Passive Smoking
Effects on Bronchial Asthma*

T. E. Dahms, Ph.D.; J. F. Bolin, M.D.; and R. G. Slavin, M.D.

Ten patients with bronchial asthma and ten control subjects were exposed to sidestream cigarette smoke (passive smoking) for one hour in an environmental chamber. All subjects showed the same increase in carboxyhemoglobin as a result of the exposure: 0.40 percent. The asthmatic group demonstrated a significant linear decrease in pulmonary function during this exposure. After one hour of smoke, FEV₁ decreased 21.4 percent, FEF25-75% decreased 19.2 percent, and FVC decreased 20.0 percent in the asthmatic patients. These alterations were readily reversible in all subjects when given inhalations of metaproterenol following the exposure. The control subjects showed no change in pulmonary function when exposed to identical conditions. These data show that nonsmokers with bronchial asthma are at risk when exposed to sidestream cigarette smoke in an environmental chamber.

The evidence regarding cigarette smoke exposure producing pulmonary changes leading to bronchospasm in asthmatic patients is only anecdotal. Speer¹ reported results of an investigation using a questionnaire given to allergic and nonallergic patients detailing their reactions to cigarette smoke. When exposed to passive smoking conditions, the allergic, nonsmoking subjects reported a greater incidence of eye irritation, nasal symptoms, cough, wheezing, sore throat, and hoarseness than did the nonallergic, nonsmoking subjects. The available data suggest an increased sensitivity of patients with bronchial asthma to cigarette smoke; however, there is currently no objective information to support the subjective data of Speer¹.

Passive smoking, the inhalation by nonsmokers of the combustion products of cigarettes from sidestream smoke and exhaled smoke, is a common form of indoor air pollution. Long-term passive exposure of both adults² and children³ to cigarette smoke can lead to a significant reduction in the function of small airways. However, if any group would be at immediate risk from cigarette exposures, it would be one whose members have an irritable airway. This report concerns the acute pulmonary responses of bronchial asthmatic patients and control subjects in a passive smoking environment. These experiments were carried out in an attempt to determine whether a factual basis exists for the anecdotal and subjective information reported by Speer¹ regarding bronchial asthmatic patients.

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METHODS

To determine more objectively the effects of passive smoking on persons who have a reactive respiratory tract, ten patients with bronchial asthma and ten control subjects were exposed to mechanically produced cigarette smoke in an environmental chamber. The control subjects were healthy, nonsmoking men and women 24 to 53 years old, who volunteered from the medical community. Five of the control subjects complained of general irritability when exposed to passive smoking environments. Nonsmoking asthmatic subjects, recruited from the St. Louis University Hospital Allergy Clinic, were men and women ranging in age from 18 to 26 years. Five of the asthmatic patients were included because they reported specific complaints when exposed to cigarette smoke; the remaining asthmatic patients were recruited at random. All subjects were fully informed, and the guidelines of informed consent were followed.

All asthmatic subjects had a previous medical history of bronchospasm and a positive methacholine challenge test. A positive methacholine test consisted of at least 20 percent fall in FEV₁ as a result of inhaling a nebulized solution of 25 mg/ml or less of methacholine. A graded methacholine challenge test⁴ was carried out at least one week before the smoke exposure on only the asthmatic subjects.

The general protocol consisted of an initial history and physical examination of the subjects to ensure that the subjects were asymptomatic. The asthmatic subjects continued taking their medication but refrained from using any bronchodilators for four hours before the experiment. Then the preexposure blood sample was drawn for carboxyhemoglobin (COHb) analysis. The subjects entered the chamber, and the control pulmonary function tests were performed after 15 minutes. The smoke generator was started, and at 15-minute intervals the pulmonary tests were repeated. Since all of the testing was carried out in the chamber, the subjects remained in the chamber for the entire 60 minutes of the exposure. After the final pulmonary function tests at 60 minutes, a second blood sample was collected for COHb analysis.

The environmental chamber used was 30 m³ in volume,
with precise humidity, temperature, air flow, and air turnover control enabling control over the exposure environment. Other conditions used were a temperature of 21 °C, relative humidity of 50 percent and an air turnover of once every 12 minutes. The smoke was produced from cigarettes (15 mg of tar and 0.15 mg of nicotine) smoked with a 30-ml puff volume at one cycle per minute to a butt length of 30 mm. The passive smoke concentration was estimated from the rate of production of carbon monoxide (CO) and particulates in combination with the room volume and the air turnover rate. The room levels of CO were confirmed by the increase in COHb of each of the subjects. Preexposure and postexposure venous blood samples were drawn, and the hemoglobin and CO content of the samples were precisely determined. All subjects averaged an increase of 0.40 percent COHb during the exposure, which, according to the model of Jones and Fagen showed that the environmental CO concentration averaged between 15 and 20 ppm over the 60-minute exposure. The particulate matter in the atmosphere of the chamber was probably less than what would be expected, owing to the precipitating action of the circulating fans and the refrigeration coils in the chamber. No measurement of particulate matter was made.

