Impairment of Lung Mucociliary Clearance in Pigeon Fanciers

Amir Hasani, M.Sc.; Margaret Johnson, M.D.; Demetri Pavia, Ph.D.;† John Agnew, Ph.D.;* and Stewart Clarke, M.D.

Lung mucociliary clearance was measured in 15 pigeon fanciers. The study group was subdivided into two: a precipitin-positive group (n = 10; mean ± SEM age 45 ± 5 years) with circulating blood precipitins and a precipitin-negative group (n = 5; mean ± SEM age 40 ± 3 years) without. Clearance was measured using an objective, noninvasive radioaerosol technique. The data for both groups were compared with those of matched control groups of healthy subjects. The mean ± SEM area under the tracheobronchial retention curves (AUC) over the 6-h observation period was 237 ± 27 %h for the precipitin-positive group compared with 177 ± 16 %h for its control group (p = 0.02)—a high AUC value denoting slow clearance. That for the precipitin-negative group was 282 ± 34 %h compared with 150 ± 15 %h for its control group (p = 0.02). Our study illustrates in pigeon fanciers involvement of the conducting airways in that a major defense mechanism of the airways—namely, mucociliary clearance—is substantially compromised. The presence or absence of precipitins appears not to be related to the degree of mucociliary clearance impairment.

(Chest 1992; 102:887-91)

AD = alveolar deposition; AUC = area under the curve; EAA = extrinsic allergic alveolitis; TBC = tracheobronchial clearance; TLCO = total lung capacity; TLCO = total diffusing capacity for carbon monoxide

The human tracheobronchial tree is swept clean of any inhaled particles and endogenous debris by mucociliary clearance and cough. Mucociliary clearance is a normal physiologic function in health, with cough a reserve mechanism in lung disease assisting mucociliary clearance, which is often impaired. Inhalation of organic material derived from pigeons is known to provoke hypersensitivity reactions (extrinsic allergic alveolitis [EAA]) in the lungs of pigeon fanciers; circulating antibodies have been demonstrated in their serum. Pathologic studies of EAA suggest that inflammation is not confined to the alveoli but also involves the bronchi and smaller airways. Pigeon fanciers have a high prevalence of chronic bronchitis, large-airways involvement, and peripheral airways obstruction in addition to the well-recognized restrictive ventilatory defect. Boyd reported that 8.4 percent of the pigeon fanciers surveyed had chronic bronchitis as their only manifestation of pigeon-related symptomatology. The classic symptoms of affected pigeon fanciers are shortness of breath, cough, malaise, and bronchitis.

To our knowledge, there is no information regarding the efficiency of lung mucociliary clearance in pigeon fanciers and specifically whether this important host defense mechanism of the lung is in any way compromised. The purpose of the present study was to compare lung mucociliary clearance in pigeon fanciers with and without circulating precipitins with that of healthy subjects tested under the same conditions.

METHODS

Subjects

Fifteen pigeon fanciers (14 male and one female) attending a national meeting for pigeon racing volunteered to participate in the study; ten pigeon fanciers had specific precipitating antibodies to pigeon precipitins (precipitin-positive group) and five had no circulating precipitins (precipitin-negative group). For comparison purposes, the data for both groups were compared with those of two historical control groups of healthy subjects. These two control groups (ten and five subjects, respectively) were selected from our bank of control data on the basis of having similar physical characteristics, smoking habits, and alveolar deposition (AD) of inhaled radioaerosol as those of the two study groups but blind as to their tracheobronchial clearance (TBC). The method of assessment of TBC used for the controls was identical to that used for assessing TBC in the pigeon fanciers. The importance of matching as closely as possible for AD was to try to ensure that initial test particle distribution in the controls was closely similar to that in the pigeon fanciers.

The smoking habits for pigeon fanciers and control subjects in the precipitin-positive and precipitin-negative groups are summarized in Table 1.

