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Breath analysis to detect recent exposure to carbon monoxide

A J Cunnington, P Hormbrey

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See end of article for
authors' affiliations

Correspondence to:
Dr P Hormbrey, Emergency
Department, John Radcliffe
Hospital, Oxford
OX3 9DU, UK;
phil.hormbrey@orh.nhs.uk

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Objectives: To determine the normal range for carbon monoxide concentrations in the exhaled breath of subjects in the emergency department and to develop a protocol for the use of a breath analyser to detect abnormal carbon monoxide exposure.

Methods: A hand held breath analyser was used to measure end expiratory carbon monoxide concentrations in 382 consenting subjects. Questionnaire data were collected to assess the effect of common sources of carbon monoxide exposure on breath carbon monoxide levels. Smokers were used as a carbon monoxide exposed group for comparison with non-smokers.

Results: The range of carbon monoxide concentrations obtained in the non-smoking group was 0–6 ppm and in the smoking group was 1–68 ppm. Smokers had a mean breath carbon monoxide concentration of 16.4 ppm and non-smokers had a mean of 1.26 ppm (95% confidence interval (CI) for difference 13.6 to 16.8 ppm). Male sex and frequent motor vehicle use were associated with slightly higher carbon monoxide concentrations (by 0.40, 95% CI 0.18 to 0.63 ppm, and 0.38, 95% CI 0.13 to 0.63 ppm, respectively) in the non-smoking group. Mean breath carbon monoxide concentrations increased in direct proportion to the number of cigarettes smoked ($p < 0.001$) and there was a negative correlation between carbon monoxide and time since last smoking a cigarette ($p < 0.001$). Altogether 23% of smokers had breath carbon monoxide concentrations in the range 1–6 ppm.

Conclusions: Breath analysis was rapid and results correlated well with carbon monoxide exposure. In this population subjects with breath carbon monoxide concentrations greater than 6 ppm should be assessed for the risk of carbon monoxide poisoning. However even carbon monoxide concentrations less than 6 ppm do not exclude carbon monoxide poisoning within the last 24 hours.

Carbon monoxide is a colourless, odourless gas produced from incomplete combustion of fossil fuels. The affinity of carbon monoxide for haemoglobin is about 240 times that of oxygen and this accounts for at least some of its toxic effect.^{1–2} Accidental carbon monoxide poisoning causes about 50 deaths in the UK each year, and including deliberate inhalation it is the major cause of death from poisoning.^{3–4} Common sources of carbon monoxide include vehicle exhaust fumes, malfunctioning heaters or poorly ventilated fires, and smoking. There is also a small endogenous production of carbon monoxide from haem metabolism.⁵

Diagnosis of carbon monoxide poisoning is difficult because the initial symptoms are very vague, often only headache, nausea or lightheadedness, but may progress rapidly to coma and death.^{6–8} The circumstances in which poisoning occurs may give a clue as to the diagnosis, for example if several members of a family are affected or someone is found unconscious in a garage.^{9–10} Carbon monoxide is aptly named the “forgotten killer” because the diagnosis often eludes medical staff until too late.¹¹ The most tragic scenario is one where a patient presents with symptoms of mild carbon monoxide poisoning, and is falsely reassured by medical staff that they have nothing but a “flu-like” illness. The patient then returns home to the source of poisoning and is found dead some hours later. However acute presentations may be just the “tip of the iceberg” since, even when not life threatening, carbon monoxide poisoning can cause chronic neurological or psychiatric sequelae.^{12–13} Groups most at risk of accidental carbon monoxide poisoning include young drivers, males, and the elderly in cold climates.¹⁴

The use of a rapid, cheap, and non-invasive diagnostic test for abnormal carbon monoxide exposure at the triage station in the emergency department may allow the detection of more cases and prevent deaths. The concentration of carbon

monoxide in end expiratory breath bears a close relationship to blood carboxyhaemoglobin (COHb) concentration^{15–16} and has been employed as a means of rapidly estimating carbon monoxide exposure.¹⁷ Hand held breath analysers are now commercially available and, although they find their main use in smoking cessation programs, are suitable for detection of carbon monoxide exposure from all causes. To our knowledge no one has yet formally defined the range of values of breath carbon monoxide in a population typical of those presenting to an emergency department. Previous studies have assessed values primarily in middle aged adult male subjects,^{15–16} and have not sought to investigate the extent of the effect of factors such as local environment, motor vehicle use or passive smoking, all of which may alter carbon monoxide concentrations.^{5–18} There is considerable variation in carbon monoxide exposure in different areas,¹⁹ and so it is important to establish a normal range for the local population at the place in which the test is to be used.

