Peripheral pooling of bronchographic contrast material: evidence of its relationship to smoking and emphysema

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Musk, A. W., Gandevia, B., and Palmer, F. J. (1978). Thorax, 33, 193–200. Peripheral pooling of bronchographic contrast material: evidence of its relationship to smoking and emphysema. Sixty-six subjects, mainly derived from various occupational groups and one-third of whom admitted to dyspnoea on exertion, have been grouped according to the appearance of their peripheral airways at bronchography with oily propyliodone. Eleven subjects showed marked peripheral pooling of radiographic contrast material, 22 showed mild or moderate pooling, and in 33 peripheral pools were absent. Pooling was not seen in non-smoking subjects. In the group of subjects without pooling, pulmonary function in non-smokers and subjects with a history of smoking was similar. Subjects with marked pooling had a significantly lower pulmonary diffusing capacity (transfer factor) and evidence of loss of pulmonary elastic recoil when compared with subjects with absent peripheral pooling. These results indicate that bronchographic peripheral pooling is associated with the physiological changes of panacinar pulmonary emphysema and suggest that a causal relationship may exist between the organic bronchiolar lesion of pooling and the peripheral parenchymal lesion of panacinar emphysema.

Peripheral accumulations of various radiographic contrast materials up to 5 mm or so in diameter have been described in antemortem and postmortem bronchograms for several decades. They have usually been described as 'peripheral pools' (Simon and Galbraith, 1953) if smooth-walled and circular, and as 'spiders' (Reid, 1955; Freimanis and Molnar, 1960), or floral forms (Simon, 1958; Duinker and Huizinga, 1962) if irregular in outline. Their pathological basis has variously been ascribed to chronic bronchitis (Christopherson, 1933; Reid and Simon, 1959; Duinker and Huizinga, 1962; Gregg and Trapnell, 1969), centrilobular emphysema (Simon and Galbraith, 1953; Leopold and Seal, 1961; Leopold and Gough, 1963; Duinker and Huizinger, 1962; Nakamura et al., 1969; Heard, 1969; Blumenthal and Greenberg, 1972; Gamsu and Nadel, 1973; Thurlbeck, 1976) or bronchiolectasis (obliterative or otherwise) (Reid, 1955; Wisoff, 1958; Simonsson, 1965). In postmortem bronchograms Reid (1955) and Heard (1969) have shown radio-opaque material pooled in dilated bronchioles whose normal diameter is less than 1 mm. Bronchioles distal to a 'pool' were shown by Reid (1955) to be obliterated, but some filling of terminal bronchioles beyond the dilated area was seen when the radiographic appearance was of 'spiders'. The bronchographic appearance of the affected lung in McLeod's syndrome (Reid and Simon, 1962) is identical. In spite of interest in the radiographic and pathological characteristics of pools and spiders there has been no previous investigation of their functional correlations.

Subjects

The subjects studied (Table 1) reflect the occupational interests of this unit. Two small but complete occupational groups (painters and welders) were asked to accept bronchoscopy as an addition to comprehensive lung function tests which were being performed on all employees because of a suspected respiratory hazard. In an attempt to assess the prevalence of peripheral pools in subjects with no known occupational
hazard, volunteers were sought from a local penitentiary. They gave informed consent and were accepted for the study if they denied current or previous chest disease when asked if they had ever had 'chest trouble'; these 'control' subjects were deliberately not selected on the basis of 'normality'. The remainder of the series, selected in retrospect, comprised patients in the care of the unit in whom both comprehensive lung function tests and bronchography were considered by the physician to be appropriate to their conventional clinical investigation. They had asthmatic or bronchitic symptoms, with some reason—such as haemoptysis or suspected localised bronchial narrowing or dilatation—for bronchography. Patients with specific or localised disorders, such as carcinoma, tuberculosis, or bronchiectasis, were not included. The usual reasons for comprehensive lung function studies, and especially lung mechanics, were the detailed assessment of disability in potential compensation claims referred for this reason and the assessment of the relative contributions of airway and parenchymal disorders where this affected decisions on therapy. Although the series is heterogeneous in origin, the method of selection does not affect the validity of a comparison of physiological findings between groups defined solely on the basis of a particular bronchographic feature, especially as peripheral pools were not found to predominate in those included on account of occupational history, clinical features, or penal servitude.

As indicated by the functional data, the series comprises mostly subjects with evidence of mild or negligible respiratory disease.

### Methods

### Symptoms

Cough and sputum were considered present if a subject admitted to cough or sputum production on most days for as many as three months each year. A subject unable to keep up with others of his own age on hills and stairs at an ordinary pace, or stating that he became short of breath on exertion more readily than others of his own age, was accepted as having 'dyspnoea'. Subjects were also asked if they had ever had asthma. 'Smokers' were those currently smoking cigarettes. 'Ex-smokers' had ceased smoking more than three months before the study. 'Non-smokers' had never regularly smoked cigarettes. No subject smoked only pipe or cigars.