Nine of the ten subjects in the precipitin-positive group had two or more of the following chest symptoms: cough, sputum, shortness of breath, and wheeze; only two of these subjects were receiving medication. One was taking inhaled salbutamol and the other was taking inhaled salbutamol, ipratropium bromide, and beclomethasone dipropionate. The last dose of medication was taken at least 2.5 h prior to the measurement of lung mucociliary clearance. In the precipitin-negative group, one subject reported shortness of breath and one other reported wheeze; none was taking medication. Informed consent was obtained from each subject prior to the commencement of the study, which was approved by the hospital's ethical practices subcommittee.

*From the Departments of Thoracic Medicine (Drs. Hasani, Johnson, Pavia, and Clarke) and Medical Physics (Dr. Agnew), Royal Free Hampstead NHS Trust and School of Medicine, London, England.
†Presently at Boehringer Ingelheim Ltd, Bracknell, England. Manuscript received October 21; revision accepted January 7. Reprint requests: Dr. Hasani, Department of Thoracic Medicine, Royal Free Hampstead NHS Trust, Pond Street, London NW3 2QG, England.
Table 1—Smoking Habits of Two Groups of Pigeon Fanciers with and without Circulating Precipitins and Their Respectively Healthy Control Groups

<table>
<thead>
<tr>
<th></th>
<th>Precipitin (+) Group</th>
<th>Precipitin (-) Group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pigeon Fanciers</td>
<td>Controls</td>
</tr>
<tr>
<td>No. of nonsmokers</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>No. of ex-smokers*</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>Tobacco consumption, pack-year</td>
<td>14±9†</td>
<td>9±7†</td>
</tr>
<tr>
<td>Tobacco consumption, pack-year</td>
<td>8</td>
<td>3</td>
</tr>
</tbody>
</table>

*Had given up cigarette smoking more than one year prior to study.
†Mean ± SEM.

Tracheobronchial Clearance

An objective, noninvasive radioaerosol technique, which has been described previously in detail,28 was used to measure TBC. Monodisperse polystyrene particles 5 μm in diameter, generated using a spinning disc generator,29 were firmly labeled with the gamma-emitting radionuclide technetium 99m (T1/2 = 6 h).29 The tracer particles were inhaled by the pigeon fanciers, under strictly controlled conditions, through the mouth while sitting in an upright position and wearing a nose clip. Single breaths of 0.45 L each were taken from approximately functional residual capacity level by each volunteer subject accompanied by an obligatory 3-s breath-holding pause to permit radioaerosol deposition by sedimentation in the small airways.30 The inspiratory flow rate was measured by a pneumotachograph and recorded on an ultraviolet recorder. The subjects were asked to gargle and drink some water to remove the remaining particles in the oropharynx or esophagus after inhaling the radioaerosol. The initial whole lung burden was measured immediately after inhalation using two collimated scintillation detectors; the degree of colimation was such that the field of view of the detectors included most of both lungs but virtually excluded the stomach. The two detectors were placed midway along the sternum axially opposite to each other and located anterior and posterior to the chest.31 Subsequently counts were made at half-hourly intervals for a total of 6 h with a final count at 24 h. All counts were corrected for radioactive background and physical decay of the radionuclide and expressed as a percentage of the initial count to adjust for unavoidable differences in the initial radioactive lung burden. The amount of radioaerosol remaining in the lung at 24 h was used to estimate "alveolar deposition," i.e., the proportion of the radioaerosol deposited in the noncollimated airways and thus not available for mucus clearance.32 Subtracting the AD from the whole lung clearance curve yielded a TBC curve.33 An index of the individual efficiency of TBC was derived for each subject by measuring the area under the curve between 0 and 6 h (AUC [0-6]) using the trapezoidal rule.32 (A small AUC represents a fast TBC.)

