Relation of expired carbon monoxide to smoking history, lapsed time, TLCO measurement and passive smoking

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Summary
We quantified the influence of lapsed time, measurement of gas-transfer factor (TL CO), and passive smoking on expired carbon monoxide (CO) levels, and then evaluated the accuracy of smoking histories against expired CO measurements in patients newly attending 'occupational' compared with 'general' chest clinics.

Expired CO levels had an estimated average rate of decline of 3.4 ppm/h in the presumed absence of further smoking, though individual rates depended necessarily on the initial levels (2.1, 3.9, 5.7 and 7.5 ppm/h, respectively, when the initial levels were 10, 20, 30 and 40 ppm). TL CO measurement was associated with a median increase in expired CO of 4.0 ppm, but passive exposure to tobacco smoke in non-smokers had negligible effect. Expired CO levels indicative of current smoking (> 8 ppm) were noted much more commonly in the current cigarette smokers (88%) than those who claimed to be current non-smokers (6.0%), but without significant difference between the non-smokers attending the occupational and general clinics (6.6% vs 5.3%).

We conclude that the lapse of 1 h and the measurement of TL CO exert mild but important influences on the expired CO level, but that passive smoking does not. 'Occupational' and 'general' patients give similarly false declarations of current non-smoking when presenting initially for clinical evaluation.

KEYWORDS
Carbon monoxide; Gas transfer factor; Smoking

Introduction
There is wide recognition that a proportion of current smokers underestimates tobacco consumption or even denies smoking entirely. From measurements of salivary cotinine and expired CO in a community-based respiratory health survey in the USA, Coultas and colleagues suggested that among self-reported current non-smokers 5.3–8.2% of males and 4.0–6.1% of females were actually smoking.\(^1\) This is consistent with community data from the UK which showed that “up to 7% of smokers and ex-smokers described themselves incorrectly as never smokers”.\(^2\) In UK smoking cessation studies, carboxyhaemoglobin levels were inappropriately high in 22% of ‘non-smoking’ participants in a secondary prevention trial following myocardial infarction and in as many as 40% of ‘non-smoking’ participants in a nicotine replacement trial.\(^3\) The validation of self-reported smoking

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Among populations with a risk of occupational lung disease, deception over smoking might be expected since a potential claim for compensation could be perceived to be weakened or invalidated otherwise. Among coal miners in the USA, for example, Lapp and colleagues reviewed questionnaire data from repeated claims for compensation and found consistent smoking histories in only 41% of 448 claimants. As many as 15% admitted to smoking initially but later claimed to have never smoked, 25% later underestimated average consumption (as described initially) by 5–50%, and 19% later underestimated average consumption by >50%. In the UK, Cockcroft noted similarly that 20% of coal miners who declared themselves light smokers were described, after death, as heavy smokers by their relatives.

Objective methods of assessing smoking habit include the measured concentrations of cotinine in plasma, saliva or urine, CO in blood (carboxyhaemoglobin) or expired air, and thiocyanate in serum or urine. Measurement of cotinine level is possibly the most sensitive and specific, but is time consuming and expensive. More practical, and almost as sensitive and specific if other sources of CO exposure can be excluded, is the measurement of expired CO. Possible limitations centre on lapsed time since last exposure to tobacco smoke; any preceding measurement of TlCO; and passive smoke exposure. Only very rarely is the expired CO level elevated through biological causes—chiefly those associated with an increased turnover of red blood cells.

The aims of this study were to evaluate these limitations prospectively and to compare the accuracy of self-reported smoking habit between patients newly attending occupational and general respiratory clinics.

**Methods**

Participants were recruited from first-time attenders at the lung function laboratory of the Royal Victoria Infirmary, Newcastle upon Tyne, UK. The laboratory supports an occupational lung disease clinic for the northeast region of England and a number of general and speciality respiratory clinics. Expired CO levels were measured routinely (whenever practical) in all new patients attending the occupational clinic during the study period August 1996–May 1998, and in alternate new patients attending one of the general clinics.

A short questionnaire was administered by pulmonary function technicians, who recorded demographic details, smoking habit, and passive smoke exposure. Tobacco consumption in the cigarette smokers was quantified by the reported average daily number of cigarettes smoked. Non-smokers were asked about passive smoke exposure on the day of the clinic visit, whether at home, on the journey, or through some other source.

CO levels were measured using the EC50 Smokerlyser (Bedfont Scientific Ltd., UK), which was calibrated 6 monthly as recommended. Each participant was asked to expire slowly through the mouthpiece after a 15 s breath-hold, by which time a steady reading was generally obtained. The test was repeated if necessary, particularly in subjects unable to hold their breath for 15 s. When practical, measurements were made on arrival at the clinic and on departure in order to determine the effect of the passage of time. Lung function tests were performed as clinically necessary, and any measurement of TlCO was recorded. Three TlCO measurements were usually made, but if the best two differed by more than 5% an additional test was carried out. An expired CO level of >8 ppm was used, by convention, to separate presumed current smokers from current non-smokers.

