

CHRONIC OBSTRUCTIVE LUNG DISEASE (COLD): A COMPARISON BETWEEN MEN AND WOMEN*

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SYNOPSIS

The characteristics of obstructive lung disease in women have not been adequately clarified, differing results having been reported by various workers. A prospective study of obstructive lung disease in 83 patients (70 men and 13 women) with a comparative analysis of the disease in men and women was therefore carried out.

Strikingly similar findings were recorded for both sexes with respect to age of onset of cough and dyspnoea, prevalence of asthma, recurrent chest infections, oedema and also on physical, haematological and electrocardiographic examination. However, a significantly greater number of women had 'pure' widespread emphysema. This was not related to smoking habits. It is probable that a genetic factor was involved.

Earlier studies (Mitchell and Filley, 1964; Burrows *et al.*, 1965) have shown that COLD is associated with a long history of cigarette smoking and a marked male predominance. As smoking is not as prevalent in women as in the men and as cigarette consumption in women smokers is usually lower, a study of COLD in women might help to uncover other aetiological factors involved in the pathogenesis of COLD in Singapore. The characteristics of obstructive lung disease in women have not been fully clarified and differing results have been reported by various workers. Burrows *et al.* (1965) observed that women frequently had a family history of chronic respiratory disease, were younger, smoked less and tended to have less of an 'inflammatory' or 'bronchitic' component than did the men. Gaensler and Lindgren (1959) also noted that women seemed to be less severely affected and suffered from a more slowly progressive form of the disease than the men. Karon *et al.* (1960), however, found that women had a much higher prevalence of infection and/or 'asthma' than the men and Coates (1968) has observed that women frequently showed progressive clinical deterioration with termination in cor pulmonale.

In view of these controversial findings, it seemed appropriate to carry out a prospective study of obstructive lung disease with a comparative analysis of the disease in men and women

so as to characterize if possible the clinical profile in women and also to observe if any differences existed between the men and women.

MATERIALS AND METHODS

Only patients who fulfilled all the following criteria were selected for study:

1. A forced expiratory volume in one second (FEV₁) of less than 60 per cent of the forced vital capacity (FVC) after inhalation of isoprenaline aerosol.
2. Absence of any 'specific' aetiology (e.g. pneumoconiosis, far-advanced pulmonary tuberculosis) for the pulmonary disability.
3. Absence of any serious illness other than COLD at the time of inclusion in the study.

A total of 108 patients with COLD were seen during a 2½-year period of study, extending from November 1966 to May 1969. However, 25 patients were excluded because they did not fulfil all the above-mentioned criteria, or who were too ill or uncooperative to be adequately evaluated.

In addition to a routine clinical history, a standard questionnaire based on the Medical Research Council's Questionnaire on Respiratory Symptoms (1960) was employed.

All patients were examined by the author using a standard technique.

A standard 12-lead electrocardiogram plus V₄R was taken in all instances. Right ventricular hypertrophy (RVH) was assessed using the grading system of Goodwin and Abdin (1959).

Posterior-anterior and left lateral chest roentgenograms were done in all instances. The criteria of Simon (1964) were used for the diagnosis of

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'widespread' or 'roentgenologic' emphysema. Bronchography was carried out in consenting fit patients because earlier work (Da Costa, 1969) had demonstrated that the morbid anatomy of the bronchial tree in COLD could be delineated up to bronchiolar level when oily propylidone (Dionosil Oily, Glaxo Laboratories Ltd., U.K.) was used.

Pulmonary function tests, performed with the subjects sitting and at rest, and femoral arterial blood gas analyses were carried out by methods described previously (Da Costa *et al*, 1971). Gas volumes were expressed at body temperature and pressure saturated with water vapour (BTPS). Predicted normal values were calculated from regression equations based on normal data obtained in our laboratory (Da Costa, 1971).

The chi-square (X^2) test and Student's *t* test were used for statistical analysis of the results.