During the 6-h observation period, all coughs were recorded and any sputum produced was collected in separate containers and weighed; its radioactive content was expressed as a percentage of the initial tracheobronchial deposition.3 At the end of the observation period, the pigeon fanciers were instructed to cough (three double coughs per minute for 5 min) and the radioactive content of the sputum samples, if any, was ascertained.

The smokers in both study groups did not smoke for at least 1 h before and throughout the 6-h observation period.

Pulmonary Function

The pulmonary function of each subject was assessed prior to the inhalation of the radioaerosol. Forced expiratory volume in 1 s (FEV1), forced vital capacity (FVC), and maximum midexpiratory flow rate between 25 and 75 percent of FVC (FEF25-75) were measured using a dry bellows spirometer. The flow rates at 25 and 50 percent of FVC (Vmax25 and Vmax50) were measured from maximal expiratory flow-volume curves using a piston-cylinder type spirometer and an X-Y plotter. The highest of three technically acceptable measurements was recorded for each pulmonary function index. Furthermore, it was possible for nine of the ten subjects with chest symptoms and circulating precipitins to attend the pulmonary function laboratory for measurement of their total lung capacity (TLC) and total diffusing capacity for carbon monoxide (DLco) using the single breath method. Predicted values were obtained based on the subject's sex, age, and height.18,19

Statistical Analysis

Statistical analysis was undertaken using the two-sample Wilcoxon.

Table 2—Mean ± SEM Physical Characteristics and Pulmonary Function Indices of Two Groups of Pigeon Fanciers with and without Circulating Precipitins and Their Respectively Healthy Control Groups

<table>
<thead>
<tr>
<th></th>
<th>Precipitin (+) Group</th>
<th>Precipitin (-) Group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pigeon Fanciers</td>
<td>Controls</td>
</tr>
<tr>
<td>No. (sex)</td>
<td>10(M)/1(F)</td>
<td>10(M)/1(F)</td>
</tr>
<tr>
<td>Age, yrs</td>
<td>45±5</td>
<td>40±3</td>
</tr>
<tr>
<td>Alveolar deposition, %</td>
<td>39±5</td>
<td>45±3</td>
</tr>
<tr>
<td>% pred FEV1</td>
<td>86±7</td>
<td>113±3</td>
</tr>
<tr>
<td>% pred FVC</td>
<td>97±7</td>
<td>117±4</td>
</tr>
<tr>
<td>% pred FEF25-75</td>
<td>71±11</td>
<td>101±10</td>
</tr>
<tr>
<td>% pred Vmax50</td>
<td>63±10</td>
<td>...</td>
</tr>
<tr>
<td>% pred Vmax25</td>
<td>45±8</td>
<td>...</td>
</tr>
<tr>
<td>% pred TLC</td>
<td>106±4</td>
<td>...</td>
</tr>
<tr>
<td>% pred TLco</td>
<td>84±12</td>
<td>...</td>
</tr>
</tbody>
</table>

*Measurements were not available.
test for unpaired data and the Kruskal-Wallis one-way analysis of variance. The level of significance was taken at \( p<0.05 \).

**RESULTS**

The data from the two groups of pigeon fanciers were analyzed separately with their respective control groups and in combination.

The physical characteristics for the pigeon fanciers and control groups together with their pulmonary function indices and AD are shown in Table 2. The table shows that subjects in the precipitin-positive group had a tendency toward reduced pulmonary function indices compared with their controls, whereas subjects in the precipitin-negative group, without symptoms, had a similar lung function compared with their controls.

The mean AD values were similar for the pigeon fanciers and healthy subjects in the precipitin-positive group; in the precipitin-negative group, the mean AD values were virtually identical (Table 2).

The AUC (0-6) was significantly larger for the pigeon fanciers in both the precipitin-positive group (\( p = 0.02 \)) and the precipitin-negative group (\( p = 0.02 \)) compared with their respective healthy control groups (Fig 1). The mean \( \pm \) SEM AUC (0-6) values for the pigeon fanciers in the precipitin-positive and precipitin-negative groups were 257 ± 27 vs 282 ± 34 % h, respectively (\( p>0.1 \)).