Descriptive statistics were derived using Minitab 11.2 (Minitab Inc., USA), together with parametric and non-parametric tests as appropriate. The method used to measure expired CO has no safety implications and is undemanding of effort. It was used more or less routinely for patients newly referred to our lung function laboratory when the study was conceived. Because of prevailing practice at that time, it was considered unnecessary to submit the protocol for ethical approval.

**Results**

The study population comprised 596 subjects, of whom 178 (30%) claimed to be current smokers and 418 (70%) current non-smokers (hereafter 'smokers' and 'non-smokers'). All underwent measurements of expired CO. Demographic details are shown in Table 1: 288 (48%) came from the occupational chest clinic and 308 (52%) from the general chest clinic. The occupational patients were a little younger (mean 54 years) than the general patients (mean 58 years) and more likely to be male (88 vs 53%), but there was no significant difference in reported smoking habit. Where data
were missing for certain analyses, the numbers of contributing participants are given in the table. Among the 178 smokers were 37 patients who used pipes or cigars but not cigarettes. They were not considered further.

Cigarettes were consumed by 141 of the smokers, of whom 124 (88%) had expired CO levels >8 ppm on arriving at the clinic. By contrast, only 25 of 418 non-smokers (6.0%) had measurements in this range (Fig. 1). Figure 2 shows that the correlation between the reported daily consumption of cigarettes and the initial expired CO level was poor (Spearman rank correlation \( r = 0.19 \)), reported consumption levels explaining very little of the variability of expired CO measurement (\( r^2 = 0.04 \)).

### Effect of lapsed time

The expired CO level was measured both on arrival in the laboratory and on departure without any intervening measurement of \( T_LCO \) in 35 of the 141 cigarette 'smokers'. Figure 3 shows the relation between the change in expired CO measurement and the lapsed time. The slope of the linear regression line was \(-0.0573 \text{ppm/min} (95\% \text{CI}, -0.095—-0.020)\), implying that in 1 h the average decline in CO level in the presumed absence of further smoking was 3.4 ppm (95% CI, 1.2–5.7). The estimate is necessarily crude, since the rate of change must depend additionally on the initial level. This is illustrated by Fig. 4, which shows that the rate of change of the expired CO level was indeed a function of the initial level, and could be estimated at \(-2.1, -3.9, -5.7 \text{ and } -7.5 \text{ ppm/h} \) when the initial levels were 10, 20, 30 and 40 ppm, respectively.

Comparable data from 77 non-smokers not undergoing \( T_LCO \) measurement showed a median change of 0 ppm (IQR 0–0 ppm).

### Effect of \( T_LCO \) measurement

The expired CO level was measured both on arrival and departure with an intervening measurement of \( T_LCO \) in 123 of the 418 non-smokers. The data were skewed and the median increase in expired CO was 4 ppm (interquartile range, IQR, 1–5 ppm) compared with 0 ppm (0–0 ppm) for the 77 corresponding non-smokers without \( T_LCO \) measurement (95% CI for the difference between the medians, 3–4 ppm, \( P < 0.001 \) Mann Whitney U test).

For 39 smokers who underwent \( T_LCO \) evaluation and paired measurements of expired CO, the median change in expired CO was \(-2 \text{ ppm (IQR, } +1—-5 \text{ ppm}) \) compared with \(-4 \text{ ppm in the corresponding 35 smokers who did not undergo } T_LCO \text{ measurement (IQR, } -1—-7 \text{). The 95\% CI for the difference between the medians was } 0-4 \text{ ppm (} P = 0.097, \text{ Mann Whitney U Test).}

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**Table 1** Study population.

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>Occupational clinic</th>
<th>General clinic</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total number</strong></td>
<td>596</td>
<td>288 (48%)</td>
<td>308 (52%)</td>
<td></td>
</tr>
<tr>
<td><strong>Mean age, years (SD)</strong></td>
<td>552</td>
<td>53.7 (13.0) (n = 253)</td>
<td>58.1 (14.3) (n = 299)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Male</td>
<td>415</td>
<td>252</td>
<td>163</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Female</td>
<td>181</td>
<td>36</td>
<td>145</td>
<td></td>
</tr>
<tr>
<td>Non smokers</td>
<td>418</td>
<td>212</td>
<td>206</td>
<td></td>
</tr>
<tr>
<td>Smokers</td>
<td>178</td>
<td>76</td>
<td>102</td>
<td></td>
</tr>
<tr>
<td>Cigarettes</td>
<td>141</td>
<td>57</td>
<td>84</td>
<td></td>
</tr>
<tr>
<td>Cigars/pipes</td>
<td>37</td>
<td>19</td>
<td>18</td>
<td></td>
</tr>
</tbody>
</table>

Gender and smoking habit compared using Chi square test. Age compared with Student t test. For significant differences at the 5% level or less, \( P \) values are given. Note that the upper half of the table contrasts all the 'occupational' and 'general' patients, while the lower half contrasts only the 141 cigarette smokers and the 418 non-smokers.
Effect of passive smoking

A total of 75 non-smokers (18%) reported exposure to passive smoke on the day of the clinic visit. The median expired CO level of these patients (3 ppm) was identical to that of the 340 non-smokers who reported no passive exposure, but the IQR reached a marginally higher level (3–5 ppm vs 3–4 ppm). In the tails of the distributions, however, the passive smokers among the non-smokers showed a striking excess of expired CO levels >8 ppm (12/75, 16%) compared with the non-smokers without passive exposure (13/340, 3.8% P<0.001, Chi-square test).
Effect of occupational referral

There was no significant difference in initial expired CO levels >8 ppm among non-smokers between the occupational clinic (14/212, 6.6%) and the general clinic (11/206, 5.3%, $P = 0.586$, Chi-square test). Among the subset of 75 who claimed passive smoke exposure, expired CO levels >8 ppm were also noted with similar prevalence among the occupational (7/38) and general patients (5/37, $P = 0.562$, Chi square).