RESULTS (Table I)

The mean age and the age distribution in the men and women in this study were similar (Fig. 1). As expected, significant differences were noted in both height and weight, the women being shorter (average, 4 inches) and lighter (average, 15 pounds) than the men (Table I).

The women also differed significantly in their smoking histories. More men than women were

opium smokers and the women, on the average, smoked less cigarettes and opium than the men.

In many other respects the sexes showed strikingly similar findings e.g. in the age of onset of cough and dyspnoea, mean duration of cough and dyspnoea, prevalence of weight loss, recurrent infection and oedema. Although a greater percentage of women were tussive and less were dyspnoeic when compared with the men this difference was not significant ($p > 0.05$). The prevalence of 'asthmatics' in the two sexes was also similar. The women seemed to show a slightly higher prevalence of chronic cough (greater than 3 months/year) and have a greater volume (more than 9 ml.) of sputum production, but again this was statistically insignificant ($p > 0.05$). Physical examination revealed similar findings in both sexes and this was also seen in the haematological and electrocardiographic findings.

Analysis of the roentgenologic findings in men and women revealed a significantly greater number of women with 'pure' emphysema ($p < 0.01$). Further analysis showed that the sex differences were not related to smoking habits (Table I). The prevalence of chronic inflammatory disease and pleural reaction in the two sexes did not differ significantly.

The functional residual capacity in men was significantly higher ($p < 0.01$) than that in the