METHODS

The use of a breath analyser was assessed in the heterogeneous population attending the minor injuries section of the emergency department of the John Radcliffe Hospital, Oxford. An additional group of students were sampled because Oxford has a large student population, some of whom live in poorly maintained accommodation and may be at increased risk of carbon monoxide poisoning. Questionnaire data were collected to determine if common sources of potential carbon monoxide exposure influenced breath carbon monoxide levels.

Abbreviations: COHb; carboxyhaemoglobin; CI, confidence interval

Box 1: Questionnaire data

- Age.
- Sex.
- Smoking status.
- Time since last cigarette/cigar/pipe was smoked.
- Number of cigarettes smoked/day (1–10, 11–20, 21–30, 31–40, or 40+).
- Exposure to other people's tobacco smoke (passive smoking).
- Use of fossil fuels or wood fire in the home.
- Use of a motor vehicle on four or more days of the week.
- Living beside a main ("A" or "B") road.
- Living in an urban or rural area based on postcode.
- Pre-existing medical problems (and specifically asthma, bronchiectasis, thyrotoxicosis, haemolytic anaemia).

Altogether 382 subjects gave informed consent to participate in this study. None of the subjects had symptoms of carbon monoxide poisoning. One hundred subjects were college students who were sampled in their accommodation. The first 20 were used to pilot the sampling technique; 282 subjects were sampled in the emergency department. All people entering the waiting area during one hour periods on 25 days, September to November 1999, were approached to participate. Subjects provided a single breath sample into a hand held solid state breath analyser (EC50, Bedfont Scientific Instruments, Upchurch, UK) in accordance with the manufacturer's instructions for use. The analyser was calibrated on a monthly basis. Subjects completed a questionnaire to assess smoking status and frequency, and whether any other factors contributed to their carbon monoxide level (box 1). Subjects were classified as smokers if they had smoked a cigarette within the last 24 hours. Passive smokers were those who considered themselves to be frequently exposed to other people's tobacco smoke. Population density, determined from postcode, was used to define urban (>10 people per hectare) or rural residence.²⁰ Subjects with medical conditions known to alter endogenous carbon monoxide production (except for asthma),^{8, 21, 22} and smokers who did not indicate how long since they had last smoked were excluded from the analysis. Asthmatics were included because asthma is common and it was important to see if self reported asthma influenced carbon monoxide levels. The peak concentration of carbon monoxide in ambient air in the centre of Oxford on each day of the study was obtained from the Department for the Environment.²³

In order to assess whether the breath analyser allowed detection of recent carbon monoxide exposure the smoking group were considered as "carbon monoxide exposed" and were compared with the non-smoking group. Data were analysed on computer using SPSS 10 software. Mean carbon monoxide concentrations were compared using the independent samples *t* test. Age was analysed by quintiles using one way analysis of variance. Proportions in groups were assessed with the χ^2 test. Trends were assessed using Pearson's correlation.

RESULTS

Approximately 50% of the subjects approached accepted to participate in the study. Of the 382 subjects who were recruited to the study 16 subjects were excluded, one with autoimmune haemolytic anaemia and 15 smokers for whom there was no record of how long ago they had last smoked.

In the pilot phase three end expiratory breath samples were obtained at 30 second intervals for each subject. In every subject the breath carbon monoxide level diminished with each successive sample, by approximately 50% each time (data not shown). In the definitive study only a single measurement was taken. In all cases it took less than two minutes from the start of explaining how to provide the sample to obtain a final value for the end expiratory breath carbon monoxide concentration.

Table 1 Summary of the characteristics of the study population; values are per cent except for age

Characteristic	Smoker (n=90) (25)*	Non-smoker (n=276) (75)*
Mean (SD) age	34.0 (14.8)	32.8 (18.2)
Male	41/66 (62)	129*/208* (62)
Asthma	10/75 (13)	32/273 (12)
Motor vehicle	43/84 (51)	112*/272* (41)
Passive smoker	61/75 (81)†	120/266 (45)†
Main road	43/86 (50)†	88/262 (34)†
Fossil fuel	70/87 (80)	208/264 (79)
Urban residence	42/68 (62)	146/235 (62)
Student	13/90 (14)†	85/276 (31)†

*Significant difference in breath carbon monoxide between groups at $p < 0.01$ (using *t* test).

