IEH assessment on

INDOOR AIR QUALITY IN THE HOME (2): CARBON MONOXIDE
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The views expressed here do not necessarily represent those of any Government Department or Agency.

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*Corrigenda to print edition*  
Page 83, Figure 3.4 - In the key to this figure the blue line now denotes carboxyhaemoglobin level (%) and the black line now denotes carbon monoxide concentrations

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Executive summary

BACKGROUND

People spend the majority of time indoors, mostly in the domestic environment, where there may be significant air pollution sources. This assessment examines available data on exposure to carbon monoxide (CO) and evaluates the likely effects on health and well-being caused by levels of CO typically found in UK homes; it was commissioned by the Department of the Environment, Transport and the Regions to contribute towards the development of the Government’s strategy on indoor air quality and the formulation of advice for the public.

REVIEW PROCESS

As a first stage in this process, the Institute for Environment and Health (IEH) prepared an extensive literature review on exposure to CO in the home and the potential health effects relating to such exposure. International experts and representatives of relevant Government departments then discussed the key issues at a workshop held in Leicester in June 1997. The primary purpose of the workshop was to ensure that the IEH review was up-to-date, accurate, balanced and comprehensive. Expert opinion on the likely health effects of exposure to CO in UK homes was sought and key knowledge gaps and research recommendations were identified. This assessment, based on the original review, incorporates the opinions of the experts at the meeting along with some additional text and data provided by workshop participants and IEH staff subsequent to the meeting.

EXPOSURE AND HEALTH EFFECTS EVALUATION

There is a large body of literature concerning indoor concentrations and the health effects of CO. However, there have to date been very few studies conducted in the UK. Outdoor CO levels can be determinants of indoor levels but, where present, the major sources of CO in the home are gas cookers and certain types of heating systems which burn gas, wood, coal or paraffin. Environmental tobacco smoke, the presence of an attached garage and the proximity of heavily trafficked roads can also affect indoor CO levels.
A recent UK study has shown typical 1-week average CO concentrations to reach 2.7 mg/m$^3$ (2.4 ppm) in the kitchens of homes where there was gas cooking, compared with 0.9 mg/m$^3$ (0.8 ppm) in kitchens where there was no gas cooking. Continuous monitoring has indicated maximum 1-hour averages of 1.9–24.5 mg/m$^3$ (1.7–21.4 ppm) in homes with gas cooking; much higher peak levels of around 180 mg/m$^3$ (160 ppm) for a 15-minute average have been associated with the use of a gas cooker grill.

Poorly installed, inadequately ventilated or malfunctioning appliances and accidentally blocked flues can also contribute to increased CO levels. Even in a sample of only 14 UK homes, a maximum 1-hour concentration of 57.0 mg/m$^3$ (49.8 ppm) was recorded in the kitchen of one home in which the boiler was malfunctioning. It is apparent that existing air quality guidelines* are likely to be exceeded in a number of UK homes. While it is not statistically valid to extrapolate the data from the small study of 14 homes in the UK to the overall situation in the UK, there is an obvious cause for concern.

**Exposure to CO is normally evaluated in terms of percentage of carboxyhaemoglobin (COHb) in the blood, but the validity of COHb as a biomarker of health effect is open to question. Although hypoxia, arising from preferential binding of CO to haemoglobin, is thought to be the main toxic mechanism by which CO acts, binding of CO to other blood components and enzymes may also play a part in its toxicity. A role in promoting atherosclerosis has been postulated for CO, although conclusive evidence is lacking, and immunological function and neurotransmission have also been investigated as possible targets for CO toxicity.**

Carbon monoxide is an important pollutant with respect to likely health effects following exposure in the home. While many of the published clinical investigations of CO intoxication in the home originate outside the UK, this does not limit their applicability. There may be differences in the types of cooking and heating appliances used but the health effects of the CO emitted from them will be broadly the same. Accidental exposures leading to acute, and sometimes fatal, health effects are well documented. Clinical reports of CO intoxication following exposure to high levels of CO have shown consistent symptoms such as headache, nausea and dizziness in the majority of patients. However, these symptoms are

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* The current World Health Organization guidelines for CO are 100 mg/m$^3$ for 15 minutes, 60 mg/m$^3$ for 30 minutes, 30 mg/m$^3$ for 1 hour and 10 mg/m$^3$ for 8 hours.
easily confused with those of other ailments, such as food poisoning or influenza, and missed or misdiagnoses of CO intoxication can therefore occur.

Numerous and varied observations have been made of the health effects of CO in controlled exposure studies. These indicate that exposure to CO can cause performance decrements in certain neuropsychological tasks and that some people, primarily sufferers of cardiovascular disease, may be more susceptible to low-level exposure to CO associated with COHb levels as low as 2%. However, the question of the COHb level at which cardiovascular indices do not differ from the norm has not been satisfactorily answered. Perhaps the most prudent conclusion to draw is that there is no threshold of effect in patients suffering cardiovascular disease.

Observed reductions in exercise duration in both healthy subjects and sufferers of cardiovascular disease are reversible on removal of the individual from the exposure source. However, few studies have measured performance during the recovery period.

**CONCLUSIONS**

The published evidence on health effects after domestic exposure points most to a hazard of acute CO intoxication from malfunctioning, unflued or poorly ventilated fuel burning appliances. It is also probable that in some homes CO levels routinely occur and persist that might possibly give rise to chronic health effects, particularly among sensitive groups (pregnant mothers, the fetus, children, the elderly and individuals suffering from anaemia and other diseases that restrict oxygen transport). Significant symptoms are generally experienced, even among normal healthy individuals, following exposure to CO concentrations high enough to produce COHb levels of about 20%. A great deal of importance would be attached to CO concentrations producing COHb levels above 10%, especially in sensitive individuals.

Although there is limited information from epidemiological studies on the health effects of CO at the low levels typically found in homes, the risk of adverse effects in healthy individuals as a result of exposure to CO in the home is thought to be low under normal circumstances (i.e. where appliances are installed and operated correctly). Nonetheless, it is prudent to continue to encourage measures which minimise CO levels, with particular attention being paid to gas combustion and other fuel-burning, especially unflued, appliances.
It is also essential to increase awareness of the symptomatology of CO intoxication among health care professionals and others to whom the public look for advice and assistance. Leaving a patient in, or returning them to, a situation from which adverse health effects might develop is unacceptable and, with vigilance, need not occur.

**MAIN RESEARCH RECOMMENDATIONS**

- More studies, primarily aimed at evaluating CO levels among representative samples of UK homes, are needed to ascertain the variability of indoor CO levels across the UK and in different types of housing.

- It would be prudent to develop strategies to ensure that representative samples of UK dwellings are included in future indoor air quality research programmes. The development of such strategies would be dependent on the specific objectives of each individual study, for example whether the research is aimed at determining the distribution of CO levels throughout the UK housing stock or whether it is aimed at targeting groups at high risk because of dwelling type or as a result of particular susceptibilities to CO exposure.

- More studies are required to determine the importance of indoor levels to overall personal exposure to CO, and particularly the significance of certain activities which may lead to high exposures. These studies should examine representative samples of the UK population and should employ methods such as relating fixed site monitoring to personal exposure measurements, questionnaire data and activity diaries. It would also be of value to investigate exposure to CO in susceptible populations such as expectant mothers and those suffering from cardiovascular disease.

- Alternative research approaches aimed at utilising new and existing data on CO exposure levels should be encouraged. Monte Carlo simulation modelling may provide a valuable means of improving the understanding of the predicted distribution of CO exposure levels in UK domestic environments.

- Studies aimed at assessing the relative contributions of various CO sources and confounding factors to indoor CO levels should be encouraged. It would seem appropriate at this stage to attempt a detailed assessment of
the prevalence of malfunctioning fuel-burning appliances in relation to high levels of CO in UK homes and to assess the relative costs and benefits of remediating the problem if one is identified.

☐ Studies are required that combine measurements of indoor CO levels, personal exposure measurements, levels of CO in expired breath samples and related levels of COHb. The use of other, indirect means for determining exposure should also be explored, for example questionnaires, medical histories, biochemical parameters and so on. Comparison of measurement methods (single point CO level versus personal exposure studies versus breath analysis of CO and thereby COHb level) could also be performed.

☐ Studies aimed at assessing the extent and level of peak CO concentrations should be encouraged. The development and validation of models relating the magnitude and frequency of peak levels to mean levels and other factors such as CO sources, housing characteristics, ventilation methods and individuals’ activity should be undertaken.

☐ Further study of long-term, low-level exposure to CO is required. Studies should be encouraged which assess the long-term CO levels typically found in UK homes. It would also be of value if the relative contributions of different CO sources to extended periods of low levels of CO in the home could be evaluated. Data obtained from such studies could usefully feed into investigations assessing the potential health effects in individuals who spend large amounts of time in the home environment.

☐ Analysis of donors’ blood COHb level, in combination with a simple questionnaire probing smoking status, occupation, basic health status, and seeking limited socioeconomic information, could be performed. This would help define the normal range of COHb levels in the UK population among healthy, adult smokers and non-smokers.

☐ Mechanisms of CO toxicity warrant further study, especially the possible consequences of CO acting as a transmitter substance and its possible involvement in vascular physiology.

☐ Studies aimed at defining more closely the relationship between COHb, exposure duration and symptom severity are required.
A more structured approach to the controlled chamber assessment of health effects should be adopted in the UK in which variables such as COHb measurement, equipment type, quality assurance procedures, testing procedures and end-points are defined and a set protocol used across study groups. This approach would produce data that could more easily be compared between groups and would help in defining dose–response relationships and thresholds of effect for CO. The recovery period following exposure as COHb levels return to normal also warrants study.

Further studies of the relationship between CO exposure and development of atherosclerosis are required.

Studies, perhaps involving occupational exposures, which examine repeated exposure to CO at levels similar to those found in UK homes, are required. The health effects investigated could be both neuropsychological and cardiovascular in nature.

It is necessary to design neuropsychological studies of CO exposure effects with specific goals in mind. For example, a better understanding is needed of the effect of CO on 1) monitoring and vigilance, 2) divided attention tasks, and 3) more complex information processing tasks. It may be useful to review the neuropsychological effects encountered in acute poisonings and determine from these the types of effects that can result from CO intoxication.

In order to assess whether CO poisoning is missed or misdiagnosed, a study of patients presenting to general practitioners and accident and emergency departments with non-specific but potentially CO related symptoms is recommended. Samples of breath could serve as a clinical diagnostic tool. (A limitation in such a study is that COHb levels may have fallen between exposure and presenting to a medical practitioner.) A relative risk scoring system could be developed to aid in determining which individual’s symptoms are more likely to be related to CO exposure.

More systematic studies aimed at investigating CO reducing factors should be undertaken. Examination of the potentially beneficial effects of the use of extractor hoods or fans in the kitchen on reducing CO levels would be of particular value owing to the link between high CO levels in the kitchen and gas cooking activity.
1 General introduction

BACKGROUND

A large proportion of people’s exposure to air pollutants occurs indoors, particularly in the home. While much is known about ambient air and workplace exposure, far less attention has been paid to the domestic environment.

Indoor air pollutants are derived from the infiltration of contaminated air from outdoors, from specific indoor sources such as combustion appliances, building materials and consumer products and from human metabolic processes. The activities and behaviour of individuals, such as cigarette smoking and painting, can influence the production and levels of indoor air pollutants. In addition, the design of a building, the provision of ventilation and the types of appliances installed can all have an impact on the levels of air pollutants in the home.

The UK Department of the Environment, Transport and the Regions (DETR) commissions research to support the development of policies on indoor air quality and the provision of appropriate information and advice. This review on carbon monoxide (CO) by the Institute for Environment and Health (IEH) was commissioned by the DETR as part of a wider research programme aimed at evaluating the risks to health and well-being from exposure to various pollutants in the home. An earlier report, commissioned under the same programme, was published by IEH in May 1996 and provided an assessment of the health effects of domestic exposure to nitrogen dioxide, formaldehyde, volatile organic compounds, house dust mites and fungi and bacteria (IEH, 1996). The present review on CO in the home is a part of the second phase of the programme which also includes environmental tobacco smoke and particulates in the domestic environment.
OBJECTIVES

This review assesses the level and extent of exposure to CO in the home and the resulting risks to the health and well-being of occupants.

This assessment incorporates:

- a review of published data on the sources of CO in the home and concentration and exposure measurements with a view to determining relevant domestic exposure ranges;
- a review of published health effects assessments to help determine the impact on health and well-being of exposure to CO at the relevant concentrations;
- an evaluation of the likely impact of exposure of people in their homes, taking into account relevant susceptible groups such as children, pregnant mothers, the elderly and those suffering from pre-existing disease such as coronary artery disease;
- recommendations for future research on exposure measurement and health impact assessment;
- suggestions for measures that may be taken to control indoor sources of CO and that may help to reduce exposure; and
- information relevant to the provision of guidance to the public about CO exposure in the home and its likely health effects.

