Smoking, lung function, and mortality

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In this issue of *Thorax* Pelkonen *et al*[1] make another contribution to the substantial body of literature relating smoking habit, lung function, and long term mortality. In this paper the effects of smoking cessation are emphasised, describing 30 years of follow up of a Finnish cohort recruited in 1959 for the Seven Countries study of coronary artery disease. It is somewhat unusual in that the study enrolled essentially all the age eligible (40–59 years) men in two localities and had extremely high rates of follow up. Lung function was measured at baseline, as were other risk factors for coronary disease such as smoking habit, blood pressure, cholesterol, and body mass index. About half of the 1600 men were smoking on entry to the study and about 37% of them quit during follow up. Baseline lung function was reasonable, with two thirds of the men having forced expiratory volume in one second in 0.75 of a second ($FEV_{0.75}$) of more than 88% of predicted normal. One third, the lowest tertile, had values below this, and presumably some were in the range of clinical obstructive disease.

Lung function predicted overall mortality after adjustment for coronary risk factors; men in the lowest tertile of lung function were significantly more likely to die than the rest, and men in the middle tertile with expiratory flows of 88–102% of predicted had a slightly higher death rate than those with better lung function. The fact that poor lung function predicts mortality has been well known for decades[2]; reduced lung function predicts death due to lung cancer, chronic obstructive pulmonary disease (COPD), and cardiovascular disease, particularly coronary artery disease. The mechanisms involved probably differ. Poor lung function—that is, reduction in expiratory flow rates—is virtually synonymous with COPD so that an association of the former with death from the latter amounts to tautology. Lung cancer has been shown repeatedly to be more common in smokers with airways obstruction than without, and the lung function effect persists after statistical consideration of the smoking habit.[3 4] On the other hand, lung function appears not to predict lung cancer in non-smokers,[5] although lung cancer in non-smokers is uncommon enough to make this kind of estimation tricky. Nevertheless it appears that, for lung cancer, the level of lung function reflects either host factors that influence cancer development in response to smoking or a particularly sensitive measure of smoking exposure. The mechanism of the lung function effect in cardiovascular mortality is even more mysterious. It appears not to be closely related to smoking in that lung function predicts cardiovascular death in non-smokers.[6] One explanation—that lung function causes cardiovascular disease by virtue of causing hypoxaemia—does not seem credible as the effect is evident at levels of lung function not associated with abnormalities of pulmonary gas exchange. There is an interesting unsolved problem here.

Pelkonen *et al* found that smoking cessation improved mortality and that this effect was not confined to men with the worst lung function at study entry. The decrease in all cause mortality was largely the result of a decrease in deaths from cardiovascular disease. A prompt decline in cardiovascular mortality and morbidity, significant within five years or less after smoking cessation, has been observed before.[7] The best estimates are that, after cessation, mortality from coronary artery disease and stroke approach those of lifetime non-smokers in some 15 years.[8] This probably relates to reductions in thromboses and in the progression of atherosclerosis, which should have nothing to do with lung function, so it is not surprising that the benefit of smoking cessation was evident at all levels of airways obstruction. However, there was some evidence to suggest a positive interaction between smoking cessation and lung function in that those with the worst lung function appeared to benefit the most. If this is true, its cause is not apparent and it re-emphasises the fact that we do not understand why poor lung function predisposes to cardiovascular disease.

Pelkonen *et al* did not observe significant decreases in mortality from lung cancer or respiratory disease after smoking cessation. This failure is consistent with other data. While there is good evidence that the incidence of lung cancer decreases after smoking cessation, it has been derived from very large cohorts studied for a very long time.[9] After cessation the incidence of lung cancer does not begin to decline for some five years and then falls gradually, not stabilising until 20 years after cessation. Even then, ex-smokers have a roughly twofold increase in lung cancer mortality compared with lifetime non-smokers.[8] The men studied by Pelkonen *et al* had been followed for 20 years after smoking cessation and lung cancer mortality in those who quit was 62% of the rate in those who did not, which is consistent with these results but not statistically significant because of the relatively small size of the Finnish cohort. The smoking induced tissue damage that produces lung cancer is not easily or quickly reversed by cessation. This probably accounts for the finding of an insignificant negative interdependence between cessation and lung function in lung cancer; those who quit with low levels of lung function were less likely to avoid lung cancer than those with better lung function.

The effects of smoking cessation in COPD have been well studied. Smoking cessation results in a very small improvement in lung function which is probably clinically insignificant. The chief benefit of cessation is that it reduces the subsequent rate of decline in lung function, at least in people with mild or moderate airways obstruction. In such individuals, who have largely preclinical disease, the benefits of cessation are clear and almost certainly lifesaving[10]; these people simply will not get symptomatic COPD. However, in patients with established symptomatic COPD the situation is less clear. Many severely ill patients with COPD spontaneously quit smoking, probably in response to their symptoms and disability, and it is hardly surprising that these patients do not do well afterwards. For this reason studies of patients with well established disease have often not shown a reduction in mortality with smoking cessation.[11 12] As the authors indicate, this probably explains their finding that deaths from respiratory diseases were more common in those who quit than in those who continued to smoke.

For the clinician the message of the Finnish paper is clear and, one hopes, consonant with routine practice. Stopping smoking is always a good thing. The 37% spontaneous quit rate observed in the cohort of Pelkonen *et al* may be

regarded as a background phenomenon; this is what middle aged Finnish men did in response to a non-smoking climate. It is our job to improve on this.

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