†Significant difference in proportions between smokers and non-smokers at $p < 0.01$ (using χ^2 test).

Complete responses to all questions were not available for all subjects.

Figure 1 Breath carbon monoxide concentrations in non-smokers.

The proportions of smokers who were also passive smokers, non-students or lived beside a main road, were significantly higher than in non-smokers (table 1). The mean breath carbon monoxide in the non-smoking group was 1.26 ppm (95% confidence interval (CI) 1.14 to 1.37) with a range from 0–6 ppm (fig 1). In the smoking group the mean was 16.4 ppm (95% CI 13.6 to 19.3) and the range was 1–68 ppm. The mean time since last smoking was 3.14 hours (range 0–24 hours). There was a significant difference between the mean breath carbon monoxide values in the smoking and non-smoking groups, mean difference 15.2 ppm (95% CI 13.6 to 16.8). Each of the factors in table 1 was compared within the non-smoking group to see if it had an independent effect on breath carbon monoxide. In non-smokers, sex and motor vehicle use were associated with significant differences. Male breath carbon monoxide was 0.40 ppm higher than female (95% CI 0.18 to 0.63). Motor vehicle use was associated with a 0.38 ppm (95% CI 0.13 to 0.63) higher carbon monoxide than in non-users.

Table 2 Breath carbon monoxide concentrations in smokers

No of cigarettes smoked	No	Range of carbon monoxide concentrations (ppm)	Mean carbon monoxide concentration (95% CI) (ppm)
1–10	41	1–46	11.9 (8.7 to 15.0)
11–20	39	2–49	17.7 (14.3 to 21.0)
21–30	5	6–68	32.8 (8.6 to 57.0)
31–40	2	33–55	44.0 (22.0 to 66.0)

Cigar and pipe smokers excluded.

Figure 2 Mean carbon monoxide concentrations in groups of smokers.

The ages of subjects ranged from 6 to 90 (mean 33.1, SD 17.4). In the non-smokers analysis by quintiles of age revealed no significant effect of age on breath carbon monoxide ($p = 0.16$). Peak daily carbon monoxide concentrations in ambient air ranged from 0.0 to 1.8 ppm (mean 0.36 ppm). There was no significant correlation between peak daily carbon monoxide level and the mean level in non-smoking subjects on those dates.

In smokers the range of breath carbon monoxide values was large, and showed considerable variation even within each band of numbers of cigarettes smoked (table 2). There was a significant negative correlation between breath carbon monoxide concentration and the length of time since the subject

last smoked within the whole population of smokers ($p < 0.001$) and the 1–10 ($p = 0.006$) and 11–20 ($p = 0.027$) cigarette/day groups individually. Twenty one of the smokers had carbon monoxide concentrations less than or equal to 6 ppm, with a mean time since last smoking of 9.0 hours (range 0–24). Fifteen of these subjects smoked only 1–10 cigarettes per day.

Mean carbon monoxide was almost directly proportional to the number of cigarettes smoked (fig 2), although the confidence intervals are very wide for the mean in each group, influenced greatly by length of time since subjects had last smoked.

DISCUSSION

Breath analysis for carbon monoxide was easy to perform and gave a final result in a short period of time. End expiratory breath carbon monoxide measurements in non-smokers in this study were distributed in a range from 0–6 ppm. This is compatible with the normal ranges based on blood COHb and expired carbon monoxide described by other researchers.^{16–24} It has been reported that in untreated asthma breath carbon monoxide may be higher than in treated asthma, but in this study we did not find raised concentrations in our subjects with self reported asthma.²² The values were significantly higher in males and in frequent motor vehicle users, but these differences were very small. Motor vehicle users may have a

Figure 3 Flow diagram for the use of a breath analyser to detect abnormal carbon monoxide exposure (CO=carbon monoxide).

slightly greater exposure than non-users to exogenous carbon monoxide in the form of exhaust fumes. Males may have greater endogenous carbon monoxide production than females, although this has not been described previously. Despite these small differences it seems safe to assume that for non-smokers in our population the normal range of breath carbon monoxide should be considered to be from 0–6 ppm. In fact the true maximum value may even be slightly lower because it is well documented that smokers do not always admit to their habit in questionnaires.²⁴