### Physical Signs

Discontinuous crackling sounds heard with a stethoscope on deep inspiration were classified as 'crackles', and 'wheeze's were recorded if a continuous musical note was heard during expiration. A requested cough under observation was graded as loose (productive) or dry by its sound (Hall and Gandevia, 1971).

### Respiratory Function Tests

Forced expiratory volume in 1 second (FEV₁) was recorded using a water-filled spirometer (W. E. Collins) or an integrated flow device (Virgulto and Bouhuys, 1973). These instruments were calibrated to give comparable results. Values were corrected to BTPS.

Single-breath carbon monoxide diffusing capacity (transfer factor Dlco) (Ogilvie et al., 1957; Cotes, 1968) and vital capacity (VC) were measured using a Resparameter Mark IV (P. K. Morgan). Washout volume was 600 ml, the volume of gas collected for sampling 700 ml, and breathing holding time 10 seconds. Inspired gas consisted of CO 0.4%, O₂ 21%, He 5%, and balance N₂. Gas analysis was by gas chromatography.

Total lung capacity (TLC) was measured in a volume-displacement body plethysmograph (Emerson) by the method of Mead (1960). Maximum expiratory flow volume (MEFV) curves were recorded in the body plethysmograph using a Fleisch pneumotachograph No. 4 and box volume. Maximum expiratory flow at 50% TLC (Vmax 50% TLC) was measured from the curves. Static deflation volume-transpulmonary pressure curves were recorded using plethysmographic volume according to the technique of Milic-Emili et al. (1964a, b) during interrupted expiration from TLC. Transpulmonary pressure was measured on a Statham differential strain gauge (PM 131 TC). Transpulmonary pressure at TLC (Pstat. at TLC) and transpulmonary pressure (relaxed) at TLC (Pstat. at TLC (relaxed)) (Colebatch et al., 1973) were taken as the mean of the three highest...

### Table 1 Bronchographic appearance and source of subjects

<table>
<thead>
<tr>
<th>Subjects</th>
<th>Pooling</th>
<th>Absent</th>
<th>Minimal/moderate</th>
<th>Marked</th>
</tr>
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<tbody>
<tr>
<td>Control</td>
<td></td>
<td>17</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td>Painters</td>
<td></td>
<td>4</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Welders</td>
<td></td>
<td>5</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Detergent enzyme workers</td>
<td></td>
<td>4</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Cotton workers</td>
<td></td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Exposed to chlorine</td>
<td></td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Hospital inpatients (no occupational hazard)</td>
<td></td>
<td>2</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>33</td>
<td>22</td>
<td>11</td>
</tr>
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</table>
measures in five separate interrupted deflation manoeuvres. Static deflation compliance (Cv stat) was taken as the slope of the volume-pressure curve over the litre above functional residual capacity. Lung volume at transpulmonary pressure of 6 cm H2O (V5 6 cm H2O) was read from the curve. The conductance of the airways upstream from the flow-limiting segment (Gs) and critical transmural pressure (Ptm) were calculated from maximum expiratory flow static recoil pressure curves over 30 to 70% of vital capacity (Leaver et al., 1973).

Closing capacity (C closing) was measured using a single-breath oxygen test (Anthonisen et al., 1969–70).

Total pulmonary resistance (Rt) was measured by the method of Mead and Whittenberger, (1952–53).

BRONCHOGRAMS

Except where the purpose of the investigation required otherwise, unilateral bronchograms were performed. The nose, pharynx, and larynx were anaesthetised topically with xylocaine 4%, and a catheter was introduced into the right main bronchus during x-ray screening. With the subject lying on his right side so as to fill the right upper lobe as selectively as possible, 10–15 ml of oily propyliodone, which is superior to aqueous propyliodone for filling the peripheral bronchial tree, were injected. The upper lobe was chosen to minimise difficulties of interpretation due to chronic bronchitic changes in the lower lobes or to inadequate peripheral filling due to sputum retention (Ogilvie, 1975). Anterior-posterior (inspiration and expiration), right lateral, and right oblique films were taken over a period of 1–2 minutes, starting as soon as filling of the peripheral airways was seen to have occurred (within two to three minutes of completing the injection). Postural drainage was instituted under supervision at the end of the study. No subject with moderate impairment of lung function was studied as an outpatient, and no adverse symptoms resulted from the investigation. One subject developed mild wheezing during bronchography, which responded to a bronchodilator aerosol. Coughing during the procedure was uncommon once satisfactory local anaesthesia had been achieved. There was no association between the occurrence of coughing and the presence of peripheral pooling. The predominant effect of coughing was to clear the airways of contrast material. All films included in the study showed adequate filling of peripheral airways.