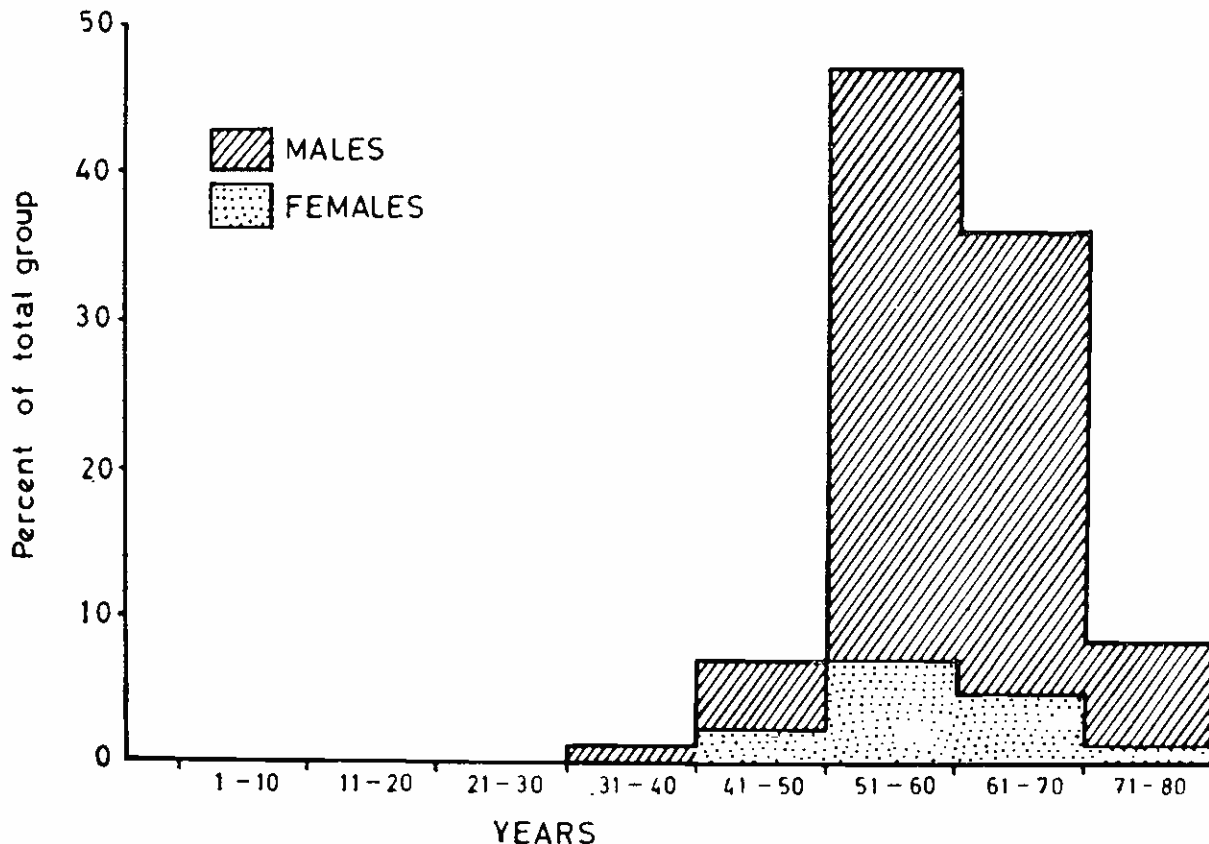


Fig. 1. Distribution of patients in the total group by age and sex.

TABLE I
FINDINGS IN MEN COMPARED WITH THOSE IN WOMEN

	Male n = 70	Female n = 13	Probability that Difference was Due to Chance*
Mean Age, Years \pm S.D.	60.5 \pm 7.5	57.6 \pm 8.5	—
Mean Height, inches \pm S.D.	63.0 \pm 2.1	59.0 \pm 2.8	<0.001
Mean Weight, pounds \pm S.D.	82.5 \pm 15.2	67.2 \pm 7.4	<0.001
SMOKING HISTORY			
'Pure' Cigarette Smokers, %	27.1	57.1	—
Opium and Cigarette Smokers, %	71.4	30.8	<0.02
RESPIRATORY SYMPTOMS, % AFFECTED			
Cough: >3 months/year	82.9	92.3	—
Sputum Vol. >9 ml./24 hours	61.6	68.6	—
Age of onset of cough, years	46.5	47.8	—
Age of onset of dyspnoea, years	50.1	54.0	—
CLINICAL CLASSIFICATION (in %) [†]			
Tussive	54.3	69.2	—
Dyspnoeic	31.4	23.1	—
Asthmatic	12.9	7.7	—
PREVALENCE OF (in %)			
Dependent ankle oedema	40.0	46.2	—
Recurrent chest infections	64.3	69.2	—
Polycythemia	15.7	23.1	—
Crepitations	68.6	84.6	—
ELECTROCARDIOGRAPHIC FINDINGS (%)			
P pulmonale	42.9	76.9	—
RVH, Grades 2-4	23.1	25.0	—
Lead I sign	65.7	69.7	—
Transitional complex beyond V ₄	65.7	69.7	—
ROENTGENOLOGICAL FINDINGS (% OBSERVED)			
Chronic Inflammatory Disease:			
'Pure'	24.3	38.5	—
As part of a 'Mixed' picture	84.3	69.2	—
Emphysema:			
'Pure' in total group	1.4	23.1	<0.01
'Pure' in opium smokers	0.0	0.0	—
'Pure' in 'pure' cigarette smokers	5.3	18.2	—
As part of a 'Mixed' picture	45.7	38.5	—
Extensive Pleural Reaction:			
In total group	37.1	7.7	—
In opium smokers	44.0	25.0	—
In 'pure' cigarette smokers	21.0	0.0	—

TABLE I (Continued)