THE REVIEW AND EVALUATION PROCESS

In order to produce an up-to-date, balanced and peer-reviewed assessment, a background review document, produced with the guidance of a small expert steering group, was subjected to thorough review and evaluation by a group of experts in the field at a workshop hosted by IEH in June 1997. The initial review document was based largely on published literature identified using recognised sources such as online databases including MEDLINE, TOXLINE, EMBASE, BIOSIS, NTIS, Scisearch and Occupation Safety and Health (NIOSH).
Although the principal aim is to assess indoor air quality in UK homes, outdoor studies, studies from other countries, controlled chamber studies and occupational exposure studies are included where they provide relevant information. While the majority of papers considered here have been subject to peer review, other literature, for example conference papers, has been used if it includes useful data.

**STRUCTURE OF THE REVIEW**

The report is structured to provide a comprehensive review of the scientific literature on CO exposure and related health effects.

In Section 2, levels of CO in indoor air, air quality guidelines, acceptable exposure limits and regulatory arrangements are considered. A review of various investigations relating to CO levels and exposure in the domestic environment is presented along with personal exposure studies. This section concludes with an evaluation of the literature on exposure in UK homes.

The third section of the review explores the relationship between CO exposure and carboxyhaemoglobin (COHb) and includes information on the methods used to measure COHb. Some of the difficulties in bridging the gap between empirical exposure data, obtained from air quality studies, and potential health effects are discussed.

Section 4 presents a review of the health effects of exposure to CO. The introduction is followed by a section that describes the general toxicology of CO. Clinical case reports and other studies are then presented to provide information on the symptoms and characteristics of CO exposure indoors. This highlights the question of susceptible groups within the population and the problematic diagnosis of CO intoxication. Next, controlled chamber studies assessing the effect of CO on the brain, heart and other systems are reviewed. The section concludes with an evaluation of the health effects.

Section 5 draws together considerations about the exposure and potential health effects of CO. Various risk situations for the domestic environment in the UK are discussed and interpreted in terms of the probable consequences to health for the UK population as a whole, as well as for particular susceptible groups.
The last section presents a final evaluation in the form of overall conclusions, and includes the identification of pertinent knowledge gaps with recommendations for future research in the field. Recommendations for relevant measures to control and reduce exposure to CO in UK homes, and for information and advice to be provided to the public, are also presented.

Throughout this review, units of CO concentration are expressed as mg/m$^3$, with ppm in parenthesis, regardless of the original units reported. Where conversion factors have been applied the following have been used: 1 ppm = 1.145 mg/m$^3$ at 25°C and 1013 millibars (1mg/m$^3$ = 0.873 ppm; WHO, 1987). Where the original measurements were reported in both mg/m$^3$ and ppm, they are reproduced here as in the original, irrespective of the conversion factor used. Where original measurements are expressed in µl/l, a conversion factor of 1.166 at 25°C and 1013 millibars is applied (molar volume of a gas at 298K and 1 atm = 24 dm$^3$).

**KEY ISSUES**

**THE ANALYSIS OF INDOOR AIR**

The evaluation of indoor air quality involves the collection, detection and measurement of representative samples of the pollutant in question from indoor air. These data can then be used to evaluate actual and potential exposures to the pollutant, and in turn recorded levels can be compared with other exposure situations or guidelines for exposure. Presented below are summaries covering the various monitoring strategies available for the study of pollutant exposure levels in indoor air, plus a brief discussion of the importance of averaging times in the interpretation of such studies.

**MONITORING STRATEGIES**

Monitoring strategies vary according to considerations such as time, location and available resources for measurement and analysis. The principal strategies for monitoring indoor air pollution and estimating exposure include instantaneous or real time monitoring, integrated or continuous monitoring and personal monitoring (Koren & Bisesi, 1996).
Instantaneous sampling typically refers to the collection of a sample over a short time period (usually less than 10 minutes) and is commonly used as a screening procedure to identify air contaminants and their related levels during the early stages of an indoor air quality study. Instantaneous strategies are also used to determine pollutant levels during specific processes, for instance when peak levels are anticipated. Sample collection and analysis are provided immediately via a direct-reading device; therefore the data represent pollutant levels at a specific time of monitoring (Koren & Bisesi, 1996).

Integrated or continuous monitoring involves the collection of a sample continuously over an extended time period (usually several hours or more). A single value representing an integration of all pollutant levels during the sampling period may be produced by allowing a sample to be run throughout the entire sampling period. Alternatively, several samples may be collected over the monitoring period, thereby providing information about fluctuations in pollutant levels at specific times and locations. In some cases individual samples may be combined and time weighted to provide a single overall time-weighted average for the whole sampling period. The primary advantage of integrated monitoring approaches is the provision of a single measure for the level of pollutant for a prolonged period of time (Koren & Bisesi, 1996).

Personal monitoring involves directly attaching an integrated monitoring device to an individual. Samples are, therefore, taken and recorded in specific locations and during specific activities. Personal monitoring allows for the measurement of pollutant concentrations in the microenvironments that people encounter, and the use of small personal exposure monitors has made possible large-scale human exposure field studies (EPA, 1991). It is worth noting that personal exposure monitoring can only give a measurement of pollutant concentrations in different microenvironments if a technique with a short sampling period is used. If a longer sampling time is employed, personal monitoring is limited to providing an integrated measurement over several microenvironments.

**AVERAGING TIMES AND THE MEASUREMENT OF AIR POLLUTANTS**

The toxicity of a particular chemical is, in part, a function of the interaction between concentration and duration of exposure. Therefore, the significance of exposure to pollutants on human health depends on both the concentrations to which people are exposed and the duration of that exposure (WHO, 1987;
Air quality standards and guidelines account for the importance of exposure duration through the use of averaging times which are, as much as possible, based on effects. For example, where knowledge is relatively complete about the exposure–response relationship, and it is known that the integral exposure is more important in terms of health effects than patterns of peak exposure, a long-term average may be recommended. The World Health Organisation (WHO) has stated that the rationale of air quality guidelines rests on the belief that “inhalation of an air pollutant in concentrations and for exposure times below a guideline value will not have adverse effects on health” (WHO, 1987).

The consideration of averaging times in any assessment of indoor or outdoor air quality is, therefore, of great importance and explicit reference should be made to the averaging times of all measurements recorded in a study. Depending on the objectives of the study this allows for:

- the meaningful comparison of levels with acceptable exposure limits and air quality guidelines for compliance considerations;
- meaningful comparison with other studies; and
- the assessment of particular exposure patterns (peak versus long-term average) in relation to health effects.

Any study which fails to make clear the averaging times of the measurements recorded is of limited value for the purposes of interpretation in relation to any of the considerations listed above.

**COMMENTS ON THE EVALUATION OF THE HEALTH EFFECTS OF INDOOR AIR POLLUTANTS**

In considering the possible consequences to health of exposure to indoor air pollutants it must be recognised that exposures generally, if not always, involve a mixture of pollutants. The evaluation of health effects is necessarily based on the assumption that exposure and health effects data are unaffected by simultaneous exposure to other contaminants. In reality, additive, synergistic or antagonistic interactions may well occur, affecting both the results and interpretation of studies. Such interactions are not necessarily obvious and may directly or indirectly affect the measurement or impact of exposure to mixtures of pollutants.
There is also uncertainty about the measurement technologies and sampling strategies employed, and for many pollutants the relative impacts of short-term peak versus long-term exposures are uncertain.

RELATING CARBON MONOXIDE EXPOSURE LEVELS TO HEALTH EFFECTS

A key issue is the link between CO exposure and likely health effects. Central to this is the use of COHb as a marker of exposure and predictor of health effects. This important relationship is discussed in Section 3.
2 Review of levels of carbon monoxide in indoor air
2.1 INTRODUCTION

The objective of this section is to review published data on the sources of CO in the home along with published concentration and exposure measurements, with a view to determining ranges of domestic exposure. Studies which relate to typical background levels in the domestic environment are reviewed first, followed by studies which provide information on peak and high background levels. Later sections cover issues relating to smoking and indoor CO levels, and to the exchange of indoor and outdoor air. Studies which have adopted personal exposure monitoring strategies are reviewed at the end of the section.

In addition to the studies examined in this report, a number of comprehensive reviews have been published covering CO concentrations in indoor air, CO exposure in the workplace and other buildings, emission studies and residential CO levels (e.g. Samet et al. 1987; Harrison et al. 1988; Lambert & Samet, 1989; Coultas & Lambert, 1991).

This section of the report deals only with the measurement of levels and exposure to CO. The various studies which have examined both exposure and health effects related to CO exposure are also discussed in detail in Section 4. Nonetheless, it is useful to note at this point that the health effects of CO are normally evaluated in terms of %COHb in the subjects’ blood; CO is currently the only air pollutant with such a specific and clinically relevant biologic marker that is a useful indicator of exposure (Coultas & Lambert, 1991). As well as COHb levels in the blood, the concentration of CO in expired breath also provides an indication of CO exposure. For the purposes of this report, it is considered that 1-hour and 8-hour averaging times provide the most useful measures of exposure for the assessment of human health effects.

Carbon monoxide is a colourless, odourless gas produced by the incomplete combustion of organic substances. Most combustion processes produce some CO, the amount depending on the availability of oxygen and the efficiency of the process. The main outdoor source of CO is petrol vehicle exhaust fumes. In the indoor environment, relevant combustion sources include gas-fuelled appliances, unvented space heaters, wood stoves and tobacco products. Exposure to high
levels of CO can lead to dizziness and headaches, lethargy, unconsciousness and even death, and there is some evidence that low levels may exacerbate conditions such as angina and have other subtle chronic effects (see Section 4). In the indoor environment, high concentrations of CO are usually associated with the operation of combustion appliances in poorly ventilated rooms or of damaged or badly installed or badly maintained appliances.

Natural background levels of CO range between 0.01 and 0.23 mg/m$^3$ (0.009–0.2 ppm; WHO, 1994). In urban traffic environments the 8-hour mean concentrations are higher, but generally less than 20 mg/m$^3$ (17.5 ppm) and in the UK 1-hour average concentrations of CO in outdoor air usually do not exceed 29 mg/m$^3$ (25 ppm; EPAQS, 1994).

As most people spend a considerable amount of time indoors, levels of CO inside the home can have a significant impact on personal exposure levels (although particular subgroups such as commuters and those working in certain occupations may be more affected by outdoor levels). In UK homes with CO sources such as gas cookers, peak concentrations of up to 60 mg/m$^3$ (52.4 ppm; the WHO air quality guideline for a 30-minute exposure to CO) have been recorded (Burr, 1995), and in other cases much higher peak levels have been associated with malfunctioning combustion appliances. However, long-term CO concentrations are generally much lower. In other indoor microenvironments in which internal combustion engines are operated with insufficient ventilation, mean levels of CO can rise to above 115 mg/m$^3$ (100.4 ppm) for prolonged periods, with much higher short-term values.

**GUIDELINES**

Since the publication of the *Air Quality Guidelines for Europe* in 1987, the WHO has produced revised Guidelines for the main air pollutants in line with advances in scientific knowledge and new developments in risk assessment methodologies. For CO these revisions did not result in any changes to the original 1987 levels. Therefore, the current WHO Guidelines for CO remain at 100 mg/m$^3$ for 15 minutes, 60 mg/m$^3$ for 30 minutes, 30 mg/m$^3$ for 1 hour and 10 mg/m$^3$ for 8 hours exposure (WHO, 1994), based on health effect considerations. Table 2.1 summarises several national and international air quality standards and guidelines for CO. There is a noticeable consistency between most of these national standards for CO, probably indicating that the mechanisms and levels of effect are better understood than for many other air pollutants.
Table 2.1 Some air quality standards and guidelines for carbon monoxide in mg/m$^3$
(ppm)