The asthmatic patients were given metaproterenol (Alupent) from an inhaler immediately following the postexposure blood sample and were removed from the chamber. Fifteen minutes later pulmonary function tests were repeated.

All pulmonary function tests were performed on a waterless spirometer (Jones-Pulmonor). Only three parameters were assessed: forced vital capacity, FVC; forced expiratory volume after 1 second, FEV1; and mean forced expiratory flow during the middle half of the FVC, FEF25-75%. At each measurement period three repetitions were carried out and the highest values were used in the analyses. A simple spirometric test was chosen to minimize the interference of the testing procedure with the potential physiologic changes due to the cigarette smoke. All of the patients had become thoroughly familiar with the apparatus during routine testing in the clinic, which reduced to a minimum problems with patient compliance and task learning.

All data were analyzed via analysis of variance, and significance for each parameter at any given time was determined using Tukey's s test. Levels of significance were determined as a result of smoke exposure by using a within-group design: asthmatic values during smoke exposure were compared with asthmatic control values (paired analysis).

**RESULTS**

The asthmatic subjects showed a highly significant decrease in pulmonary function throughout the exposure to the sidestream cigarette smoke (Table 1). The FVC decreased significantly after 15 minutes of exposure (P < 0.01), from 3,395 ml to 3,135 ml. After one hour of smoke exposure the FVC had decreased on an average of 680 ml, or 20.0 percent. The control subjects showed no change in FVC as a result of exposure to the same conditions. In the asthmatic patients the FEV1 fell throughout the exposure, but did not become statistically significant until 30 minutes. After 60 minutes FEV1 had fallen 520 ml (21.4 percent) in the asthmatic subjects, whereas the controls showed a slight but insignificant increase in FEV1 after 60 minutes of smoke exposure. All ten of the asthmatic patients had reductions in both FVC and FEV1. The FEF25-75% in the asthmatic group also decreased throughout the exposure to the sidestream cigarette smoke, but the decrease did not reach statistical significance until 30 minutes (P < 0.05). In the asthmatic group the FEF25-75% decreased from 1.95 L/sec before exposure to 1.61 L/sec (19.2 percent) after 60 minutes.

The decrease in FEF25-75% may have been due

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**Table 1—Group Mean Data of Pulmonary Response to Passive Smoking**

<table>
<thead>
<tr>
<th>Test</th>
<th>Duration of Passive Smoke Exposure</th>
<th>15 min After Bronchodilator</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
<td>15 min</td>
</tr>
<tr>
<td>FVC</td>
<td>Control group</td>
<td>4,490 (±291)</td>
</tr>
<tr>
<td></td>
<td>% Change</td>
<td>4.3</td>
</tr>
<tr>
<td></td>
<td>Asthmatic group</td>
<td>3,395 (±190)</td>
</tr>
<tr>
<td></td>
<td>% Change</td>
<td>-7.45 †</td>
</tr>
<tr>
<td>FEV1</td>
<td>Control group</td>
<td>3,625 (±222)</td>
</tr>
<tr>
<td></td>
<td>% Change</td>
<td>3.9</td>
</tr>
<tr>
<td></td>
<td>Asthmatic group</td>
<td>2,475 (±173)</td>
</tr>
<tr>
<td></td>
<td>% Change</td>
<td>-8.6</td>
</tr>
<tr>
<td>FEF25-75%</td>
<td>Control group</td>
<td>4.09 (±53)</td>
</tr>
<tr>
<td></td>
<td>% Change</td>
<td>0.5</td>
</tr>
<tr>
<td></td>
<td>Asthmatic group</td>
<td>1.95 (±24)</td>
</tr>
<tr>
<td></td>
<td>% Change</td>
<td>10.9</td>
</tr>
</tbody>
</table>

*Values given are ± SEM. All values in asthmatic group are significantly different from control values at all measurement periods (P < 0.01).
†Values significantly different from preexposure (P < 0.05).
‡Values significantly different from preexposure (P < 0.01).
in part to decreases in lung volume, since the FVC also fell. However, on an individual-by-individual basis, the changes in FEF25-75% did not correlate in all cases with a decrease in FVC. For example, the 60-minute exposure values of FVC in two of the asthmatic subjects fell 36 percent and 22 percent, but their respective FEF25-75% fell only 4 percent and 6 percent. However, the three largest responders in FEF25-75%, 44, and 25 percent, also had FVC decreases of 33, 23 and 24 percent respectively. Two of the subjects had greater percentage decreases in FEF25-75% than in FVC, the inverse of the other eight subjects. Therefore, not all subjects showed the same pattern of pulmonary responses to the smoke exposure.