FINDINGS IN MEN COMPARED WITH THOSE IN WOMEN

	Male n = 70	Female n = 13	Probability that Difference was Due to Chance*
PULMONARY FUNCTION TESTS			
RV, L., mean \pm S.D.	3.33 \pm 1.6	2.67 \pm 0.72	—
Per cent of predicted RV, mean \pm S.D.	204 \pm 65	170 \pm 42.8	—
FRC, L., mean \pm S.D.	4.35 \pm 1.07	3.32 \pm 0.62	<0.01
Per cent of predicted, FRC, mean \pm S.D.	156 \pm 35.7	123 \pm 23.4	<0.01
TLC, L., mean \pm S.D.	5.36 \pm 1.08	4.14 \pm 0.70	<0.001
Per cent of predicted, TLC, mean \pm S.D.	114 \pm 22.2	106 \pm 15.9	—
RV/TLC, per cent, mean \pm S.D.	60 \pm 9.5	66 \pm 7.1	<0.05
FVC (after isoprenaline), L., mean \pm S.D.	2.00 \pm 0.52	1.27 \pm 0.27	<0.001
Per cent of predicted, FVC, mean \pm S.D.	67 \pm 17.3	60 \pm 14.6	—
FEV ₁ , L., mean \pm S.D.	0.78 \pm 0.30	0.51 \pm 0.17	<0.01
Per cent of predicted, FEV ₁ mean \pm S.D.	38 \pm 13.4	31 \pm 12.1	—
SaO ₂ , %, mean \pm S.D.	89 \pm 7.1	84 \pm 13.3	—
PaCO ₂ , mm. Hg., mean \pm S.D.	50 \pm 9.0	52 \pm 11.7	—

*Dashes indicate a *P* value greater than 0.05. As more than 20 findings have been compared in this table, a *P* value less than 0.01 would be a more desirable level of significance.

†Based on the classification proposed by Mitchell and Filley (1964).

women even when calculated as per cent of predicted, 55 per cent of women and only 13 per cent of men having values within the normal range. No significant difference, however, was observed between the sexes with regard to their residual volumes. Thus the expiratory reserve volume in males exceeded that in the females.

DISCUSSION

It has been well established that COLD occurs predominantly in middle-aged males with a long history of cigarette smoking (Fletcher *et al*, 1964; Mitchell and Filley, 1964; Burrows *et al*, 1965). This was confirmed in this study. Women were also affected, but to a much lesser extent. The ratio of males to females in this study was 5.4:1. Similar findings have been reported by Gaensler and Lindgren (1959). Mitchell and Filley (1964) and Burrows *et al* (1965), however, found a much higher male to female ratio (9:1), whereas Karon *et al* (1960) and Snider *et al* (1962) reported much lower male to female ratios of 2:1 and 1:1, respectively. However, the latter two studies were not strictly comparable as Karon's patients were restricted to young adults and Snider analysed routine autopsies of subclinical emphysematous patients.

In contrast to the findings of Burrows *et al* (1965) and Webster *et al* (1968), COLD in women in this study appeared to have a higher prevalence (though not statistically significant) of a 'bronchitic' or 'inflammatory' component than in the men; women more often having a chronic cough with expectoration and more frequently noting the occurrence of cough before the onset of dyspnoea. Also, the women had a slightly greater prevalence of heart failure, recurrent chest infections, cyanosis and crepitations. Moreover, the similar impairment of lung function and electrocardiographic abnormalities noted in women suggested that the disease was at least of equal severity, if not more severe, in women. If these findings are adequately representative, then the much higher cigarette and opium consumption combined with a longer duration of smoking in the men should have resulted in a more severe, possibly more 'bronchial' type of COLD as reported by Burrows *et al* (1965) and Webster *et al* (1968). This was not seen in the present study. It is possible that a genetic factor may be involved. Unfortunately, it was not possible to carry out family studies adequately in the present series as most of the patients were migrants from China and had left behind their relatives on coming to Singapore. Also, multiple environmental factors

and the late age of onset of the illness made it difficult to assess the importance of a genetic factor in this instance (McKusick *et al*, 1963).

An increased prevalence of a positive family history in females has been noted by a number of workers (Karon *et al*, 1960; Burrows *et al*, 1965; Webster *et al*, 1968). Recently, Laurell and Eriksson (1963) noted an association between a deficiency of α_1 -antitrypsin and "degenerative pulmonary disease". The distinguishing features of this disease include an early age of onset of familial panlobular emphysema, a greater than expected proportion of affected females and progressive dyspnoea without much evidence of chronic bronchitis in the early stages (Talamo *et al*, 1966). As facilities for the study of serum alpha₁-antitrypsin levels are now available, this aspect is being studied at the present time. It is thus not certain that women in this series had a different type of illness with a greater inherited susceptibility than the men. This aspect would seem to merit further investigation.

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