<table>
<thead>
<tr>
<th>Country/Organisation</th>
<th>Averaging time</th>
<th>Concentration$^a$</th>
<th>Comments</th>
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<tbody>
<tr>
<td>WHO</td>
<td>15 min</td>
<td>100 (90)$^b$</td>
<td>Ambient and outdoor</td>
</tr>
<tr>
<td></td>
<td>30 min</td>
<td>60 (50)$^b$</td>
<td>air quality</td>
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<tr>
<td></td>
<td>1 h</td>
<td>30 (25)$^b$</td>
<td></td>
</tr>
<tr>
<td></td>
<td>8 h</td>
<td>10 (9)$^b$</td>
<td></td>
</tr>
<tr>
<td>UK (EPAQS)</td>
<td>8 h</td>
<td>11.5 (10)</td>
<td>Ambient air quality</td>
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<td>US EPA</td>
<td>1 h</td>
<td>40 (35)</td>
<td>Ambient air quality</td>
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<tr>
<td></td>
<td>8 h</td>
<td>10 (9)</td>
<td>Ambient air quality</td>
</tr>
<tr>
<td>ASHRAE$^c$</td>
<td>8 h</td>
<td>10 (9)</td>
<td>Recommended standard for indoor air</td>
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<td>Canada</td>
<td>2 h</td>
<td>26 (23)</td>
<td>Ambient air quality</td>
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<tr>
<td></td>
<td>8 h</td>
<td>14 (12.6)</td>
<td>Ambient air quality</td>
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<td>Sweden</td>
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<td>40 (35)</td>
<td>Threshold limit value</td>
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<td>Finland</td>
<td>1 h</td>
<td>30$^d$ (25)</td>
<td>Ambient air quality</td>
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<td></td>
<td>8 h</td>
<td>10$^d$ (9)</td>
<td>Ambient air quality</td>
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<td>Poland and the former USSR</td>
<td>2 h</td>
<td>2.3 (2)</td>
<td>Ambient air quality</td>
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<td></td>
<td>8 h</td>
<td>1.5 (1)</td>
<td>Ambient air quality</td>
</tr>
<tr>
<td>Japan</td>
<td>1 h</td>
<td>11.5 (10)</td>
<td>Building sanitation management standard</td>
</tr>
<tr>
<td></td>
<td>2 h</td>
<td>23 (20)</td>
<td>Ambient air quality</td>
</tr>
<tr>
<td></td>
<td>8 h</td>
<td>11.5 (10)</td>
<td>Ambient air quality</td>
</tr>
<tr>
<td>Korea</td>
<td>1 month</td>
<td>9 (8)</td>
<td>Ambient air quality</td>
</tr>
<tr>
<td></td>
<td>8 h</td>
<td>23 (20)</td>
<td>Ambient air quality</td>
</tr>
<tr>
<td></td>
<td>8 h</td>
<td>11.5 (10)</td>
<td>Indoor air environmental standard</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Underground spaces</td>
</tr>
<tr>
<td>Saudi Arabia</td>
<td>1 h</td>
<td>40 (35)$^b$</td>
<td>Ambient air quality</td>
</tr>
<tr>
<td></td>
<td>8 h</td>
<td>10 (9)$^b$</td>
<td>Ambient air quality</td>
</tr>
</tbody>
</table>

From Ritchie & Oatman (1983); Lambert & Samet (1989); Rowe et al. (1989); EPA (1991); Alm et al. (1994), EPAQS (1994); Lambert & Samet (1994); Ström et al. (1995); Arashidani et al. (1996); Rogers & Saffell (1996); Sohn (1996)

$^a$ Guidelines and standards originally reported as ppm unless otherwise indicated; values in mg/m$^3$ have been calculated using a conversion factor of 1 ppm = 1.145 mg/m$^3$

$^b$ Guideline or standard originally reported as both ppm and mg/m$^3$. Different conversion factors may have been used and approximations made

$^c$ ASHRAE: American Society of Heating, Refrigeration and Air Conditioning Engineers

$^d$ Guideline or standard originally reported as mg/m$^3$ only
UK REGULATIONS

The safety aspects relating to the installation and use of gas appliances are largely governed by the Gas Safety (Installation and Use) Regulations 1994\(^a\) as twice amended by the Gas Safety (Installation and Use) (Amendment) Regulations 1996\(^b\). These regulations revoke previous controls specified under the Gas Safety (Installation and Use) Regulations 1984 and the Gas Safety (Installation and Use) (Amendment) Regulations 1990\(^c\).

Under the regulations, persons may not carry out work in relation to a gas fitting unless they are adequately trained and experienced and are a member of an approved body, namely CORGI (the Council for Registered Gas Installers). Any person involved in the installation of a gas appliance must ensure that they are familiar with the appropriate standards for gas fittings and that the materials they use are to those standards. Most gas appliances are subject to the requirements of the Gas Appliances (Safety) Regulations 1995\(^d\), and may carry a recognised standard mark.

With regard to existing gas fittings, the regulations are designed to ensure that any alterations to premises where gas appliances are fitted do not detrimentally affect the safety of the gas fitting, its flue or means of ventilation. Any alterations to the premises must take into account changes which may affect ventilation, including changes to windows, air bricks and extractor fans. The regulations also cover the possible effects of double glazing or cavity wall insulation on ventilation efficiency.

A gas appliance and its associated fittings must be installed and maintained in such a way as to ensure its safe use. In particular, the supply of a permanent and sufficient amount of air must be available to safeguard proper combustion and the installer must take into account room size, presence of double glazing, and location of air bricks and vents to ensure that the space where the appliance is fitted is adequately ventilated. Equally, installers must ensure the adequacy and effectiveness of any flue to which an appliance is fitted.

With regard to the maintenance of gas appliances, businesses (including landlords) are duty bound to ensure that each appliance is checked annually by a competent person registered with CORGI. A proper record concerning the maintenance of the gas appliance has to be kept and made available to tenants.

\(a\) SI 1994/1886  
\(b\) SI 1996/550 and SI 1996/2541  
\(c\) SI 1984/1358 and SI 1990/824  
\(d\) SI 1995/1629
At the point of manufacture, safety aspects of all gas appliances (excluding those intended for industrial purposes), including portable ones, are governed by the Gas Appliances (Safety) Regulations 1995 which implements the European Union (EU) Gas Appliance Directive. The UK regulations are implemented primarily through the use of safety standards, most of which are now EU harmonised. The standards impose requirements for the safe installation and use of gas appliances and frequently include instructions to users.

**SOURCES OF INDOOR CARBON MONOXIDE**

As CO is one of a number of air pollutants emitted from combustion sources into indoor air, the determination of emission rates (mass of pollutant per unit of fuel input) of CO from combustion appliances is useful, for example:

- as a guide to the design of an indoor air monitoring strategy;
- as an input for indoor air modelling;
- as an aid to the ranking of important indoor sources; and
- in the development of effective risk management strategies.

Emissions of CO in the domestic environment may be classified as accidental or as resulting from the intentional use of combustion devices. Accidental emissions may result from the improper use of combustion appliances and from faulty flues and appliances; other non-intentional sources include the ingress of polluted air from attached garages or from the outdoor environment. Ventilation efficiency is important; for example, the spillage of combustion products (mainly carbon dioxide) from an appliance operating under poor ventilation conditions in a room or compartment may be great enough to affect the efficient operation of the appliance, which in turn may lead to elevated emissions of CO. This type of process, known as vitiation, may be caused by the downdrafting of combustion products as a result of inadequate ventilation measures, or in some cases by extreme weather conditions whereby the fluid dynamics of a usually efficient flue system may be adversely affected. Accidental emissions can lead to very high indoor CO levels which may result in acute and sometimes fatal health effects.

The sources of indoor CO and emission rates of CO have been extensively reviewed by the US Environmental Protection Agency (EPA; EPA, 1991).
Although the types of appliances used in the USA may differ from those in the UK, the overall factors affecting emission rates are broadly similar. The key conclusions from the EPA are therefore relevant and are summarised below.

- Most CO emissions come from the intentional use of partially vented or unvented combustion appliances such as gas cookers and other appliances including water heaters, unvented gas space heaters, unvented kerosene heaters and wood- or other solid-fuel-burning appliances.

- Emissions of CO from gas cookers and other appliances may be evaluated by direct sampling of emitted combustion gases as they pass through a quartz hood above the source or by the mass-balance or chamber approach. The latter involves the examination of changes in CO concentration over time in relation to outdoor concentrations, source emission rates, air exchange rates and pollutant removal rates. For gas hobs, emission rates of CO are generally assessed using a standard water load in a cooking pan. Emission rates of CO from gas cookers and other appliances are dependent on a number of factors such as the source type (e.g. number of pilot lights and burner design), condition of the appliance (e.g. age and maintenance), use patterns (e.g. frequency and length of use) and ventilation efficiency.

- CO emissions are highly variable between gas cookers as well as between individual burners on the same appliance. Operating a gas cooker with an improperly adjusted flame can lead to very high emission rates (up to and above a fivefold increase compared with a properly adjusted flame). Emissions are generally comparable for hobs, ovens and pilot lights and between sampling techniques.

- Emissions from unvented gas space heaters are very variable, but tend to be comparable with gas cooker emissions. Infrared gas space heaters produce higher emissions than convective or catalytic appliances. For unvented kerosene space heaters, radiant appliances produce higher emissions than convective appliances. For these types of sources, the wick setting has a significant effect with a low setting producing the highest CO emission rates.

- Fewer data are available for wood- and other solid-fuel-burning appliances. It is, however, likely that non-airtight wood burning stoves and fireplaces may produce substantial amounts of CO compared with airtight appliances. Tobacco smoking is also a source of indoor CO with emission rates varying between tobacco brands and with the total number of cigarettes smoked.
The EPA review concludes that owing to the high variability in emission rate data, further work is necessary to develop a fuller understanding of the factors affecting CO emissions. It also points to the paucity of emission rate data available for the residential setting. Such data tend to be more variable and to indicate higher rates than those measured in chamber or test house studies.

Levels of CO of potential importance to health may be produced even by a well functioning gas appliance, particularly when operated in a poorly ventilated building. For example, a flame touching a surface cooler than the ignition temperature of the gaseous portion of the flame can result in the production of CO: the temperature of water-filled coils in a water heater cannot rise appreciably above the boiling point of water and a flame playing on these coils may emit substantial quantities of CO. Thus situating even a properly functioning heater in a poorly or insufficiently ventilated room may lead to elevated levels of CO (Hamilton & Hardy, 1974; Thomsen & Kardel, 1988).

Some data obtained from tests conducted on a range of appliances commonly used in UK homes are presented below (Table 2.2). The concentrations of CO are those measured in the combustion products from the appliances, which would either pass through flues to the open air or, in the case of a grill and some sink water heaters, be diluted by the ventilation of the room. All measurements were made using non-dispersive infrared instruments under laboratory conditions with the appliances being operated in the same manner as they would in a domestic situation.

<table>
<thead>
<tr>
<th>Appliance</th>
<th>Approximate CO concentrations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inset fuel effect fire</td>
<td>115–286 (100–250)</td>
</tr>
<tr>
<td>Surface combustion grill</td>
<td>143 (125)</td>
</tr>
<tr>
<td>Floor mounted combi boiler</td>
<td>52–172 (50–150)</td>
</tr>
<tr>
<td>Sink water heater</td>
<td>27 (25)</td>
</tr>
<tr>
<td>Back boiler unit</td>
<td>27 (25)</td>
</tr>
<tr>
<td>Gas front fire to back boiler unit</td>
<td>11 (10)</td>
</tr>
<tr>
<td>Floor mounted open flue boiler</td>
<td>&lt;11 (&lt;10)</td>
</tr>
<tr>
<td>Box radiant fire</td>
<td>&lt;11 (&lt;10)</td>
</tr>
</tbody>
</table>

Data supplied by the UK Health and Safety Executive
2.2 MEASUREMENT DEVICES FOR CARBON MONOXIDE

The studies presented in the next section (Section 2.3) have employed a variety of sampling strategies and a number of different measurement devices, primarily indicator tubes, electrochemical detectors and infrared analysers. In some cases the devices were operated under passive diffusion controlled conditions, while in others active sampling methods were employed whereby air is pumped through the CO measuring device. The accuracy and precision of the measurements recorded vary, and are largely determined by the type of measuring device and calibration procedures used. Whichever method or instrument is used, it is essential that the results are validated by frequent calibration with samples of known composition similar to the unknowns. A brief summary is given below describing the analytical basis of the various measuring devices used in the studies reviewed and their relative accuracies.

INDICATOR TUBES

These devices operate on the basis of colorimetric analysis and include, for example, Dräeger diffusion tubes and Shepard type colorimetric indicating tubes. Indicator tubes may be of two types — ‘length of stain’ indicator or colorimetric tubes. Both types are based on a sealed glass tube filled with a chemically coated solid sorbent impregnated with an appropriate chemical reagent. Concentrations of CO in the sampled air are then calculated according to the length of stain or the intensity and shade of colouration. While these techniques are simple and inexpensive, they are open to interference by other gases and are, therefore, relatively imprecise, with a typical accuracy of ± 25% (EPA, 1991; Koren & Bisesi, 1996). In the case of Dräeger diffusion tubes, errors of up to ± 50% for long-term exposure measurements may arise (Ross, personal communication).
ELECTROCHEMICAL DETECTORS

Many studies have used electrochemical detectors to measure indoor levels of CO under both passive and active sampling conditions. The device used most frequently in the studies summarised in this review is based on the production of an electrical current in an aqueous solution by the electrochemical oxidation of CO to CO$_2$ at a noble metal electrode (EPA, 1991). The concentration of CO reaching the electrode is dependent on its rate of diffusion through a permeable membrane, which in turn is determined by the CO concentration in the sampled air. The electrical current generated by the reaction is proportional to the concentration of CO in the sampled air. Measurements obtained using this method are generally very sensitive and selective. However, interference may be caused by a range of substances including acetylene, ethylene, hydrogen, ammonia, nitric oxide, nitrogen dioxide and sulphur dioxide. In the studies (which provided clear information on precision and relative accuracy) reviewed in the following section, precision for electrochemical methods varied between 0.2 and 2.3 mg/m$^3$ (0.2 ppm and 2.0 ppm) with a relative accuracy between ± 6.6% and ± 15%. Personal exposure monitors generally work on the electrochemical basis and usually have a small pump which sends air actively onto the sensing cell and chemical filters, as well as removing any interfering chemicals (EPA, 1991).