The asthmatic subjects' preexposure pulmonary function values were considerably lower than those values of the control subjects (Table 2). The average values for the asthmatic subjects also were less than the predicted normal values for the measurements used in the study: FVC, 79.2 percent; FEV1, 73.7 percent; and FEF25-75%, 51.5 percent of predicted. This is in contrast to the control subjects, whose values all were within 93 to 104 percent of predicted values. Therefore, the decreases in pulmonary function in the asthmatic subjects as a result of the passive smoking presented further risk to already compromised respiratory system. One asthmatic patient had an audible wheeze at 60 minutes of exposure.

Following the exposure to the passive smoking conditions, the asthmatic patients were given meta-proterenol via an inhaler. Fifteen minutes later the pulmonary function tests were performed. Two of the asthmatic subjects improved with the bronchodilator but did not return to their preexposure status; however, the remaining asthmatic patients returned to baseline or above. The subjects who did not return to baseline had the greatest decreases in FEV1 and FVC and were among the highest responders in FEF25-75%. The group responses showing a return to baseline values are shown in Table 1.

All subjects, control and asthmatic, incurred the same subjective degree of eye and nasal irritation. Both the control and asthmatic groups increased their COHb concentrations to the same extent as a result of the exposure (Table 3). The control group's COHb increased 0.43 percent, from 0.62 percent to 1.05 percent (P < 0.01), and the asthmatic group increased 0.38 percent from 0.82 to 1.20 percent (P < 0.01). There was no statistical difference in the elevation in COHb between the groups, suggesting identical exposure for each group. There was also no relationship found between the slight differences in individual increments in COHb and their corresponding decrements in pulmonary function.

The methacholine challenge test results indicate that this group of asthmatic patients was moderately sensitive to methacholine. Five of the asthmatic subjects responded with a 20 percent decrease in FEV1 (threshold criterion) with the lowest dose of 0.075 mg/ml in the nebulizer; one responded at 0.15 mg/ml, two at 0.62 mg/ml, and two at 1.25 mg/ml. The dose required for confirmation of asthma is 25 mg/ml, a value considerably above that for anyone in this group of asthmatic patients. No significant relationships were found between methacholine sensitivity and pulmonary response, primarily because of the small size of the sample. Seven of the subjects show such a relationship, but the inclusion of the other three skewed the data and remove any significance.

**DISCUSSION**

The evidence from this investigation clearly demonstrates that passively encountered cigarette smoke produces an increase in airway resistance in patients

*Table 2—Subject Description and Baseline Pulmonary Function Values Before Exposure to Passive Smoking*

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Age Range, yr</th>
<th>VC Mean ± Pred</th>
<th>FEV1 Mean ± Pred</th>
<th>FEF25-75% Mean ± Pred</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control subjects</td>
<td>10</td>
<td>24-53</td>
<td>4,490 ± 291</td>
<td>3,625 ± 222</td>
<td>4.09 ± 0.05</td>
</tr>
<tr>
<td>Asthmatic patients</td>
<td>10</td>
<td>16-39</td>
<td>3,395 ± 190</td>
<td>2,475 ± 173</td>
<td>1.95 ± 0.24</td>
</tr>
</tbody>
</table>

*Values ± SEM.
†Value significantly different from controls at P<0.05.

*Table 3—Increases in Carboxyhemoglobin as a Result of Exposure to Sidestream Cigarette Smoke*

<table>
<thead>
<tr>
<th>Group</th>
<th>Preexposure % COHb at 60 min of Exposure</th>
<th>% Increase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control subjects</td>
<td>0.62% ± 0.08</td>
<td>1.06 ± 0.08</td>
</tr>
<tr>
<td>Asthmatic patients</td>
<td>0.82% ± 0.10</td>
<td>1.20 ± 0.09</td>
</tr>
</tbody>
</table>

*Values ± SEM.
†Values significantly different from preexposure values where P<0.01.
with bronchial asthma. This increase in resistance was demonstrated by a significant decrease in both FEV₁ and FEF25-75% after 30 minutes of exposure to the cigarette smoke. The decrease in pulmonary function was linear over the 50-minute exposure, reaching a total decrement of approximately 20 percent of control values in all parameters at 60 minutes. The identical conditions produced no measurable effects in control subjects.