Figure 2 gives the mean \( \pm \) SEM tracheobronchial retention curves for the whole study group of 15 pigeon fanciers vs the 15 matched, healthy subjects used as controls. Tracheobronchial clearance for the pigeon fanciers was significantly reduced (\( p<0.01 \)) compared with the control group.

Mean \( \pm \) SEM AUC (0-6) was 263 ± 24 vs 170 ± 10 % h (\( p = 0.02 \)) for the five nonsmoking pigeon fanciers compared with their respective controls. Furthermore, the mean \( \pm \) SEM AUC (0-6) was 323 ± 40 vs 169 ± 39 % h (\( p>0.10 \)) for the four currently smoking pigeon fanciers compared with their respective controls. Within the pigeon fanciers group, there was no significant difference in AUC (0-6) between the smoking categories.

Nine of the 15 pigeon fanciers (six in the precipitin-positive group) coughed during the 6-h observation period. The range of the number of coughs per subject was 2 to 21. Of these nine subjects, five (four in the precipitin-positive group) produced sputum (range of wet weight, 0.2 to 1.9 g) containing tracheobronchial radioactive deposition in the range of 0.3 to 7.8 percent.

At the end of the 6-h observation period, only two pigeon fanciers, both in the precipitin-positive group, produced sputum under instructed coughing (wet weight, 0.7 and 0.9 g) containing percent tracheobronchial radioactive deposition of 0.1 and 1.2 percent, respectively. The mean \( \pm \) SEM tracheobronchial retention values for the 15 pigeon fanciers before and after instructed coughing at 6 h were similar (20 ± 4 vs 21 ± 4).

**DISCUSSION**

Although both FEV\(_1\) and FVC for the pigeon fanciers in the precipitin-positive group were within the "normal" range, they were, nevertheless, significantly reduced compared with the matched control group. This observation together with the reduced...
flow rates for the tests of small airway function (FEF25-
75, Vmax50 and Vmax25) may well reflect the early
stages of onset of chronic bronchitis, which has been
reported to be present in a proportion of pigeon
fanciers. Since both TLC and total diffusing capacity
were within the normal range for the pigeon fanciers
in the precipitin-positive group, it is unlikely that
restrictive defect, a well-known phenomenon in
pigeon fanciers, was present in our population.

Pigeon fanciers in the precipitin-negative group,
with minimal chest symptoms, demonstrated normal
results of lung function tests with the exception of
Vmax25, which was on average only 54 percent of
predicted. The clearance of radioaerosol from the
lungs depends on its initial site of deposition within
the airways. In general, radioaerosol deposited prox-
imally will be cleared more rapidly from the lungs
than radioaerosol deposited peripherally within the
lungs. In our study, we were able to ensure, as far as
possible, that the radioaerosol deposition within the
lungs (ie, AD) of the pigeon fanciers was similar to
that of the healthy control subjects in both precipitin-
positive and precipitin-negative groups. It is not fea-
sible to study a control group prospectively since it is
impossible to ensure similar radioaerosol deposition
within the lungs of the healthy subjects and the pigeon
fanciers. Historical controls were therefore selected
from a group who inhaled radioaerosol at different
flow rates to achieve a range of ADs.

Tracheobronchial clearance of the pigeon fanciers
in both groups was found to be significantly reduced
compared with their respective healthy control groups
(Fig 1). This finding indicates that the presence or
absence of circulating precipitins is not related to
defective mucociliary clearance. This finding in our
study group would also suggest that level of exposure
is immaterial to the degree of impairment in TBC.
Taking all pigeon fanciers as a whole group (Fig 2),
similar retardation was seen in TBC at a higher level
of significance because of the increased number of
subjects.