INFRARED ANALYSERS

Methods which utilise the non-dispersive infrared technique are generally accepted as the most reliable measurement method for CO (EPA, 1991); CO is detected by absorption of a discrete wavelength of infrared light. Absorption is proportional to the concentration of CO in the sampled air (Koren & Bisesi, 1996). Modern non-dispersive infrared instruments include the gas filter correlation technique which is able to detect minimum concentrations of 0.05 mg/m$^3$ (0.04 ppm). These devices tend to be relatively insensitive to flow rates, require no wet chemicals, are sensitive over wide concentration ranges and have short response times. (It should, however, be noted that older non-dispersive infrared devices may be open to interference by water vapour).
2.3 CARBON MONOXIDE LEVELS AND EXPOSURE IN THE HOME

2.3.1 TYPICAL LEVELS OF CARBON MONOXIDE IN THE HOME

Studies which provide information on background levels of CO in the home are reviewed in this section. Data that help to address typical ranges in background CO concentrations and factors that may affect these levels are presented. Information from UK studies is summarised along with studies from other countries that provide pertinent information.

In a pilot study for a nation-wide investigation into factors affecting health and health attitudes among the UK population, CO levels in the breath and indoor air of a sample of 168 adults were taken in their own homes (Cox & Whichelow, 1985). The sample was randomly selected to represent the socioeconomic distribution of the UK population. Subjects comprised 86 men and 82 women aged between 18 and 74 years and were selected from the electoral registers of Bristol and Bury St Edmunds using a stratified randomised procedure. Measurements of CO were made using a battery-powered portable Ecolyzer (a type of electrochemical CO monitor) with samples generally being collected in the subject’s living room. Information about the type of home heating systems was noted.
Ambient CO levels in the subjects’ homes ranged from 0 to 48.1 mg/m$^3$ (0–42 ppm) [sampling and averaging times not given] with the higher levels found in homes with radiant gas fires, wood fires, coal or wood stoves or paraffin heaters. The lower concentrations were almost always recorded in homes with non-CO-generating (non-combustion) heating appliances.

Background CO levels in UK homes were also measured as part of an assessment of the impact of a mechanical ventilation and heat recovery system on house dust mite numbers in the homes of asthmatics (Wiech & Raw, 1995). Four different intervention strategies — the presence or absence of a mechanical ventilation and heat recovery system, and the use or not of a high efficiency vacuum cleaner — were assessed in 40 homes, each including at least one asthmatic patient. The homes were monitored for temperature, humidity, CO, nitrogen dioxide, volatile organic compounds and house dust mite numbers.

Dräeger passive diffusion tubes, placed in the kitchen, living room, one individual’s bedroom and outside, were used to measure CO levels. Sampling was conducted on three occasions immediately before intervention and was intended to continue for four occasions immediately following intervention. The exact length of time for which each of the tubes was exposed was calculated for each of the three readings, taken approximately 3, 8 and 14 days in each monitoring period. Levels of CO immediately before (October 1994) and immediately after (November 1994) intervention was initiated were compared, as an experimental control procedure. All indoor readings were below 3.4 mg/m$^3$ (3 ppm). Comparison of the average measurements before and after intervention revealed that the installation of a mechanical ventilation and heat recovery system had no effect on CO levels in the kitchen, but there was a small but statistically significant reduction in the levels recorded in the living room (p<0.005) and bedroom (p<0.01).

Similar background CO levels were also recorded in a recent study by Ross (1996) when continuous and passive monitoring of CO in homes in the UK was conducted. The study aimed to provide data on peak levels and integrated exposure to various indoor air pollutants, and also investigated the impact of mechanical ventilation such as cooker extractor hoods on the levels of indoor combustion products.

Fourteen homes were monitored over a period of 1 week: six had gas cooking appliances only, two had electric cooking appliances only and six had both gas and electric cooking appliances. Eight of the homes used gas for cooking in
conjunction with an extractor hood or fan in the kitchen. Levels of CO were monitored using an EIT Sensor-Stik continuous electrochemical detector for passive sampling in the kitchen, living room and bedroom, and Dräger direct-reading colorimetric diffusion tubes, also in the kitchen, living room and bedroom. Questionnaire data were collected concerning home layout, methods of cooking, heating and ventilation measures as well as actual cooking activities. Experimental measurements from the study are presented in Table 2.3 and frequency distributions of weekly and peak measurements taken in homes with gas appliances are shown in Figures 2.1 and 2.2. Typical 24-hour exposure profiles for a home with gas only appliances (Home B) and a home with electricity only appliances (Home C) are shown in Figures 2.3 and 2.4.

Weekly average CO levels were calculated using recordings taken by both methods of sampling. In gas cooking homes the average levels in the kitchen ranged from 0.3 to 2.7 mg/m³ (0.3–2.4 ppm) for the electrochemical detector and from 0.2 to 1.9 mg/m³ (0.2–1.7 ppm) for the Dräger tubes. For measurements in the living room of gas cooking homes, CO levels ranged between 0.2 and 2.5 mg/m³ (0.2–2.2 ppm) for the electrochemical detector and 0.2 and 0.9 mg/m³ (0.2–0.8 ppm) for the Dräger tubes, and in the bedroom levels were 0.5–2.1 mg/m³ (0.4–1.8 ppm) for the electrochemical detector and 0.2–1.1 mg/m³ (0.2–1.0 ppm) for the Dräger tubes. It should be noted that the measurements recorded in Home I are omitted from these ranges. High background CO levels in this home were associated with a faulty boiler, as discussed in the next section.

A number of studies conducted elsewhere, in Italy and the USA, have recorded similar background levels of CO to those measured in the limited number of UK studies. In a survey of 60 flats in a building block in Parma, Italy, measurements were made to assess residential levels of radon and CO in an attempt to gain an insight into the way in which the gases accumulated in the domestic environment (Malanca et al., 1993). Using a gas filter correlation analyser, CO was measured in samples taken from the kitchen on two separate occasions [specific sampling and averaging times not given].

Mean values of the two CO measurements were used for statistical calculations; where high values were recorded measurements of CO were also taken in the lounge and bedrooms of the same home. The overall average CO concentration was 3.3 mg/m³ (2.9 ppm); average concentrations of CO in homes with gas stoves were higher (3.9 mg/m³; 3.4 ppm) than in homes with furnace radiator systems (2.6 mg/m³; 2.3 ppm). Generally, high concentrations in the kitchen were associated with high levels in the other two rooms sampled. The types of windows
Table 2.3 Continuous and passive sampling of carbon monoxide in mg/m³ (ppm) in 14 UK homes

<table>
<thead>
<tr>
<th>Home</th>
<th>Fuel</th>
<th>Room</th>
<th>Electrochemical CO measurements</th>
<th>Dräger tube</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Max. 1-minute average (±5%)</td>
<td>Max. 1-hour average (±5%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Weekly average (±5%)</td>
<td>Weekly average (±50%)</td>
</tr>
<tr>
<td>B</td>
<td>G</td>
<td>K</td>
<td>49.3 (43.1)</td>
<td>18.9 (16.5)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>L</td>
<td>7.1 (6.2)</td>
<td>6.0 (5.2)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>B</td>
<td>17.2 (15.0)</td>
<td>9.4 (8.2)</td>
</tr>
<tr>
<td>D</td>
<td>G</td>
<td>K</td>
<td>10.9 (9.5)</td>
<td>7.9 (6.9)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>L</td>
<td>12.4 (10.8)</td>
<td>10.9 (9.5)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>B</td>
<td>13.5 (11.8)</td>
<td>10.8 (9.4)</td>
</tr>
<tr>
<td>F</td>
<td>G</td>
<td>K</td>
<td>6.0 (5.2)</td>
<td>1.9 (1.7)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>L</td>
<td>4.2 (3.7)</td>
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<td></td>
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<td>B</td>
<td>12.4 (10.8)</td>
<td>4.6 (4.0)</td>
</tr>
<tr>
<td>H</td>
<td>G</td>
<td>K</td>
<td>24.0 (21.0)</td>
<td>10.3 (9.0)</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td>B</td>
<td>9.0 (7.9)</td>
<td>7.9 (6.9)</td>
</tr>
<tr>
<td>M</td>
<td>G</td>
<td>K</td>
<td>15.5 (13.5)</td>
<td>6.6 (5.8)</td>
</tr>
<tr>
<td></td>
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<td>8.5 (7.4)</td>
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</tr>
<tr>
<td></td>
<td></td>
<td>B</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>N</td>
<td>G</td>
<td>K</td>
<td>13.3 (11.6)</td>
<td>9.3 (8.1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>L</td>
<td>8.8 (7.7)</td>
<td>3.5 (3.1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>B</td>
<td>3.2 (2.8)</td>
<td>3.1 (2.7)</td>
</tr>
<tr>
<td>A</td>
<td>G/E</td>
<td>K</td>
<td>13.9 (12.1)</td>
<td>7.7 (6.7)</td>
</tr>
<tr>
<td></td>
<td></td>
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<td>5.3 (4.6)</td>
<td>4.1 (3.6)</td>
</tr>
<tr>
<td>G</td>
<td>G/E</td>
<td>K</td>
<td>9.5 (8.3)</td>
<td>5.7 (5.0)</td>
</tr>
<tr>
<td></td>
<td></td>
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<td></td>
<td>B</td>
<td>5.6 (4.9)</td>
<td>5.3 (4.6)</td>
</tr>
<tr>
<td>J</td>
<td>G/E</td>
<td>K</td>
<td>68.5 (59.8)</td>
<td>57.0 (49.8)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>L</td>
<td>121.4 (106.0)</td>
<td>29.5 (25.8)</td>
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<td></td>
<td></td>
<td>B</td>
<td>20.3 (17.7)</td>
<td>16.9 (14.8)</td>
</tr>
<tr>
<td>I</td>
<td>G/E</td>
<td>K</td>
<td>15.0 (13.1)</td>
<td>9.8 (8.6)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>L</td>
<td>3.9 (3.4)</td>
<td>3.2 (2.8)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>B</td>
<td>3.7 (3.2)</td>
<td>3.4 (3.0)</td>
</tr>
</tbody>
</table>
which were installed in the home were recorded to assess whether window type (double glazed or old wooden frame) affected the accumulation of CO in the dwelling. Double glazed windows were shown to have a moderate but statistically insignificant effect on CO levels.

In a US study designed to determine normal levels of CO in the home in non-summer months, urban and rural households were examined in Colorado during 1975 (Rench & Savage, 1976). In total 80 households were involved in the study (60 urban and 20 rural) and CO measurements were taken in the family room and the kitchen as well as outside the home. A Model Series 2000 Ecolyzer was used to determine CO levels [sampling and averaging times not given]. The study also collected data on types of heating systems, age of house and various socioeconomic factors. Visits for monitoring purposes were made between 17:00 h and 19:30 h. The final results were analysed as a mean CO concentration and as an adjusted value, by subtracting outdoor levels from the indoor measurements. Unadjusted figures were

### Table 2.3 (continued)

<table>
<thead>
<tr>
<th>Home</th>
<th>Fuel</th>
<th>Room</th>
<th>Electrochemical CO measurements</th>
<th>Dräger tube</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Max. 1-minute average (±5%)</td>
<td>Max. 1-hour average (±5%)</td>
</tr>
<tr>
<td>K</td>
<td>G/E</td>
<td>K</td>
<td>30.3 (26.5)</td>
<td>16.7 (14.6)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>L</td>
<td>25.2 (22.0)</td>
<td>6.5 (5.7)</td>
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<td></td>
<td></td>
<td>B</td>
<td>24.8 (21.7)</td>
<td>3.3 (2.9)</td>
</tr>
<tr>
<td>L</td>
<td>G/E</td>
<td>K</td>
<td>26.2 (22.9)</td>
<td>24.5 (21.4)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>L</td>
<td>7.1 (6.2)</td>
<td>6.6 (5.8)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>B</td>
<td>4.5 (3.9)</td>
<td>4.1 (3.6)</td>
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<td>C</td>
<td>E</td>
<td>K</td>
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<td></td>
<td></td>
<td>B</td>
<td>1.9 (1.7)</td>
<td>1.7 (1.5)</td>
</tr>
<tr>
<td>E</td>
<td>E</td>
<td>K</td>
<td>3.5 (3.1)</td>
<td>3.3 (2.9)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>L</td>
<td>2.9 (2.5)</td>
<td>2.4 (2.1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>B</td>
<td>2.7 (2.4)</td>
<td>2.6 (2.3)</td>
</tr>
</tbody>
</table>

From Ross (1996), additional data provided by the Building Research Establishment

- a All homes located in suburban areas. Homes B and D are flats, all others are two-storey houses
- b E, electricity; G, gas
- c B, bedroom; K, kitchen; L, living room
- d Additional unpublished data for maximum 1-hour averages supplied by the Building Research Establishment
- e High levels of CO recorded in this home were associated with the operation of a faulty boiler

levels in indoor air
Figure 2.1 Frequency distributions of weekly average carbon monoxide measurements (mg/m$^3$) for twelve UK homes.
Figure 2.2 Frequency distributions of maximum 1-hour average carbon monoxide measurements (mg/m³) for twelve UK homes

From Ross (1996) and additional data provided by the Building Research Establishment
Figure 2.3 Carbon monoxide exposure profile (24-hour) for a gas cooking appliance home

Data provided by the Building Research Establishment
Figure 2.4 Carbon monoxide exposure profile (24-hour) for an electricity cooking appliance home

- **a** Kitchen
- **b** Living room
- **c** Bedroom

Data provided by the Building Research Establishment
useful to assess human exposure and health effects, whilst the authors considered that adjusted figures were needed for comparisons between subsamples.

