pH was more acidic in smokers. Smokers had more emphysematous changes and reduced airway lumen area on HRCT.

Smoking does seem to increase the severity of asthma and morbidity.‡ We extend these findings, showing increased respiratory symptoms among smokers as well as a trend toward increased emergency department visits and absenteeism from work or school (p = 0.05 to p < 0.1). It was somewhat surprising that this was not reflected in Asthma Control Questionnaire or Quality of Life Questionnaire scores, contrary to what had been reported, suggesting that patients may adapt to their disease or that long-term control is not always properly assessed by measures of control parameters obtained in the recent past. This may also be related to a quality-of-life benefit from smoking.

Mean baseline FEV1 was normal in our two groups of patients, reflecting the fact that we only included patients with mild-to-moderate asthma and that their cumulative years and degree of smoking were lower than what we usually find in COPD patients. We also selected between 18 to <45 years of age in order to minimize the possibility of including patients with only smoking-induced COPD. The findings of this study may have been different in a more severe asthmatic population, but we wanted to include corticosteroid-naïve asthmatic patients in order to assess airway inflammation without the interference of these medications. The influence of smoking on the perception of respiratory symptoms was also likely to be better assessed without the confounding effect of the antiinflammatory medications and the smoking associated COPD.

Nevertheless, the ratio of FEV1/FVC was lower in smokers, suggesting increased airway obstruction. Bronchodilator response was similar, contrary to what is found in COPD patients, while there was evidence of more marked lung hyperinflation in asthmatic smokers. Smokers had also more evidence of small airways dysfunction as shown by changes in FEF25–75% and lung hyperinflation. However, baseline and postmethacholine inspiratory capacity were similar in the two groups, suggesting that methacholine-induced bronchoconstriction was not associated with an increase in lung hyperinflation.

Furthermore, with the same degree of airway hyperresponsiveness in our two groups, perception scores for breathlessness before and after methacholine challenge were similar. Janson-Bjerklie et al12 reported that there was a significant negative relationship between age and the magnitude of dyspnea, and between cigarette pack-year and dyspnea intensity, suggesting the possibility of impaired perception of breathlessness among smoking patients. Com-

Table 4—HRCT Results

<table>
<thead>
<tr>
<th>Variables</th>
<th>Smokers</th>
<th>Nonsmokers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients, No.</td>
<td>16</td>
<td>23</td>
</tr>
<tr>
<td>Emphysematous changes, %</td>
<td>18.8</td>
<td>4.4</td>
</tr>
<tr>
<td>Bronchiectasis, %</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Heterogeneity of lung parenchyma, %</td>
<td>18.8</td>
<td>8.7</td>
</tr>
<tr>
<td>Inspiratory</td>
<td>18.8</td>
<td>8.7</td>
</tr>
<tr>
<td>Expiratory</td>
<td>68.8</td>
<td>69.6</td>
</tr>
<tr>
<td>Airway measurements</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total area, mm²</td>
<td>27.2 ± 11.3</td>
<td>34.1 ± 12.0</td>
</tr>
<tr>
<td>Area of bronchial lumen, mm²</td>
<td>9.4 ± 4.9</td>
<td>13.8 ± 5.9†</td>
</tr>
<tr>
<td>Airway wall thickness, mm²</td>
<td>17.8</td>
<td>20.3</td>
</tr>
</tbody>
</table>

*Data are presented as mean ± SD unless otherwise indicated.
†p < 0.05.
pared to this previous study, our patients may not have been old enough or have smoked sufficiently to observe such change.

Another parameter analyzed in our study was airway inflammation, mainly assessed by induced-sputum analysis. Our findings are in keeping with those of Chalmers et al., who observed an increase in total cells and neutrophils in induced sputum of smoking asthma patients. As for COPD, even in normal subjects, cigarette smoking seems to induce an increase in neutrophils in the airways. Sunyer et al40 also found that smoking increased neutrophils in peripheral blood of nonasthmatic patients but not in those with asthma. In our study, although there were slightly more eosinophils in the smoking group, this difference was not statistically significant. However, the increased number of bronchial cells in induced sputum may reflect increased airway epithelial damage from smoking and associated desquamation.

Other noninvasive measures of airway inflammation, such as exhaled nitric oxide analysis and various substances or pH in exhaled air condensate, have been developed. In our study, we used a new method to obtain exhaled air condensate to measure changes in pH. These changes were lower in smokers, an increased acidity of airway fluid being in keeping with a more marked inflammatory process.

With regard to HRCT, Park et al.43 reported from HRCT studies that patients with bronchial asthma had bronchial wall thickening in addition to bronchiectasis (in 17.5% of patients), emphysema (5.3%), and mosaic pattern of lung attenuation (17.5%). Our study shows a similar prevalence of emphysematous changes in nonsmoking asthmatics, while it was higher in smokers. Paganin et al.44 also demonstrated the presence of emphysema-like changes on HRCT of asthmatic patients.

Kondoh et al.45 reported evidence of emphysema that correlated with cigarette consumption in smoking subjects with chronic asthma and irreversible airway obstruction. We also previously compared HRCTs in two populations: patients with COPD and nonsmoking asthma patients with a component of irreversible airflow limitation. Emphysematous changes were observed in most COPD patients but only in a few asthma patients, while bronchial wall thickening was more frequent in asthma. In smoking asthma patients, the observed airway wall and lung parenchyma alterations and their consequences on pulmonary function, along with the change in type of airway inflammation, may explain recent observations of “resistance” to corticosteroid therapy as compared with nonsmoking asthmatics.47–50 It was intriguing that in our present study, the airways of smokers were smaller than nonsmokers; but, although it could be due to smoking, we cannot exclude that the slightly higher number of women in smoking patients could have influence this finding. However, when we corrected the airway lumen area for height and sex, the difference between the two groups was still significant.

Smoking asthma patients can therefore be considered as a specific group, intermediate between nonsmoking asthma and COPD patients, with a mixture of the features of both diseases. Indeed, although they have asthma, they also have, as demonstrated in this study, features of early COPD, such as airway neutrophilia, lung hyperinflation, lower lung diffusion capacity, increased baseline airway resistance, and increased emphysematous changes on HRCT. They also have an increase in sputum interleukin-8 cytokine expression, as well as a response to therapy closer to what is found with COPD than with asthma. This may be due to progressive changes of the same type as those found in COPD but to a much smaller degree. It would therefore be of interest to follow these patients to determine the time course of those changes over time. It is possible that this population has coexisting asthma and early COPD, or simply that smoking has modulated the asthmatic pathophysiology.

Finally, it is possible that some of the features observed in smoking asthma patients could have been observed in smoking patients without a diagnosis of asthma. Nevertheless, we now have evidence that smoking changes the expression and pathophysiology of asthma, and our focus was on how smoking changed the features of asthma.

In conclusion, this study supports the concept that smoking asthma patients show different features than nonsmoking asthma patients, particularly a larger number of neutrophils in airway fluid. Mild emphysematous changes were found on HRCT in approximately one of five smokers, despite a relatively moderate smoking exposure, suggesting an increased susceptibility to cigarette smoke in these patients. Further studies should be done to explore these features and how they affect response to therapy, in order to suggest the most appropriate treatments for these patients.

ACKNOWLEDGMENT: We are grateful to Johanne Lepage for her help conducting this study; Serge Simard for his suggestions on statistical analysis; Philippe Prince for his help with induced-sputum analysis; and Michel Laviolette, François Malks, Yvon Cormier, and Lori Schubert for reviewing the manuscript.

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