At the conclusion of the study an agreed grading of the severity of peripheral pooling was made by a panel of three observers1, without knowledge of the clinical, functional, or occupational histories, as ‘marked’ (Fig. 1), ‘moderate’, ‘minimal’ (Fig. 2), or ‘absent’.

Preliminary analysis of the results showed the ‘minimal’ and ‘moderate’ groups to be indistinguishable by clinical or functional criteria, and they were therefore combined.

Peripheral dye accumulations were further classified according to their resemblance to ‘pools’ or ‘spiders’. At a later reading the bronchographic signs of chronic bronchitis in the larger bronchi of the right lung were noted, the relevant features sought being mucous diverticula, irregularity of the bronchial walls and lumina, and evidence of excess mucus secretion (Gregg and Trapnell, 1969; Ogilvie, 1975).

STATISTICAL METHODS

Age was related to the presence of peripheral pooling (Table 2). Because the age differences between the groups could account for differences in pulmonary function, adjusted mean values for the bronchographically defined groups were deter-

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Table 2  Bronchographic appearance, age, and height

<table>
<thead>
<tr>
<th>Pooling</th>
<th>Absent</th>
<th>Minimal/ moderate</th>
<th>Marked</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of subjects</td>
<td>33</td>
<td>22</td>
<td>11</td>
</tr>
<tr>
<td>Mean age (years ±1 SD)</td>
<td>40·2 ± 8·5</td>
<td>46·4 ± 6·6*</td>
<td>54·2 ± 9·1**</td>
</tr>
<tr>
<td>Mean height (metres ±1 SD)</td>
<td>1·71 ± 0·08</td>
<td>1·75 ± 0·05</td>
<td>1·70 ± 0·06</td>
</tr>
</tbody>
</table>

Statistical significance of differences from group with absent pooling (Student's t test) *P < 0.05, **P < 0.01.

Results

Within the group of subjects without pooling, the measurements of pulmonary function did not differ significantly between cigarette smoking categories. The pulmonary function results of non-smokers was therefore combined with those of ex-smokers and current smokers for comparison with the subjects with marked and mild/moderate pooling.

The prevalence of clinical abnormality was higher in subjects with abnormal bronchograms (Table 3). No peripheral pooling was found in the bronchograms of non-smokers. Crackles and a loose cough were significantly more frequent in subjects with pools than in those without. Smoking was significantly related to the presence of cough and sputum; only one non-smoker admitted to cough and sputum, and only 10 smokers denied cough and sputum (P < 0.001). In this series, no association was found between peripheral pooling and the bronchographic signs of chronic bronchitis in larger, more central bronchi.

Table 3  Bronchographic appearance and clinical features

<table>
<thead>
<tr>
<th>Pooling</th>
<th>Absent</th>
<th>Minimal/ moderate</th>
<th>Marked</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of subjects</td>
<td>33</td>
<td>22</td>
<td>11</td>
</tr>
<tr>
<td>Smoking history</td>
<td>Smokers</td>
<td>Ex-smokers</td>
<td>Non-smokers</td>
</tr>
<tr>
<td>Cough and sputum</td>
<td>17 (51-5)</td>
<td>15 (68-2)</td>
<td>9 (81-8)</td>
</tr>
<tr>
<td>Dyspnnoea on exertion</td>
<td>7 (21-2)</td>
<td>8 (36-3)</td>
<td>5 (45-3)</td>
</tr>
<tr>
<td>Past history 'asthma'</td>
<td>7 (21-2)</td>
<td>5 (22-6)</td>
<td>2 (18-2)</td>
</tr>
<tr>
<td>Physical chest signs</td>
<td>Crackle**</td>
<td>Wheezes</td>
<td>Loose cough*</td>
</tr>
<tr>
<td>Bronchographic signs of chronic bronchitis†</td>
<td>8 (24-2)</td>
<td>13 (39-3)</td>
<td>10 (6)</td>
</tr>
</tbody>
</table>

Figures in parentheses are % column totals.
Statistical significance of differences between bronchographic groups (x² analysis) *P < 0.05, **P < 0.01.
†Mucous diverticula, irregularity of bronchial walls and lumina, excessive mucus secretion in airways.
There were significant changes, not explicable in terms of age differences, in the lung function of subjects with peripheral pooling of bronchographic material (Tables 4 and 5); lung function in subjects with mild or moderate pooling was intermediate between those with absent pooling and those with marked pooling. In the presence of peripheral pooling, forced expiratory flow (as reflected by FEV$_1$ and FEV$_1$/VC) was decreased with preservation of vital capacity, closing capacity was raised, lung volume at transpulmonary pressure 6 cm H$_2$O was increased with lower maximum transpulmonary pressures and increased pulmonary compliance, and pulmonary diffusing capacity was reduced. Figure 3 shows the mean static deflation volume-pressure curves for the three groups, together with the mean curves for 10 normal subjects (mean FEV$_1$, 3.7 l) and 10 subjects with exertional dyspnoea due to pulmonary emphysema (mean FEV$_1$, 1.3 l) published by Colebatch et al. (1973). The changes found in subjects with peripheral pooling were in the direction of those found in structural panacinar pulmonary emphysema—loss of pulmonary elastic recoil and diminished pulmonary diffusing capacity but