No significant differences were observed between the rural and urban dwellings. For both unadjusted and adjusted figures, CO levels were consistently higher in the kitchen than in the family room, across all groups, and in all cases the recorded outdoor levels were lower than those found inside the home in either room. The mean unadjusted value of ambient CO in the kitchen across all groups was 3.5 mg/m$^3$ (3.1 ppm) and in the family room 2.9 mg/m$^3$ (2.5 ppm). Critical analysis of factors such as the contribution of heating system and age of house to CO levels proved to be difficult, as these potential determinants were not uniformly distributed throughout the rural and urban socioeconomic groups, making it hard to separate the confounding factors. However, it was clear that homes with wall space heaters tended to have significantly higher levels of CO in both the kitchen and the family room (p<0.10).

Hawthorne et al. (1986) described a study on a range of indoor pollutants, including CO, in 40 homes in Tennessee. Carbon monoxide measurements were taken during a warm-weather period (April–July 1982) and a winter period [dates not reported]. Active sampling was used to monitor CO, during a single visit (approximately 6 hours in duration), using an instrument incorporating an electrochemical sensor with a detection limit of 1.2 mg/m$^3$ (1 µl/l)*. Information on the characteristics of the homes, fuel types and insulation measures was also collected.

Concentrations of CO during the warm-weather period were generally low and frequently around the level of detection of 1.2 mg/m$^3$ (1 µl/l). Monitoring protocols for this phase were modified to concentrate on a comparison between homes with combustion appliances and those without. Single-day measurements were conducted in ten homes with potential CO sources and ten control homes with no such source. Continuous monitoring was undertaken using an electrochemical voltametric detector. Unfortunately, the CO monitor used was sensitive to temperature changes, but based on the readings that were valid, levels of CO were not significantly increased during the winter measurement phase.

Further work on the effect of combustion appliances on residential air pollutant levels was conducted by Leaderer et al. (1984). A case–control field study aimed to assess pollutant exposures and acute health effects associated with the use of kerosene space heaters in over 150 homes. The homes, located in Connecticut,

* The authors reported levels in µl/l rather than ppm
were monitored during January to April 1983. Levels of CO were monitored in a selection of homes during a 2-week period in which measurements were made in the living room, bedroom and outdoors.

Continuous CO monitoring took place in 14 homes (13 with kerosene space heaters and one without but with a gas cooker) with a range of continuous sampling times of between 43 and 209 hours and heater use of between 9 hours 30 minutes and 67 hours 30 minutes [specific sampling and averaging times not given]. Levels of CO were almost always below 10 mg/m$^3$ (8.7 ppm) with only one residence recording levels above this. The concentrations at the two indoor sampling locations were generally similar, suggesting rapid mixing of the pollutant throughout the residence.

Principal sources of indoor CO were again evaluated by Lebowitz et al. (1984) in Tucson, Arizona. The main purpose of the study was to appraise the interaction between indoor and outdoor exposures in relation to health in an epidemiological study. Duplicate, and highly correlated, grab bag samples and a Bendix CO Infrared analyser were used to measure CO in the home. The measurements were conducted for 72 hours on one occasion in each home during a period of 2 years. Subjects also provided details about the residence and types of heating and cooking systems used in the home.

Concentrations of CO tended to be low, with averages of the two indoor spot readings generally around 2.7 mg/m$^3$ (2.4 ppm). Outdoor readings were lower than 4.4 mg/m$^3$ (3.8 ppm) and analysis showed that indoor CO was significantly correlated with that of outdoor CO ($r = 0.6$, $p<0.003$). Analysis also revealed that indoor CO was associated with gas cooker use (borderline $0.05<p<0.10$), but not with environmental tobacco smoke, gas burning furnaces, hot water heaters or washer/dryer appliances.

A positive correlation between gas cooker use and CO levels in the home was also identified in a study by Stock et al. (1984) which involved a field survey of indoor air quality in 164 mobile homes in Texas. Indoor and outdoor environmental sampling was conducted for a range of air pollutants, including CO, typically over a 7-hour period of continuous monitoring. Indoor samples were taken in the living room and CO was measured using a dual-sensor electrochemical monitor.

Average indoor CO levels of 1.6 mg/m$^3$ (1.4 ppm; SD 1.5 mg/m$^3$ or 1.3 ppm) were recorded, with 94% of the homes having concentrations below 4.0 mg/m$^3$ (3.5 ppm). For all the homes monitored the average CO concentrations for those
using gas cookers were two to three times higher than corresponding outdoor levels. This finding was supported by another study designed to appraise interactions between indoor and outdoor exposures to CO in which it was revealed that while indoor levels of CO tended to be low, they were frequently higher than those found outside during many times of the day (Lebowitz et al., 1984). Interestingly, Stock et al. (1984) observed that even homes using electric appliances tended to exhibit higher CO levels than outdoor, although the magnitude of the difference was less. This suggested the presence of other CO sources in addition to domestic fuel-burning appliances in mobile homes.

SYNOPSIS

The key findings of studies which have examined issues relating to typical background levels of CO in the domestic environment are presented in Table 2.4.

Background levels of CO in UK homes are generally in the range of about 0.3–2.7 mg/m³ (0.3–2.4 ppm), although these figures are based on limited data. Factors affecting background CO levels include the presence of combustion appliances, location and time of day (for example, background levels in the kitchen are frequently higher than elsewhere in the home, particularly with gas cooking activity) and the exchange of indoor and outdoor air. Because of the limited data for the UK domestic environment, a number of other studies have been considered. Data from these suggest similar background levels in the home, with the majority of measurements ranging from 1.1 to 4.0 mg/m³ (1–3.5 ppm).

2.3.2 PEAK AND HIGH BACKGROUND LEVELS OF CARBON MONOXIDE IN THE HOME

This section concentrates on studies which provide information on peak levels and high background concentrations of CO in the home. Data for the UK which help to address issues relating to high exposures, such as the conditions which may lead to short-term and, in some cases, longer-term elevated levels of CO, are presented. Other studies which provide information relevant to these considerations are also summarised.
### Table 2.4 Summary table of typical background carbon monoxide levels in mg/m³ (ppm) in the home

<table>
<thead>
<tr>
<th>Study reference &amp; country</th>
<th>Measurement</th>
<th>CO levels</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cox &amp; Whichelow (1985) UK</td>
<td>CO detected and measured by a portable Ecolyzer in the living room</td>
<td>0–48.1 (0–42)</td>
<td>Higher levels recorded in homes with combustion appliances, lower levels in homes with non-CO-generating heating appliances</td>
</tr>
<tr>
<td>Wiech &amp; Raw (1995) UK</td>
<td>CO detected and measured by Dräeger passive diffusion tubes in the kitchen, living room and bedroom</td>
<td>All readings below 3.4 (3)</td>
<td>Installation of a MVHR had no effect on CO levels in the kitchen but was related to small reductions in CO levels in the living room and bedroom</td>
</tr>
<tr>
<td>Ross (1996) UK</td>
<td>Weekly average measurements by electrochemical detector and Dräeger passive diffusion tubes</td>
<td>CO levels*, electrochemical detector</td>
<td>Differences in measurements due to differences in instrument precision and accuracy</td>
</tr>
<tr>
<td>Malanca et al. (1993) Italy</td>
<td>CO detected and measured by gas filter correlation analyser in kitchen</td>
<td>Overall average</td>
<td>Higher concentrations in kitchen were generally associated with high levels in lounge and bedroom</td>
</tr>
<tr>
<td>Rench &amp; Savage (1976) USA</td>
<td>CO detected and measured by Ecolyzer</td>
<td>Mean CO level, unadjusted figures</td>
<td>No significant differences between urban and rural homes</td>
</tr>
</tbody>
</table>

#### Total CO levels

<table>
<thead>
<tr>
<th>Kitchen</th>
<th>Family room</th>
<th>Outside</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>3.5 (3.1)</td>
<td>2.9 (2.5)</td>
</tr>
<tr>
<td>Rural</td>
<td>2.2 (1.9)</td>
<td>2.2 (1.9)</td>
</tr>
<tr>
<td>Urban</td>
<td>4.0 (3.5)</td>
<td>3.4 (2.7)</td>
</tr>
</tbody>
</table>

#### Socioeconomic group

<table>
<thead>
<tr>
<th>Socioeconomic group</th>
<th>Upper</th>
<th>Middle</th>
<th>Lower</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2.1 (1.8)</td>
<td>3.3 (2.9)</td>
<td>6.8 (5.9)</td>
</tr>
<tr>
<td></td>
<td>1.9 (1.7)</td>
<td>2.3 (2.0)</td>
<td>4.9 (4.3)</td>
</tr>
<tr>
<td></td>
<td>1.0 (0.9)</td>
<td>1.3 (1.1)</td>
<td>0.8 (0.7)</td>
</tr>
</tbody>
</table>

Note: (*) refers to electrochemical detector and Dräeger passive diffusion tubes.
**Table 2.4 (continued)**

<table>
<thead>
<tr>
<th>Study reference &amp; country</th>
<th>Measurement</th>
<th>CO levels</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hawthorne <em>et al.</em> (1986) USA</td>
<td>CO detected and measured by electrochemical instrument</td>
<td>All levels around 1.1 (1.0)</td>
<td>CO levels similar for both summer and winter time monitoring</td>
</tr>
<tr>
<td></td>
<td>40 homes in Tennessee</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leaderer <em>et al.</em> (1984) USA</td>
<td>Continuous CO monitoring in living room, bedroom and outside</td>
<td>All measurements except one were below 10 (8.7)</td>
<td>CO levels were similar for all sampling locations in the home</td>
</tr>
<tr>
<td>Lebowitz <em>et al.</em> (1984) USA</td>
<td>CO detected and measured by grab bag samples and COIR analyser</td>
<td>Average indoor spot levels, 2.7 (2.4) All outdoor levels, &lt;4.4 (3.8)</td>
<td>Weak positive correlation between indoor and outdoor CO levels</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Very weak association between gas stove use and indoor CO levels</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>No relationship between indoor CO levels and environmental tobacco smoke or other combustion appliances</td>
</tr>
<tr>
<td>Stock <em>et al.</em> (1984) USA</td>
<td>Continuous CO measurement by electrochemical instrument</td>
<td>Average, 1.6 (1.4) 94% &lt;4.0 (3.5)</td>
<td>Gas cooker homes had CO levels 2 to 3 times higher than outdoors</td>
</tr>
<tr>
<td></td>
<td>164 mobile homes in Texas</td>
<td></td>
<td>All homes tended to have higher indoor CO levels than outdoor ones, including all electric homes</td>
</tr>
</tbody>
</table>

COIR, carbon monoxide infrared; MVHR, mechanical ventilation and heat recovery system

* Levels measured in Home I not included
In a limited research programme covering five homes in the UK, the effect of cooker type on indoor CO levels was examined in three homes, two with gas cookers (sites 1 and 3) and one with only electric appliances (Site 2; Stevenson, 1985). In the other two homes the effect of heating with unflued appliances was examined. Measurements were made in the kitchens at sites 1–3 using an Ecolyzer 2000 series electrochemical CO monitor. The measurements (based on 15-minute averages) were all taken whilst the homes were in normal use, and the occupants kept a diary of when specific appliances were used.

At Site 1, all peak CO concentrations in the kitchen were directly related to gas cooker use with a characteristic pollution pattern of sharp rises in CO whenever the cooker was in use. Typically these peaks ranged between approximately 10.3 mg/m³ and 22.9 mg/m³ (9–20 ppm). Levels decayed quite quickly once the cooker ceased to be in use, although background levels remained above those expected for the outdoor environment. The author suggested that the relatively high background level in the kitchen was associated with the continuous use of five pilot lights on the cooker in question. However, the study gave no indication whether any CO measurements were made with the pilot lights turned off, making it difficult to draw any firm conclusions. Gas was used for central heating via a back boiler in the living room, where a gas fire was also operated, and these may also have contributed to the raised background levels of CO in this home.

