EDITORIAL

Occupation and chronic obstructive pulmonary disease (COPD)

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Chronic bronchitis, defined as increased cough and sputum production, is well established as an occupational disease independent of cigarette smoking, which is a major confounding factor. The relevance of industrial exposure to the development of airflow obstruction (chronic obstructive pulmonary disease (COPD)) is more controversial. Good data exist linking the inhalation of cadmium fume to the development of emphysema. The pathology of airflow obstruction due to other occupational exposures is less clear. The principal measure of occupational bronchitis with airflow obstruction is accelerated loss of forced expiratory volume in one second (FEV_1); and epidemiology is the principal tool for investigation. Using these methods, many workers have established links between occupational exposure and disease, which will be reviewed.

From an occupational standpoint tobacco smoking is unique, in that the pollutant is put into the mouth and deliberately inhaled in concentrations far exceeding occupational exposures. Despite this, less than 20% of smokers develop significant airflow obstruction. The factors which determine whether an individual smoker develops airflow obstruction are usually unknown. There are two ways in which an occupational agent may act: 1) by promoting the deleterious effects of smoking; or 2) by acting in a manner similar to tobacco smoking, requiring other promoting factors before an effect is seen. Examples will be given of both of these mechanisms. From a pragmatic point of view, it is highly unlikely that the mixed agents in tobacco smoke are the only cause of significant COPD. The widespread habit of tobacco smoking in industrial populations has delayed the recognition of other factors contributing to disease, as it is only possible to examine the independent risks of smoking and occupational exposures when a reasonable proportion of those occupationally exposed are lifelong nonsmokers.

The studies of specific workforces are often difficult to interpret, as workers commencing exposure in jobs with a high risk of lung disease have even better lung function than the normal worker, and losses from a cohort are higher in those with disease, leading to lower estimates of risk as an increasingly smaller proportion of survivors are followed-up. These problems have been overcome by sampling the general population away from the workplace. Such studies suffer from less selection bias (but exclude those who have died prematurely), and have less satisfactory estimates of occupational exposure, usually including a greater proportion of those with low exposure and, thus, reducing the relative risks of exposure. Such studies have included a general older working population in Beijing (China) [1], an urban and rural population in Norway [2], a rural population in Northern Italy [3], and two studies of city dwellers designed to investigate air pollution in France [4] and the USA [5]. Different outcome measures have been used, but all show significant excess risks with occupation. In general, dust exposure is associated with higher risks of reduced lung function than gas or fume exposure [1, 5], with relative risks of around 1.5.

General population samples have been studied longitudinally in Paris [6], Cracow (Poland) [7], Zutphen (Holland) [8] and Bergen (Norway) [9]. The Zutphen study again started with a community sample, using a job matrix to link symptoms and diagnoses with the occupation. The study has been analyzed longitudinally, initially using the time, intensity and duration of exposure. The longitudinal analysis found a cumulative 25 yr incidence of chronic nonspecific lung disease of 27.9%. Incidence density ratios were calculated, and ratios for smoking increased from 1.5 for light smokers to 4.5 for those smoking more than 20 cigarettes daily.

Increased risks of chronic nonspecific lung disease (which includes asthma), were found in a number of occupations which are shown in table 1. A further analysis of this study, by the same group, appears in this issue of the Journal [10], using a different job exposure matrix generated from the sample itself. It is disappointing that the results of the reanalysis are less clear than the original analysis, perhaps because of the lack of differentiation between the proportion of the workforce exposed to a particular agent, and its intensity. The mortality analysis was limited by the small number of deaths (33 out of 799) due to chronic nonspecific lung disease. Nevertheless, for occupational groups where at

Table 1. – Relative risk of chronic nonspecific lung disease incidence from the Zutphen (Holland) study [8]

Occupation	Relative risk
Textiles and tailors	2.37
Construction and cement	2.29
Transport	2.09
Furnace	2.07
Wood and paper	1.72
Farmer	1.58

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least 50% of the sample reported dust exposure, the relative risk of dying from chronic nonspecific lung disease was 1.47, compared with 2.0 for each 10 yrs smoked. The Zutphen study alone found an increased incidence of chronic nonspecific lung disease in workers with solvent exposure. The solvent exposed workers included painters, who have been found to have the highest incidence of occupational asthma in the UK, which might account for this finding. Some of these problems have been avoided in the other longitudinal population studies. Construction, outdoor or cement exposed workers were also at excess risk in Cracow [7]. Workers exposed to quartz or silica were at increased risk in all four longitudinal studies (longitudinal decline in FEV_1 about 60 ml·yr^{-1} [6]). Farmers, grain workers, foundry workers (or workers exposed to chromium, nickel or platinum in the Norwegian study), woodworkers and workers exposed to excess heat, including furnace workers, are identified as increased risk groups in several studies. Sulphur dioxide exposure was associated with greater declines in FEV_1 in Bergen.