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negligible changes in pulmonary resistance or the relationship between maximum expiratory flow and transpulmonary pressure.

Bronchographic differentiation of pools and spiders proved uninformative in that no significant differences emerged between these two groups in terms of clinical or functional criteria. Both appearances were found with equal frequency in all grades of severity and in accordance with the experience of others (Reid, 1955; Freimanis and Molnar, 1960); one-third of the cases could not be classified as showing predominantly one or the other. There was no suggestion that earlier films differed from later films in the proportions of pools and spiders. Reid (1955) suggests a different pathological explanation of these two radiological entities.

Discussion

It was not considered reasonable in this study to assess the repeatability of the bronchographic appearance of pooling by carrying out a second procedure on any of the subjects. We had to accept the evidence of others (Reid, 1967) that pools represent organic bronchiolar lesions although we recognise that technique may have led to some imprecision in the grading of bronchiograms. Similary, it was not the aim of this study to investigate observer variation in the recognition of pooling. It was our impression that the three observers had little disagreement in the grading of the radiographs.

In panacinar pulmonary emphysema the fragmentation of the fibre network of the lung (Wright, 1961) is reflected in a decrease in pulmonary elastic recoil (Colebatch et al., 1973). Alveolar septa are lost and the vascular bed is destroyed (Reid and Heard, 1963), resulting in a decrease in pulmonary diffusing capacity (Bates, 1958; Bedell and Ostiguy, 1967). The demonstration of these functional changes in subjects with peripheral pools indicates that the bronchographic changes correlate with (panacinar) emphysema.

Cigarette smoking in this and other studies (Auerbach et al., 1963; Thurlbeck, 1963; Anderson et al., 1964) is common to the abnormalities demonstrated clinically, physiologically, and radiographically despite the fact that only one-third of our subjects admitted to dyspnoea on exertion. It appears that pools are not as closely related to disability as to bronchitis clinically and emphysema physiologically. Other studies (Park et al., 1969; Colebatch et al., 1973) in fact suggest that emphysema is not necessarily accompanied by disability, which commonly requires an additional component of bronchial disease.

The absence of a correlation between peripheral pools and the bronchographic features of chronic bronchitis in central airways may be a function of our choice of the right upper lobe for bronchographic assessment (Ogilvie, 1975) and the relatively mild disability in the present series of subjects: the greater the involvement of proximal airways, the more likely it is that respiratory disability will be manifest (Park et al., 1969). Alternatively, it may be that there is not necessarily a close association between the central and the peripheral consequences of cigarette smoking that is, between pools and the other generally accepted bronchographic criteria of chronic bronchitis.

The pathological evidence of Reid (1955) indicates that pooling results from bronchiolitis obliterans, and an identical bronchographic appearance is seen in the affected lung of unilateral emphysema in McLeod's syndrome (Reid and Simon, 1962). The association that we have shown between pooling and functional changes of panacinar emphysema supports a causal relationship between bronchiolitis and destruction of the parenchyma of the lung beyond the bronchiolar abnormality. In the adult subjects we have studied it appears that the pulmonary overinflation we have shown, which is typical of pulmonary emphysema, is due to collateral ventilation of air spaces distal to obliterated bronchioles. The observation that overinflation is not usually seen as a result of bronchiolitis in the developing lung of McLeod's syndrome is presumably due to arrested growth of the affected lung. Our results are compatible with those of Ogilvie (1975), who showed that patients with more frequent pooling have a more rapid rate of clinical deterioration. These studies underline the importance of disease in the small airways in the likely pathogenesis and progression of chronic obstructive lung diseases, a fact for which there is already considerable epidemiological evidence.

We are most grateful to Professor Margaret Turner-Warwick and Professor Bryan Williams for their assistance in grading the bronchographic appearances, and to Professor H. J. H. Colebatch and Dr. Geoffrey Field for advice in the preparation of this report and for their contribution to the laboratory investigation. Our thanks are due also to Dr. R. Williams for performing some of the bronchograms and to Dr. V. Kalyanasundaram, Mr. P. Owen, Mrs. R. Tester, and Mrs. Elizabeth Khoo for technical and clerical assistance.

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