At Site 3 the data suggested that only the gas cooker (rather than central and water heating systems) had a discernible effect on indoor CO levels, with peak concentrations exclusively associated with cooking activity. In this home, peak levels ranged from approximately 10.3 to 182 mg/m³ (9–160 ppm). Particularly high peaks were associated with the use of the grill. In contrast to Site 1, background levels were similar to those expected outside at this location. This could possibly be explained by the absence of pilot lights on the cooker.

The all-electric home had much lower CO levels than those expected in the outdoor environment at that location. No noticeable peaks were recorded and all measurements were below 10.3 mg/m³ (9 ppm).

It should be noted that conclusions drawn from this study are based on a limited number of measurements which may not be typical of the UK as a whole. Nonetheless, the evidence suggests, as do other studies covered in this report, that cooking with gas can produce CO concentrations that exceed those typical of outdoor air.
In the study conducted by Ross (1996; detailed in the previous section), analysis showed that gas cooking was the most important source of peak CO concentrations in the home, with one exception (Home I), which was associated with the use of a faulty boiler. Peak CO measurements were usually recorded in the kitchen at times of cooking activity and tended to be two to three times higher than normal background (range of peak levels in the kitchen for homes with gas cookers 6.0–49.3 mg/m³ (5.2–43.1 ppm) for maximum 1-minute averages or 1.9–24.5 mg/m³ (1.7–21.4 ppm) for maximum 1-hour averages). Peak levels in the living room and bedroom were usually lower than in the kitchen (Home I is omitted from these ranges). In Home I with the faulty boiler, two large peaks were observed: 68.5 mg/m³ (59.8 ppm) for maximum 1-minute averages or 57.0 mg/m³ (49.8 ppm) for maximum 1-hour averages in the kitchen, and 121.4 mg/m³ (106 ppm) for maximum 1-minute averages or 29.5 mg/m³ (25.8 ppm) for maximum 1-hour averages in the living room. The lowest peak levels were recorded in the two homes which used only electricity for cooking; 4.0 mg/m³ (3.5 ppm) kitchen, 2.3 mg/m³ (2.0 ppm) living room, 1.9 mg/m³ (1.7 ppm) bedroom and 3.5 mg/m³ (3.1 ppm) kitchen, 2.9 mg/m³ (2.5 ppm) living room and 2.7 mg/m³ (2.4 ppm) bedroom for maximum 1-minute averages (see Table 2.3). All peak levels except for the house with the faulty boiler were below the WHO recommended guidelines for CO.

The contributions of certain combustion appliances in the home to peak and raised indoor CO levels have also been identified by a number of studies conducted elsewhere in Europe and in the USA. Very high levels of up to 700 mg/m³ (600 µl/l)* were recorded in homes with geysers in the Netherlands (Brunekreef et al., 1982). In this study the CO production potential of geysers (an instantaneous water heater usually located in the kitchen, often connected to the shower and generally not directly vented to the outside) was established. At the time of the study, 70% of Dutch homes made use of such heating devices. Homes (n = 254) in two Dutch cities, Arnhem and Enschede, were investigated during November and December 1980. Enschede was unusual at the time as it had a special maintenance system in operation which provided servicing to about 80% of the geysers in the city. Arnhem was more typical of the Netherlands as a whole with a smaller provision of servicing operations.

Measurements of CO were made in the home using an Ecolyzer 2000 monitor at breathing height (1.5 m), and the experimental procedure involved simulating normal geyser use patterns by operating it for 15 minutes. Measurements were

* The authors reported levels in µl/l rather than ppm
made immediately before and after the geyser was operated and again 15 minutes after the geyser had been switched off [specific sampling and averaging times not given]. Analysis revealed that a larger percentage of homes in Arnhem had levels of CO above 29.2 mg/m³ (25 µl/l) than homes in Enschede. Across both cities, a level of 58.3 mg/m³ (50 µl/l) was exceeded in 17% of cases (50 µl/l represented the Installation Code Standard for domestic geysers at the time). In some cases a level of more than 700 mg/m³ (600 µl/l) was recorded. The presence of a vent and the type of burner were both found to affect levels of CO at breathing height. In 3% of the cases, water heaters with a flue produced CO concentrations above 29.2 mg/m³ (25 µl/l), while 50% of the homes in which unvented geysers with a primary aerated burner were in use had CO levels in excess of 29.2 mg/m³ (25 µl/l). Although geysers are not in common use in UK homes now, these results may have important implications for possible delayed health effects of long-term exposures to high CO levels for individuals who have previously lived in homes which were fitted with geysers.

Lebret et al. (1987) conducted a study using real-time measurements to determine the transient peak concentrations of CO and nitrogen dioxide in relation to the use of unvented gas appliances. Levels of CO were measured using a dual-range Ecolyzer 2000 monitor in 12 homes in a suburban area of the Netherlands. Samples for CO measurement were drawn from three indoor locations (kitchen, bedroom and living room) and one outdoor location. Thermocouples were used to monitor the use of the cooking range and geyser in the homes. The indoor locations were sampled eight or nine times an hour and outdoor samples were taken once an hour. The measurements were conducted over periods of between 135 and 273 hours.

Maximum 1-minute average CO levels ranged from 5 to 108 mg/m³ (4.4–94.3 ppm) in the kitchen, 4 to 28 mg/m³ (3.5–24.4 ppm) in the living room and 4 to 48 mg/m³ (3.5–42 ppm) in the bedroom. Maximum 1-hour averages ranged from 3 to 56 mg/m³ (2.6–48.9 ppm) in the kitchen, 2 to 26 mg/m³ (1.7–22.7 ppm) in the living room and 1 to 26 mg/m³ (0.9–22.7 ppm) in the bedroom. Overall mean CO levels outdoors were almost always lower than levels recorded in the homes. Analysis of CO levels against time of day in the three sampling locations showed the presence of sharp peaks in CO levels in the kitchen when gas appliances were in use. These peak patterns were reflected in the living room and bedroom but were of smaller magnitude.

The contribution of combustion appliance use in the home was also highlighted in the study in Parma, Italy by Malanca et al. (1993; detailed in previous section)
[specific sampling and averaging times not given] where the highest instantaneous CO concentrations were recorded in two homes where gas heating systems were operated (15.8 mg/m$^3$ and 14.6 mg/m$^3$; 13.8 and 12.7 ppm). It was noted, however, that the latter reading was taken from a home where the stovepipe valve was closed. The lowest instantaneous measurement of 0.2 mg/m$^3$ (0.2 ppm) was recorded in a flat with a furnace; slightly higher levels (0.7 mg/m$^3$; 0.6 ppm) were recorded in other homes with furnace radiator heating systems.

Moriske et al. (1996) conducted a study in Germany to investigate the effects of different domestic heating systems on indoor air pollution, including CO levels. Carbon monoxide levels were measured in 16 homes during the winter heating period and also during the non-heating summer period. The sample comprised seven coal-burning homes, one with an open wood-burning fireplace, and eight centrally heated homes. All homes were inhabited by non-smokers. Measurements were taken during a 3-week period in the winter and a 2-week period in the summer. During the monitoring periods normal living conditions were documented, such as the structural condition of the home and ventilation measures. Measurements of CO were made indoors using an automatic monitor recording 30-minute values.

Maximum CO concentrations recorded were consistently higher in homes with coal- or wood-burning heating systems than in those with central heating. However, one exception was noted in a centrally heated home where levels reached 64.1 mg/m$^3$ (56 ppm). These levels were associated with a central heating stove in the basement of the block of flats in which the home was located which had a malfunctioning exhaust system.

Elevated levels of CO were recorded by Schaplowsky et al. (1974) in an early survey conducted between November 1972 and March 1973, which attempted to define the extent and nature of long-term exposure to low levels of CO in the living environment across the USA. With the cooperation of 25 local public health authorities, residential air samples were taken from dwellings randomly selected from high risk neighbourhoods. In the same study blood samples were taken from children attending day centres, schools and health centres in the neighbourhoods. Issues relating to health effects in this study are detailed and discussed in Section 4.

Measurements of CO were made using Shepard-type colorimetric indicating tubes placed in locations in a total of 1820 homes where there were fuel-burning appliances [sampling and averaging times not given]. In 16.8% of the homes CO
levels were above 11.5 mg/m³ (10 ppm) in at least one area in which a fuel-burning appliance was located. Elevated CO concentrations of around 229 mg/m³ (200 ppm) were reported in a number of dwellings.

In a continuation of the above study, monitoring was extended over 1974 and 1975 to investigate the incidence and nature of CO poisonings and identify criteria that could be used to predict the incidence of such poisonings (Pattenaude et al., 1976). Levels of CO were measured, using either a Bendix Gastic pump with length of stain tubes or an MSA colorimetric CO tester [sampling and averaging times not given]. An ambient air measurement was made in each home, and for each individual fuel-burning appliance CO was monitored at a point 3 feet from the front of the appliance at waist height. Results of the study indicated that while water heaters and furnaces were the least likely appliances to produce elevated levels of CO, when they did they tended to produce the highest average levels (246.2 mg/m³ (215 ppm) and 144.3 mg/m³ (126 ppm) respectively). Conversely, the kitchen cooker was the most likely appliance to produce elevated levels of CO but the levels emitted tended to be lower (77.9 mg/m³; 68 ppm).

Lao et al. (1982) investigated levels of CO associated with wood stove use and other fuel-burning appliances in 27 homes in Craven County, North Carolina. The results indicated, as have others, that residential CO concentrations were correlated with the general condition of the house and the heating system used. Levels were higher in houses in poor general condition and also in those using wood-burning heaters as opposed to gas- or oil-fuelled appliances. Heating systems were switched on for a 24-hour period and measurements made in the primary living areas. The highest concentrations [specific sampling and averaging times not given for peak measurements] of CO were 27.5 mg/m³ (24.0 ppm) but most homes showed peak values of under 11.5 mg/m³ (10.0 ppm). Most peak values were of short duration, lasting between 10 minutes and 1 hour.

The effects of gas cooker use on indoor levels of CO was also investigated by Goldstein et al. (1988). Measurement of real-time CO concentrations during a simulated cooking cycle was made using an Ecolyzer Model 2000 CO monitor. From the time the gas was turned on measurements were made in sequence at heights of 15, 91, 168 and 229 cm from the floor for 2.5 minutes. Three cycles were conducted in this manner covering a total period of 30 minutes. A final cycle of measurements was made (1 minute each) from 36–40 minutes after start up, after which the gas was turned off. The results confirmed that elevated CO levels were associated with gas cooker use in the home. The average level of CO at breathing height 30 cm from the gas cooker while it was in operation was
approximately 16 mg/m$^3$ (14 µl/l)* compared with an average baseline level of 1.7 mg/m$^3$ (1.5 µl/l). Levels of CO began to fall off approximately 15 minutes after the cooker was shut off.

SYNOPSIS

The key findings relating to peak and high background levels of CO are summarised in Table 2.5.

From the limited amount of data available for the UK, it is clear that the use of gas cookers and unflued heating appliances plays a major role in determining patterns of peak CO levels in the home. Recorded peak levels in the kitchens of UK homes with gas cookers range from 1.9 to 24.5 mg/m$^3$ (1.7–21.4 ppm) for 1-hour averages and levels of up to 183.2 mg/m$^3$ (160 ppm) for a 15-minute average have been recorded, with the highest levels associated with the use of a gas grill. The presence of malfunctioning appliances may also lead to high peak concentrations. For example, maximum 1-minute average levels of 121.4 mg/m$^3$ (106 ppm) were measured in the living room of a home where a faulty boiler was in operation. In UK homes fitted with electrical appliances only, no noticeable peaks have been recorded and all maximum levels have been below 10.3 mg/m$^3$ (9 ppm).

Because of limited data for the UK, other studies have been considered. These also highlight the contribution of combustion appliances, unflued appliances and malfunctioning appliances to peak and high background levels of CO in the home. In some of the studies which considered the impact of heating systems on CO levels, it was observed that levels even higher than those associated with gas-fuelled heating systems were linked to coal and wood burning.