In an attempt to explain these results, comparisons can only be made with the effects of active smoking, since so little information is available regarding acute physiologic responses to passive smoking. The difference between the two conditions might be one merely of degree, i.e., smoke concentration. Nadel and Comroe¹⁰ demonstrated that airway resistance increased immediately when healthy subjects smoked a single cigarette. This bronchoconstriction was thought to be due to a reflex initiated by the particulate matter in the smoke.¹⁰,¹¹ The increase in airway resistance seen in the asthmatic subjects in this study required 30 minutes of inhalation of the diluted sidestream smoke to produce significant decrements in the pulmonary parameters used to assess airway resistance. When a cigarette is burned under the conditions used in these experiments, the sidestream smoke will contain more than three times the particulate mass of the mainstream smoke. The mainstream smoke inhaled in active smoking is diluted in only the tidal volume before reaching the airways, whereas the sidestream smoke particles are diluted in the volume of the entire room. This results in a 10⁴-fold difference in the inhaled particulate concentration between active smoking and passive smoking. If the particulate matter were the stimulus for the responses seen in the asthmatic subjects, their airways would have to be considerably more sensitive to particulates than the controls.

The bronchoconstriction resulting from the active smoking of one cigarette in healthy nonsmokers is thought to be a reflex¹⁰,¹² mediated via particulates stimulating parasympathetic pathways. Bronchial asthmatic patients are characterized by hyperactivity of the bronchi to various stimuli resulting in increased airway resistance that is manifested in the extreme as paroxysmal and reversible wheezing and dyspnea. The specific mechanisms that can lead to bronchial asthma are unknown, but several factors can definitely cause a significant increase in airway resistance in asthmatic patients. Inhaled aerosols of histamine, acetylcholine, methacholine, and dust particles cause much greater bronchoconstriction in asthmatic patients than in normal subjects. Asthmatics with their obstructive type of ventilatory function have been found to have a larger than normal intrapulmonary deposition of inhaled particulates, and the range of sites of deposition is shifted proximally.¹³ Therefore, the asthmatic subjects probably responded to the passive smoke because they had an increased sensitivity of bronchial receptors and perhaps a greater number of particles deposited on the hypersensitive airways.

Although particulates have been implicated¹⁰,¹² as the primary stimulus, the gaseous phase cannot be completely ruled out as a possible causative agent in the response of the airways in the bronchial asthmatic patients to passive smoking.

The effects reported here were not influenced by the maximal inspiratory and expiratory maneuvers used in the testing procedure. The subjects, control and asthmatic groups, repeated the FVC maneuvers three times with a 15- to 30-second interval between maneuvers. If any of these influences had played a role, a definite order effect would have been seen in the FEV₁ and FEF25-75% values. No order effect was seen, suggesting that deep inspiration and expiration had no effect on the results of this investigation.

We were not able to exclude the possibility that these changes in pulmonary function were emotionally related to cigarette smoke. Horton et al¹⁴ have shown a high correlation between emotional responses in specific airway conductance and sensitivity to methacholine or histamine. The emotional response described by Horton et al¹⁴ was manifested immediately, whereas the subjects exposed to the sidestream cigarette smoke in the present study did not show a significant change in airway resistance until 30 minutes of exposure. Although an emotional component could have been present, increasing with duration of exposure, the portion of the response due to emotion cannot be determined. Also the range of methacholine sensitivity in the asthmatic patients in this study who specifically complained of cigarette smoke irritation was quite large, i.e., it was not the subjects most sensitive to the methacholine who felt particularly bothered by the smoke.

The exposure conditions were representative of moderate environments, and all the asthmatic subjects felt that they had been exposed to similar environmental conditions in their lives. However, many asthmatic patients avoid such situations. The atmospheric carbon monoxide concentration range of 15 to 20 ppm is within the range of hourly averages reported¹⁵,¹⁷ for taverns and nightclubs of 3 to 29 ppm. Some hourly averages for such locations occasionally reached 36 to 42 ppm. The air turnover in the environmental chamber used for these experiments is similar to that found in and recommended.
for various environments.18

Long-term exposure to environmental cigarette smoke results in changes in pulmonary function of nonsmokers suggestive of small airway disease.2 These effects, however, were measured after a minimum of 20 years of exposure of the subjects to a smokey environment. The passive smoking environment may pose a more immediate threat to persons with a reactive respiratory tract. In 1974 it was recommended that reactive persons in the population be studied because adverse effects of environmental tobacco smoke may occur at very low concentrations among atopic patients and persons who otherwise have a reactive respiratory tract.18 The results of this initial investigation indicate that patients with bronchial asthma do respond adversely when actively exposed to environmental cigarette smoke. Aronow18 recently reported that under conditions of acute exposure to smoke, some angina patients are also at additional risk of suffering anginal attacks. It is still to be determined to what extent these results can be generalized to the entire groups of people with these chronic diseases.

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