Many occupational studies have been carried out in situations where pneumoconioses or byssinosis also occur, making it more difficult to separate the airway effects of COPD from these other pathologies. Workers exposed to coal, silica and cotton are all at increased risk of accelerated loss of FEV_1, which in general is greater in smokers than nonsmokers, *i.e.* the occupational effect is promoting the effect of cigarette smoke. The converse is seen in isocyanate workers, where the predominant effect is in nonsmokers [11].

Cough and sputum are associated with increasing cotton dust exposure [12]. High levels of cotton dust exposure in former Yugoslavia, India and China have been associated with increasing annual declines in FEV_1 in longitudinal studies [13, 14]. In England, the loss of FEV_1 was found to be of similar order to that of smoking [15]. In the USA, in workers with low exposures, an effect of cotton dust on loss of FEV_1 was seen only in smokers[16]. This study showed effects in nonsmokers at higher levels of cotton dust exposure levels.

Early studies showed that lung function in miners with uncomplicated pneumoconiosis was similar to miners without pneumoconiosis [17]. This was interpreted as implying that silica or coal dust exposure had no effect on lung function in the absence of progressive massive fibrosis. More recent studies confirm the lack of effect of radiological pneumoconiosis on lung function, but show that increasing silica or coal dust exposure is associated with reducing levels of FEV_1 and forced vital capacity (FVC); *i.e.* the effect on lung function is acting independently of the effect of the nodular shadows on the chest X-ray. Studies in South African gold miners have shown reductions in FEV_1 in workers with and without silicosis. After controlling for radiological silicosis the annual loss of FEV_1 attributed to mining was 8 ml·yr^{-1}, and that due to smoking 20 cigarettes·day^{-1} was 6.9 ml·yr^{-1} in black miners who were more heavily exposed to silica and smoked less than white miners [18]. The studies on white miners [19] showed that the contribution to FEV_1 loss due to silica (236 ml for average lifetime exposure) was estimated to be about half that of smoking 20 cigarettes daily for 30 yrs (552 ml). The relationship between death from COPD, silica exposure and smoking has suggested a multiplicative risk model in this group [20]. Exposure in early adult life appeared to have more effect than later exposure. Using attributable risk, 5% of the deaths were due to silica exposure, 59% from the combination of silica and smoking, and 34% from smoking.

The relationship between smoking, coal dust exposure and COPD has been studied in UK coal miners and is complex. The attributable risk of dust exposure for an FEV_1 less than 80% predicted is less for smokers than nonsmokers, but the attributable risk for an FEV_1 less than 65% predicted is about twice as high for smokers as nonsmokers [21] (*i.e.* smoking is more likely to lead to severe airflow obstruction than coal dust exposure, the reverse being true for less severe disease). It is often argued that the average loss of FEV_1 is small in relation to that likely to cause significant disability. It depends on whether all the exposed population decline at a rate close to the mean, or whether there is wide variation, as in the effect of cigarette smoking. The evidence tends to favour a large clinically significant effect in a few individuals. This has been calculated on the basis of 35 yrs exposure to the mean level of exposure per 1,000 workers. For coal miners, a lifetime exposure of 122.5 gh·m^{-3} would result in 80 out of 1,000 having a 20% loss attributed to dust, and 12 out of 1,000 a 35% loss. The comparable attributable risks for smokers are 66 out of 1,000 and 23 out of 1,000, respectively. The highest group cumulative dust exposure for the South African gold miners was only 21.3 gh·m^{-3}, a tenth of that of the highest exposure group of British coal miners. Despite this, the attributable risk for an FEV_1 less than 80% was 4.9 for silica exposed gold miners *versus* 1.5 for coal miners [21].

Cadmium fume exposure is the best example of a particular occupational exposure causing a specific variety of COPD, namely emphysema. Cadmium has a very long half-life in the body (4–19 yrs), allowing total exposure to be estimated reasonably accurately many years after exposure has ceased, as it is stored in the liver. The most complete study has been survivors from a foundry manufacturing copper-cadmium alloy. For those with the highest exposure, the mean excess loss of FEV_1 (compared with similarly smoking industrial controls), was 398 ml, for diffusing capacity of the lung for carbon monoxide (D_{LCO}) the reduction was 1.58 mmol·min^{-1}·kPa, with a dose/effect gradient for lesser exposure groups. Nineteen percent of the cadmium workers and 3% of the controls had a gas transfer measurement less than 1.96 SD from the predicted values. Carbon monoxide transfer coefficient (K_{CO}) correlated significantly with cumulative exposure [22].

There is now growing evidence that airways obstruction (COPD), as well as cough and sputum, are caused by exposures other than tobacco smoke, and that occupational exposures, particularly to dusts, are amongst such causes. As the working population smokes less, the significance of occupational exposures causing

COPD will increase. It is now time to extend the observations on miners exposed to coal dust and silica to other populations, with similarly careful studies to define the relationship between exposure and disease.

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