* The authors reported levels in µl/l rather than ppm
Table 2.5 Summary table of typical peak and high background carbon monoxide in mg/m³ (ppm) levels in the home

<table>
<thead>
<tr>
<th>Study reference &amp; country</th>
<th>Measurement</th>
<th>CO levels</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stevenson (1985) UK</td>
<td>Ecolyzer electrochemical measurement</td>
<td>Peak ranges for kitchen measurements</td>
<td>Author suggested pilot lights on gas cooker contributed to high background levels of CO at Site 1</td>
</tr>
<tr>
<td></td>
<td>Five homes as follows:</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Sites 1 &amp; 3 gas cooker (kitchen measurement)</td>
<td>Site 1 10.3–22.9 (9–20)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Site 2 all electric (kitchen measurement)</td>
<td>Site 3 10.3–183.2 (9–160)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Site 4 paraffin heater (living room measurement)</td>
<td>Site 4 &lt;10.3 (&lt;9)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Site 5 butane heater (living room measurement)</td>
<td>Site 5 10.3–183.2 (9–160)</td>
<td></td>
</tr>
<tr>
<td>Ross (1996) UK</td>
<td>Measurement of maximum levels using electrochemical detector</td>
<td>Ranges of peak levels, 1-min average</td>
<td>Gas cooking was the most important source of peak CO levels, except in the home with the faulty boiler</td>
</tr>
<tr>
<td></td>
<td>14 homes in the UK</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>G</td>
<td>Kitchen 6.0–49.3 (4.2–12.4)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>E</td>
<td>Living room 3.5–4.0 (2.3–2.9)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>G&amp;E</td>
<td>Bedroom 9.5–30.3 (6.3–26.5)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Home with faulty boiler</td>
<td>(8.3–26.5) (2.3–22.0)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(5.2–43.1) (3.7–10.8)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(3.1–3.5) (2.0–2.5)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(1.7–2.4)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(11.6–30.3) (7.9–25.2)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(6.3–26.5) (2.3–22.0)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(3.7–24.8)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(3.2–21.7)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(68.5)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(59.8)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(121.4)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(106)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(20.3)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(17.7)</td>
<td></td>
</tr>
<tr>
<td>Brunekreef et al. (1982)</td>
<td>Electrochemical measurement of CO following use of a geyser</td>
<td>Frequency distribution of CO levels at breathing height</td>
<td>The presence of a vent and type of burner strongly affected CO levels</td>
</tr>
<tr>
<td>The Netherlands</td>
<td>254 homes in two Dutch cities</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>CO level</td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td></td>
<td>&lt;11.6 (&lt;10 µl/l)</td>
<td>154</td>
<td>63</td>
</tr>
<tr>
<td></td>
<td>12.8–58 (11–50 µl/l)</td>
<td>50</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>59.2–116 (51–100 µl/l)</td>
<td>25</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>&gt;116 (&gt;100 µl/l)</td>
<td>17</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>missing values</td>
<td>8</td>
<td>–</td>
</tr>
<tr>
<td>Study reference &amp; country</td>
<td>Measurement</td>
<td>CO levels</td>
<td>Comments</td>
</tr>
<tr>
<td>--------------------------</td>
<td>-------------</td>
<td>-----------</td>
<td>----------</td>
</tr>
<tr>
<td>Lebret et al. (1987)</td>
<td>Real-time measurement by electrochemical and monitoring of cooker and geyser use</td>
<td>Maximum 1-minute averages</td>
<td>Overall mean CO levels were generally lower than outdoor levels</td>
</tr>
<tr>
<td>The Netherlands</td>
<td></td>
<td>Kitchen 5-108 (4.4-94.5)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Living room 4-28 (3.5-24.4)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bedroom 4-48 (3.5-42.0)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>12 homes in a suburban area</td>
<td>Maximum 1-hour averages</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Kitchen 3-56 (2.6-48.9)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Living room 2-26 (1.7-22.7)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bedroom 1-26 (0.9-22.7)</td>
<td></td>
</tr>
<tr>
<td>Malanca et al. (1996)</td>
<td>CO detected by gas filter correlation analyser in kitchen</td>
<td>Highest instantaneous level: home with gas heating 15.8 (13.8)</td>
<td>Levels of CO were not affected by presence of double-glazed windows</td>
</tr>
<tr>
<td>Italy</td>
<td></td>
<td>Lowest instantaneous level: home with furnace heating 0.2 (0.2)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>60 flats in a building block in Parma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moriske et al. (1996)</td>
<td>30-minute measurements with an automatic monitor</td>
<td>Maximum recorded level, 64.1 (56)</td>
<td>Maximum level was found in a centrally heated home affected by a malfunctioning central stove in a basement</td>
</tr>
<tr>
<td>Germany</td>
<td></td>
<td></td>
<td>CO levels were consistently higher in homes with coal or wood burning systems rather than centrally heated ones</td>
</tr>
<tr>
<td></td>
<td>16 homes during winter and summer</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Schaplowsky et al. (1974)</td>
<td>CO measurement with colorimetric indicating tubes</td>
<td>CO levels according to dwelling type</td>
<td>Elevated CO levels of up to 229 mg/m³ were recorded in a number of homes</td>
</tr>
<tr>
<td>USA</td>
<td></td>
<td>Type</td>
<td>% &gt; 11.5 (10.0)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Single</td>
<td>16.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Multiple</td>
<td>15.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mobile</td>
<td>24.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Other</td>
<td>23.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Total</td>
<td>16.8</td>
</tr>
</tbody>
</table>
### Table 2.5 (continued)

<table>
<thead>
<tr>
<th>Study reference &amp; country</th>
<th>Measurement</th>
<th>CO levels</th>
<th>Comments</th>
</tr>
</thead>
</table>
| Pattenaude *et al.* (1976) USA | Bendix Gastic pump with stain tubes or MSA colorimetric CO monitor Measurements taken in proximity to fuel-burning appliances | Average CO levels by fuel-burning appliance type  
Appliance % Appliances tested emitting CO | Kitchen oven = 36.4  
Space heater = 15.9  
Furnace = 3.4  
Water heater = 2.6 | Kitchen oven was the most likely appliance to produce elevated CO levels  
Furnace and water heaters were most likely to produce the highest levels |
| Lao *et al.* (1982) USA | CO measured in 27 homes with fuel-burning appliances | Maximum recorded levels, 27.5 (24.0)  
Most peaks were below 11.5 (10.0) | Most peaks were of short duration lasting for between 10 minutes and 1 hour  
Higher levels were associated with homes in general poor condition and also homes using wood burning appliances |
| Goldstein *et al.* (1988) USA | Real-time measurement by electrochemical detector during a simulated cooking cycle | Average background level ~1.7 (1.5 µl/l)  
Average levels associated with cooker use ~16 (14 µl/l) | CO levels began to decline following maximum levels approximately 15 minutes after the cooker was shut off |

E. electricity only; G. gas only; G&E, gas and electricity
Carbon monoxide is an important component of environmental tobacco smoke and a number of studies which have considered the effects of environmental smoke on indoor levels of CO are presented below.

In the study by Cox and Whichelow (1985; described in Section 2.3.1) the levels of CO in the breath and indoor air were investigated among a randomly selected sample of 168 smoking and non-smoking adults in the UK. Levels of CO in the breath of smokers ranged from 3.4 to 114.5 mg/m$^3$ (3–100 ppm), with 74% of smokers exceeding breath CO levels of 11.5 mg/m$^3$ (10 ppm). Levels in non-smoking individuals ranged from 2.3 to 68.7 mg/m$^3$ (2–60 ppm) with 79% recording levels below 6.9 mg/m$^3$ (6 ppm). It should be noted that the non-smoker with the highest breath CO level of 68.7 mg/m$^3$ (60 ppm) was excluded from further analysis because of occupational exposure to high CO levels through the use of gas welding equipment.

In non-smokers there was a close correlation ($r = 0.952$, $p<0.001$) between breath and ambient CO levels and in these cases it was observed that the type of domestic heating system could markedly influence ambient CO in the home. Analysis of measurements taken in environments where non-CO-generating heating appliances were in use demonstrated that smokers also contribute to indoor levels of CO (though to a lesser extent than CO-generating combustion appliances). For example, for non-CO-generating homes with non-smokers, CO levels never exceeded 4.6 mg/m$^3$ (4 ppm), whereas in a similar room with smokers 21% of the values were above this level with a range of 0–18.3 mg/m$^3$ (0–16 ppm). This difference was significant for the rooms of all smokers ($p<0.05$).

Kirk et al. (1988) conducted a study on environmental tobacco smoke levels in a range of smoking and non-smoking environments across Great Britain. The assessments were based on a number of pollutant measurements, including estimates of CO levels in work, home, leisure and travel situations. The study was conducted over three 10-week periods covering 2912 sampling sites across
Great Britain. Monitoring was fairly evenly distributed between the four situations: home (19%); work (25%); leisure (27%); and travel (29%).

CO was measured actively; each sampling event lasted for 30 minutes and CO readings were logged during this period every 2 minutes. Mean CO values for different activities in smoking and non-smoking environments (summarised in Table 2.6), indicate that there were no significant differences between smoking and non-smoking environments for any of the sampling situations (p>0.05), suggesting that indoor levels of CO are mostly determined by sources other than environmental tobacco smoke.

A moderate impact of tobacco smoking on indoor levels of CO in the Netherlands was identified by Lebret et al. (1987) who recorded slightly elevated CO levels in the living rooms of smokers when gas appliances were not in use. While the CO levels associated with the use of certain combustion appliances were higher than those associated with tobacco smoking activity, the results nonetheless suggested a small but noticeable impact of smoking on indoor levels of CO. This source is liable to be more important in some non-domestic (e.g. leisure) environments than in the home.

**SYNOPSIS**

It is difficult to draw any firm conclusions about the impact of the CO component of environmental tobacco smoke on the levels of CO in the home. However, from the limited data available, it is probable that the presence of tobacco smoke can cause slightly elevated levels of CO indoors, although other sources of CO are of greater significance.

---

### Table 2.6 Overall mean levels of carbon monoxide in mg/m³ (ppm) for particular sampling situations

<table>
<thead>
<tr>
<th>Sampling situation</th>
<th>Smoking environment</th>
<th>Non-smoking environment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CO level n</td>
<td>CO level n</td>
</tr>
<tr>
<td>Travel</td>
<td>3.3 (2.9) 283</td>
<td>3.1 (2.7) 235</td>
</tr>
<tr>
<td>Work</td>
<td>2.5 (2.8) 221</td>
<td>2.4 (2.1) 450</td>
</tr>
<tr>
<td>Home</td>
<td>2.6 (2.3) 139</td>
<td>2.1 (1.8) 549</td>
</tr>
<tr>
<td>Leisure</td>
<td>3.2 (2.8) 676</td>
<td>2.5 (2.2) 104</td>
</tr>
</tbody>
</table>

From Kirk et al. (1988)
2.3.4 CARBON MONOXIDE FROM VEHICLE EXHAUST AND THE EXCHANGE OF INDOOR AND OUTDOOR AIR

The exchange of indoor and outdoor air may influence levels of CO in the home and the presence of vehicle exhaust fumes in outside air or in an attached garage can lead to increased exposure to CO indoors. A number of studies which provide information on CO and the ingress of polluted outdoor air into the indoor environment are considered below.

The possible contribution of vehicle exhausts to CO exposure was identified by Kirk et al. (1988). In this study (detailed above), the highest mean CO levels (5.7–6.9 mg/m³; 5–6 ppm) were observed during car journeys. In non-smoking situations, statistical analysis revealed that higher CO levels were associated with travel, with concentrations significantly higher than those in home and work situations.

Other studies have indicated that ingress of polluted outdoor air can result in elevated indoor levels of CO. Field et al. (1992) found that during the December 1991 pollution episode in London, levels of CO inside an office building closely followed the recorded patterns of outdoor CO concentrations. Indoor CO levels were monitored continuously using a 2008-AH Dasibi instrument (which unfortunately gave intermittent readings due to a detector problem) and outdoor levels were recorded continuously using an APNA-35DE Horiba instrument. Prior to the pollution event, average indoor CO concentrations were 2.4 mg/m³ (2.1 ppm, SD 0.9 mg/m³); these were elevated to an average of 9.9 mg/m³ (8.6 ppm; SD 3.3 mg/m³) during the event (16.00h, 11.12.91 to 23.00h, 15.12.91). Average ambient CO levels were recorded as 2.0 mg/m³ (1.75 ppm; SD 0.9 mg/m³) prior to the onset of the pollution episode, increasing to 10.0 mg/m³ (9 ppm; SD 3.6 mg/m³) during the event. [When considering the data from this study, it should be borne in mind that the severity of the December 1991 pollution episode in London was particularly unusual.]
A number of US studies have provided empirical evidence to suggest that indoor levels of CO can be affected by the exchange of indoor and outdoor air and that the presence of vehicle exhaust fumes can play an important role in determining indoor levels. Hawthorne et al. (1986) observed that two houses located near a busy road had higher levels (<7.0 mg/m$^3$; <6 µl/l)* than other homes in the same study, suggesting an influx of outdoor air. Increased CO levels (1.2–19.8 mg/m$^3$; 1–17 µl/l) were also recorded in homes with a basement garage within which car engines had been running for 3 minutes. Figure 2.5 presents the predicted pattern of ambient CO levels with distance from a road.

Similar positive correlations between the presence of attached or underground garages and CO levels indoors have been recorded in other US studies. For example, Nagda et al. (1983) found elevated CO levels in offices with underground garages in Washington and Denver and Akland et al. (1985) found increased CO levels in homes with basement garages.

* The authors reported levels in µl/l rather than ppm.

Figure 2.5 Predicted pattern of ambient carbon monoxide concentrations with distance from a road

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levels associated with houses with attached garages in Washington. A study by Wallace (1983), which investigated CO levels in the air and the breath of employees in an underground office (with associated garage) in Washington, showed consistently elevated CO levels of between 13.7 and 25.2 mg/m³ (12–22 ppm).