Discussion

The measurement of expired CO is disarmingly easy (gentle expiration over a few seconds after a brief

Figure 3  Effect of lapsed time in clinic on change in expired CO level. Linear regression: $y = -1.028 - 0.0573 \times$ (95% CI for slope $-0.095$ to $-0.02$).

Figure 4  Effect of initial expired CO level on rate of change during time in clinic. Linear regression: $y = -0.32 - 0.18 \times$ (95% CI for slope $-0.31$ to $-0.05$).
expired CO levels do correlate closely with smoking histories and the corresponding measurements of expired CO. Others have shown that, in general, expired CO levels do correlate closely with specific cotinine assays, and we believe that in most clinical settings the measurement of expired CO reliably reflects smoking habit. However, interpretation of the result is likely to be more effective with adjustment for lapsed time since last cigarette, any measurement of TLCO, and passive smoking.

It is evident from a number of epidemiological studies that the dichotomous separation of 'smokers' from 'non-smokers' often provides greater power for assessing the effects of smoking than the reported level of tobacco consumption. It is assumed that smokers are less likely to deny they are smokers, than they are to underestimate their levels of consumption. Thus, 'smoking' is readily shown to have an effect on lung function, but the effect of a pack-year is estimated with much less confidence. Our results support this. A great majority of the cigarette smokers (88%) had expired CO levels above the diagnostic threshold of >8 ppm compared with a minority only (6.0%) of those who claimed to be non-smokers. It is likely that the latter were current smokers, and that inaccuracy due to categorical denial was low. This is consistent with other studies and does not enhance current knowledge. By contrast, the reported daily consumption of cigarettes correlated very poorly with the initial measurement of expired CO (i.e. that before any TLCO test). Although lapsed time and smoking pattern (puff frequency and inspiratory depth) may have contributed to this, we think the major determinant is likely to have been a more substantial inaccuracy over reported consumption levels.

Our estimate that the expired level of CO declined on average by 3.4 ppm/h in the presumed absence of further exposure is necessarily crude, since the concentration is known to decrease logarithmically (by half in 2–5 h in episodes of CO poisoning, depending on the level of physical activity and the partial pressure of inspired oxygen). The absolute rate of decline consequently depends on the initial level, but at low concentrations pertinent to cigarette smoking the actual average is of practical value. The range that can be estimated from these observations is –2.1– –7.5 ppm/h with initial measurements of 10–40 ppm. These imply a half-life of 3–4 h, which is consistent with general experience, though half-life clearance rates at persistently low levels of exposure are not necessarily comparable to those associated with a single episode of poisoning. For light (but not heavy) smokers our findings imply that a lapsed time of 1–2 h could readily allow the expired CO level to fall into the normal (non-smoking) range.

By contrast, the increase in expired CO associated with the measurement of TLCO (median 4 ppm) could elevate values in non-smokers into the smoking range. Ideally, the expired CO level should be measured first, but if it is measured after the TLCO the value obtained can be adjusted accordingly. In comparison, the effect of passive smoking was not meaningful, though relevant lapsed times since last exposure often exceeded 1–2 h. We noted, however, that among the non-smokers who reported passive exposure there was a much higher proportion with expired CO levels >8 ppm than among non-smokers without such exposure. Since the median levels were not different and the IQRs were very similar, these extreme values are more likely to reflect deception over active smoking than any effect of passive smoking.

We had speculated that discordance between smoking histories and expired CO measurements might be greater among subjects from an occupational clinic compared to a general clinic, but we did not observe this. The degree of discordance was similar in both groups of subjects, and entirely consistent with other studies assessing the accuracy of smoking histories in general populations. Nevertheless, an investigation of coal miners did show that the likelihood of inaccuracy (false denials and under-reporting of consumption levels) increased with repeated evaluations associated specifically with compensation claims. Our assessment of the current ‘occupational’ population provided the first opportunity for a specialist evaluation, and so any consideration of compensation was probably remote when the participants first visited the lung function laboratory.

We conclude that the measurement of expired CO level is useful in clinical practice as an objective means of checking the accuracy of the smoking history. Interpretation of the result should take account of the effects of lapsed time (an average
decline of 3–4 ppm/h) and the measurement of TcCO (a median increase of 4 ppm). Passive smoking appears to exert no meaningful influence, nor does an initial referral for specialist evaluation of lung disease of possible occupational origin.

References