Smokers had very much higher breath carbon monoxide levels than non-smokers. The mean breath carbon monoxide increased in direct proportion to the carbon monoxide exposure (number of cigarettes smoked) in the smoking group. This indicates that breath analysis is reliable over the range of carbon monoxide exposures seen here. Our data suggest that in smokers it is very difficult to assign a maximum normal value since this will depend on how many and what type of cigarettes they smoke, how recently they have smoked, how deeply they inhale, and what they have been doing since smoking.⁵ The decrease in breath carbon monoxide with repeated sampling probably reflects the fact that the equilibrium of blood carbon monoxide with alveolar carbon monoxide levels is not established instantaneously and may itself be affected by smoking.²⁵ It is sensible to bear this in mind when testing subjects.

It has been reported that symptoms due to carbon monoxide poisoning do not usually occur until the COHb concentration reaches values of 16%–20%, in normal subjects.^{6–8} A COHb of 20% corresponds to an end expiratory breath carbon monoxide value of approximately 130 ppm.¹⁵ This is greatly in excess of the values achieved in this study where none of the subjects had symptoms of carbon monoxide intoxication. However there is often reported to be little correlation between COHb and clinical status, and it is recognised that symptoms may persist even when COHb has fallen substantially. This may be due to irreversible damage caused by hypoxia, free radical generation, binding of carbon monoxide to myoglobin and cytochrome enzymes or interaction with the endogenous heme-oxygenase and nitric oxide systems.^{2–6, 26–27} Thus the time since exposure must be considered and it must be determined whether breath carbon monoxide may have been damagingly high at the time the subject left the source of exposure. This can be calculated using the half time for elimination of carbon monoxide breathing room air as 4–5 hours or from a nomogram.²⁸ This fact is particularly important for subjects who may have been exposed to carbon monoxide in the home or workplace at levels sufficient to be harmful, but may have left the scene of intoxication some hours before being seen in hospital. It is possible for someone with symptomatic carbon monoxide poisoning to present to a doctor within 24 hours of leaving the site of exposure and to have a normal breath carbon monoxide when measured. In such cases it is essential not to send the victims back to the site of exposure. Altogether 23% of the smokers in our study had carbon monoxide concentrations as low as the non-smoking group with a mean time since last smoking of nine hours, equivalent to two half times for carbon monoxide elimination.

The Chief Medical Officer has repeatedly urged doctors to remain aware of the risk of carbon monoxide poisoning during winter months.²⁹ We suggest the use of the breath analyser at the triage station in the emergency department (fig 3). Where there are features compatible with carbon monoxide exposure, and no other obvious cause, a breath sample should be taken before any oxygen is given. It is essential that the sample is properly obtained to avoid the need for repeating samples at short intervals and obtaining a falsely low reading. A breath carbon monoxide greater than 6 ppm requires a specific consideration of the possibility of carbon monoxide poisoning. In this assessment potential exogenous and endogenous sources of carbon monoxide should be considered in addition to

Key points

- The diagnosis of carbon monoxide poisoning often eludes medical professionals.
- Portable breath analysers are available for the quantitative determination of carbon monoxide concentrations.
- This study shows that the use of a breath analyser in the emergency department is rapid and can detect recent carbon monoxide exposure.
- A protocol has been developed to use a breath analyser to help to detect abnormal carbon monoxide exposure.
- This may help to prevent the diagnosis of carbon monoxide poisoning from being overlooked by medical staff.

factors that increase vulnerability to carbon monoxide poisoning and may lower the threshold at which it becomes harmful. The time since potential exposure must also be considered.

We have reported the first description to our knowledge of breath carbon monoxide levels in a heterogeneous and clinically relevant population with consideration of the effect of potential confounding factors. We propose that breath analysis is routinely used in the triage situation for assessment of patients with symptoms compatible with carbon monoxide exposure. Further studies are now warranted to investigate the effectiveness of testing for carbon monoxide exposure in this way.

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Authors' affiliations

A J Cunningham, Emergency Department, King's College Hospital, London, UK

P Hormbrey, Department of Accident and Emergency, John Radcliffe Hospital, Oxford

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