It is unlikely that cigarette smoking confounded
the interpretation of the observed data since TBC in the
nonsmoking pigeon fanciers was slower (significantly)
than in the corresponding control group. It is of interest
that the average retardation in TBC in the currently
smoking pigeon fanciers compared with their control
subjects was greater in magnitude than in the non-
smoking group (154 vs 93 %h). Although the number
of subjects in each group is low, it is possible that
smoking and exposure to pigeons may have a cumula-
tive adverse effect on TBC. The apparent lack of a
difference in TBC between smoking groups within the
pigeon fanciers can be attributed to differences in
physical characteristics and AD (eg, AD for the
nonsmoker was 42 ± 6 percent vs 33 ± 5 percent for
the smokers).

Cough appears to have played a small part in the
overall TBC, with only five pigeon fanciers producing
sputum during the 6-h observation period. This finding
together with any help in TBC due to unproductive
coughing would result in an underestimate of the
degree of reported impairment in lung mucociliary
clearance. The lack of any significant enhancement in
TBC at 6 h following instructed coughing would
suggest that the undue retention of the radioaerosol
was beyond the reach of productive coughing (ie,
probably beyond the seventh generation on Weibel's
model of the human lung and/or due to lack of
appropriate hypersecretion that is necessary for pro-
ductive coughing). It is of interest that the degree of
lung mucociliary clearance impairment in pigeon
fanciers within the precipitin-negative group was com-
parable to that seen for those subjects in the precipitin-
positive group with reduced lung function and in-
creased symptomatology. This is consistent with the
reported apparent lack of relationship between degree
of impairment of lung mucociliary clearance and
pulmonary function indices in patients with chronic
bronchitis.

Our study has demonstrated that lung mucociliary
clearance is compromised in pigeon fanciers. This is
further evidence of involvement of the large airways
in these groups of subjects. Any reduction of lung
mucociliary clearance will tend to increase the resi-
dence time of any inhaled antigen. Inhaled antigen
has been shown to result in reduced lung mucociliary
clearance and undue retention of lung secretions has
been reported to result in atelectasis, thereby
giving rise to an increased incidence of chest infec-
tions.

Avian precipitins have been shown to have a role,
as a noninvasive test, in the diagnosis of bird breder's
disease. Our study using an objective, noninvasive
technique has demonstrated that lung mucociliary
clearance is compromised in pigeon fanciers irrespec-
tive of the presence or absence of avian precipitins.
Our data, albeit on a small number of subjects, appear
to demonstrate that mucociliary clearance may have,
at best, a limited relationship to immune activation in
pigeon fanciers. The detection of an abnormal clear-
ance in pigeon fanciers with absence of avian precipi-
tins may be akin to the observation by Lourenco and
associates of abnormal mucociliary transport in
asymptomatic smokers. Smokers who develop chronic
bronchitis, where chest symptoms are present, are
known to have impaired mucociliary clearance. In
such cases, abnormal mucus transport may be an early
indicator of the disease process. Delayed clearance
may represent one aspect of a vicious circle with
prolonged retention at airway sites of inhaled antigen
itself promoting a further decline in the efficacy of

Lung Mucociliary Clearance in Pigeon Fanciers (Hasani et al)
mucociliary mechanism. This, in turn, could cause undue retention of lung secretions and thereby an increased incidence of chest infections.33

The clearance deficit demonstrated in this study provides further evidence that pigeon fanciers suffer lung abnormalities involving the conducting airways.

REFERENCES

5 Boyd G. Pulmonary function changes in pigeon fancier's lung. Respir Med 1990; 84:5-7
12 Few JD, Short MD, Thomson ML. Preparation of Tc-99m labelled particles for aerosol studies. Radiochem Radioanal Lett 1970; 5:275-77
14 Thomson ML, Pavia D. Long-term tobacco smoking and mucociliary clearance. Arch Environ Health 1973; 24:66-9
33 Pavia D. Acute respiratory infection and mucociliary clearance. Eur J Respir Dis 1987; 71:219-26