Since 1972, measurements of hourly average CO concentrations have been performed with continuous analysers at fixed point locations in the UK. Monitoring data for selected UK sites are shown in Table 2.7. Since 1989 the geographical spread and size of the network has expanded considerably, and it currently covers 41 operational monitoring sites (Department of the Environment/Scottish Office, 1997). Although there is no clear evidence of a downward trend in urban CO concentrations, there are indications that rural concentrations are beginning to decrease. Lower outdoor levels are likely to be the result of increasingly stringent vehicle emission standards, although meteorological variability cannot yet be ruled out as a contributory factor.

A number of indoor air quality studies have included measurements of outdoor CO levels. On the basis of these studies the relationships between indoor and outdoor CO levels have been evaluated and are summarised in Table 2.8. Indoor CO concentrations are often higher than outdoor values, suggesting that the presence of combustion sources in the indoor environment is an important factor.

Table 2.7 Carbon monoxide monitoring data in mg/m³ (ppm) for calendar years 1990–1995 for selected UK sites

<table>
<thead>
<tr>
<th>Site</th>
<th>Year</th>
<th>Annual average</th>
<th>Maximum 1-hour average</th>
<th>Maximum 8-hour running average</th>
</tr>
</thead>
<tbody>
<tr>
<td>London,</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1990</td>
<td>3.3</td>
<td>(2.9)</td>
<td>21.1 (18.4)</td>
<td>17.7 (15.5)</td>
</tr>
<tr>
<td>Cromwell Road</td>
<td>1991</td>
<td>3.8 (3.3)</td>
<td>21.4 (18.7)</td>
<td>15.9 (13.9)</td>
</tr>
<tr>
<td>(kerbside)</td>
<td>1992</td>
<td>3.2 (2.8)</td>
<td>12.6 (11.0)</td>
<td>10.0 (8.7)</td>
</tr>
<tr>
<td></td>
<td>1993</td>
<td>2.5 (2.2)</td>
<td>14.4 (12.6)</td>
<td>10.4 (9.1)</td>
</tr>
<tr>
<td></td>
<td>1994</td>
<td>2.2 (1.9)</td>
<td>12.3 (10.7)</td>
<td>11.6 (10.1)</td>
</tr>
<tr>
<td></td>
<td>1995</td>
<td>2.1 (1.8)</td>
<td>11.1 (9.7)</td>
<td>7.7 (6.7)</td>
</tr>
<tr>
<td>Birmingham,</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1992</td>
<td>0.7</td>
<td>(0.6)</td>
<td>16.3 (14.2)</td>
<td>12.4 (10.8)</td>
</tr>
<tr>
<td>City centre</td>
<td>1993</td>
<td>0.7 (0.6)</td>
<td>5.2 (4.5)</td>
<td>4.4 (3.8)</td>
</tr>
<tr>
<td></td>
<td>1994</td>
<td>0.7 (0.6)</td>
<td>16.1 (14.1)</td>
<td>11.1 (9.7)</td>
</tr>
<tr>
<td></td>
<td>1995</td>
<td>0.7 (0.6)</td>
<td>10.5 (9.2)</td>
<td>7.9 (6.9)</td>
</tr>
<tr>
<td>Leicester</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1994</td>
<td>0.7</td>
<td>(0.6)</td>
<td>10.1 (8.8)</td>
<td>6.8 (5.9)</td>
</tr>
<tr>
<td>1995</td>
<td>0.6</td>
<td>(0.5)</td>
<td>11.6 (10.1)</td>
<td>9.0 (7.9)</td>
</tr>
<tr>
<td>Bexley</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1994</td>
<td>0.6</td>
<td>(0.5)</td>
<td>9.6 (8.4)</td>
<td>5.2 (4.5)</td>
</tr>
<tr>
<td>1995</td>
<td>0.5</td>
<td>(0.4)</td>
<td>7.1 (6.2)</td>
<td>5.4 (4.7)</td>
</tr>
</tbody>
</table>

From Department of the Environment/Scottish Office (1997)
<table>
<thead>
<tr>
<th>Study</th>
<th>Indoor/outdoor ratio</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Field et al. (1992)</td>
<td>1.2</td>
<td>Measurements taken prior to the December 1991 London pollution episode</td>
</tr>
<tr>
<td>UK</td>
<td></td>
<td>Indoor levels measured in an office building</td>
</tr>
<tr>
<td>Lebret et al. (1987)</td>
<td>1.0–2.0</td>
<td>Indoor measurements taken in the kitchen, living room and bedroom</td>
</tr>
<tr>
<td>The Netherlands</td>
<td></td>
<td>of Dutch homes</td>
</tr>
<tr>
<td>Rench &amp; Savage (1976) USA</td>
<td>19.0</td>
<td>Indoor CO levels consistently higher than outdoor levels</td>
</tr>
<tr>
<td>(USA)</td>
<td>18.0</td>
<td></td>
</tr>
<tr>
<td>Kitchen</td>
<td>3.9</td>
<td></td>
</tr>
<tr>
<td>Living room</td>
<td>2.9</td>
<td></td>
</tr>
<tr>
<td>Rowe et al. (1989)</td>
<td>Office block 0.68</td>
<td>Based on simultaneous measurement of indoor and outdoor air in</td>
</tr>
<tr>
<td>Saudi Arabia</td>
<td>Office block 0.68</td>
<td>Riyadh, Saudi Arabia</td>
</tr>
<tr>
<td></td>
<td>Hotel 0.78</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Residence 0.36</td>
<td></td>
</tr>
<tr>
<td>Stock et al. (1984) USA</td>
<td>2.0–3.0</td>
<td>Indoor CO levels consistently higher than outdoor levels for homes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>with gas cookers</td>
</tr>
<tr>
<td>Lebowitz et al. (1984) USA</td>
<td>0.63</td>
<td>Indoor measurements based on average of two spot readings</td>
</tr>
</tbody>
</table>
affecting CO exposure levels. However, some studies have recorded higher outdoor levels than indoor levels, again indicating that the ingress of polluted air from outside can be an important source of CO indoors. Polluted air outside is most commonly attributed to motor vehicle exhaust emissions; petrol vehicle exhaust emissions account for 71% of the total estimated emissions of CO in the UK (Department of the Environment/Scottish Office, 1997).

SYNOPSIS

Indoor levels of CO are frequently higher than those found outside, particularly when a CO-generating source such as a combustion appliance is present. However, evidence suggests that the ingress of polluted air from outdoors can increase CO levels indoors and this may have implications for homes in heavily trafficked areas. Indoor CO levels of 3.4–9.9 mg/m³ (3.0–8.6 ppm) have been attributed to the exchange of indoor and polluted outdoor air. These measurements represent an increase of between 2.3 and 7.5 mg/m³ (2–6.5 ppm), around 200–500%, as a result of the ingress of polluted air from outside. The presence of an attached garage has also been identified as a potential source of increased CO levels, with concentrations of up to 25.2 mg/m³ (22 ppm) being recorded in such conditions.

2.3.5 PERSONAL EXPOSURE STUDIES

Personal exposure studies allow the measurement of pollutant concentrations encountered by individuals as they move through different microenvironments during the course of their daily activities. The use of small personal exposure monitors has enabled researchers to conduct large-scale field studies, and as such they have made a significant contribution to the determination of typical exposure patterns to a range of pollutants. Because of the absence of personal exposure studies conducted in the UK, a number of studies from other countries are discussed here.

Personal 1-hour mean CO exposure measurements were made by Alm et al. (1994) for 55 pre-school children (aged 3–6 years) who attended two day care centres in
Töölö and Vallila in Helsinki, Finland. The investigation, conducted in the autumn of 1990 and the winter and spring of 1991, was designed to examine the relationship between ambient air monitoring data and personal exposure assessment. The children carried a personal exposure monitor for approximately 22 hours (most children took part on more than one monitoring day). The personal exposure monitor contained a passive electrochemical monitor connected to a datalogger which recorded 1-minute average ppm values for CO. The recorded values were then converted to moving 1-hour averages in mg/m³ at 0°C for analysis. Ambient air quality was measured by stationary non-dispersive infrared devices situated near major roads in Vallila and Töölö.

Results showed that the principal contributory factors affecting total personal exposure to CO were traffic fumes outdoors and the presence of gas cookers, attached garages and cigarette smoke indoors. The mean exposure of children in homes with gas cookers was 2 mg/m³ (1.7 ppm) in Vallila and 1.9 mg/m³ (1.7 ppm) in Töölö. For children in homes with electric cookers mean exposure was 0.9 mg/m³ (0.8 ppm) in Vallila and 1.0 mg/m³ (0.9 ppm) in Töölö. The Finnish national ambient air quality guideline for CO for a 1-hour average of 30 mg/m³ (26.2 ppm) was exceeded among children from homes with gas cookers in 0.7% of the sample in Vallila and 3% in Töölö. For children from homes with electric cookers the guideline was exceeded by 0.1% of the sample in Vallila and 2.6% of the sample in Töölö. Although the presence of gas cookers made a small contribution to overall personal exposure, they were of little significance unless the appliance was malfunctioning. In the analysis of the contributions made by cooker type to CO exposure, consideration was also given to potentially confounding factors. These included home/building characteristics, whether tobacco was smoked in the home and the mode of transport used by the children between their home and day centre. There were no noteworthy differences between the locations and cooker types except when the presence of tobacco smoking in homes equipped with gas stoves in Vallila was considered, where CO concentrations were higher.

In a study by Maroni et al. (1996), personal exposure measurements were made to characterise the total daily personal exposure to a variety of air pollutants, including CO, as well as to estimate the relative importance of home, workplace and journey exposures to overall personal exposure. The study was conducted in the metropolitan area of Milan during May to June 1995. It involved 50 office workers (25 male, 25 female; comprising 33 non-smokers, 17 smokers; mean age 38.6 ± 10.4 years).
Each individual was issued with a personal and a stationary CO monitor. The stationary measurements were taken in the subjects’ homes (kitchen and bedroom), workplaces and outside during commuting activity. These measurements were only taken during office hours and at home when the subject was present. The personal exposure monitors were used to take passive measurements over the period of 1 day. Activity diaries were completed by each subject. Daily personal exposure was calculated and the contribution of each microenvironment to the total daily personal exposure was determined.

Average daily CO exposure for all subjects was $2.2 \pm 0.8 \text{ mg/m}^3$ ($1.9 \pm 0.7 \text{ ppm}$) and the relative contribution of indoor exposure in the home and workplace was greater than outdoor exposure. The relative contributions as percentages of total personal exposure were: home 50.1%; office 32.9%; and commuting 17%. However, mean CO levels during commuting activity were generally higher than those recorded indoors. The study emphasises that although indoor levels of CO may be relatively low, exposure in the home accounts for the most significant contribution to total daily personal exposure because of the length of time spent there.

Nagda et al. (1983) presented results from an early pilot study on average exposure levels to CO in indoor environments, indoor exposure distributions and conditions associated with particularly high exposures, and the degree of correspondence between indoor and ambient measurements of CO. The survey covered 58 subjects, yielding 197 person-days of sampling data over a period of 11 weeks starting in October 1982. The study was carried out in Washington DC and measured total 24-hour exposure to CO among housewives, construction workers and office workers.

A General Electric CO detector, based on electrochemical principles, combined with a Custom Instruments signal integrator was used to measure exposures. Subjects also completed activity cards, particularly to record each time a change in microenvironment was made. Average exposure for all subject groups was $1.7 \text{ mg/m}^3$ ($1.5 \text{ ppm}$) in the residential setting. Exposures in the work place were slightly higher ($2.1 \text{ mg/m}^3$; $1.8 \text{ ppm}$) and exposure in other buildings for all groups combined was $3.4 \text{ mg/m}^3$ ($3.0 \text{ ppm}$) with highest exposures recorded in restaurants and recreation facilities. About 8% of the residential exposures were above $5.7 \text{ mg/m}^3$ ($5 \text{ ppm}$) with a large majority of these occurring in homes with gas cookers, some elevated exposures also occurred in apartments with underground garages. In the worst case of residential exposure, the US EPA 8-hour ambient air quality standard for CO of $10 \text{ mg/m}^3$ ($9 \text{ ppm}$) was exceeded.
with exposure to 15.3 mg/m³ (13.4 ppm) over a 9-hour period. This was caused by the simultaneous use of two kerosene space heaters in the home.

In a widely cited study designed to develop a methodology for measuring frequency distributions of CO exposure in an urban population, personal exposure monitoring data were collected in Washington DC and Denver, Colorado during the winter of 1982–1983 (Akland et al., 1985; Jungers et al., 1985). Non-institutionalised, non-smoking residents aged between 18 and 70 years were studied and the investigation aimed to achieve approximately 1000 person-days of exposure data for each city. Data were collected using questionnaires, activity diaries and a personal exposure monitor designed to operate continuously for 24 hours. Residential indoor exposures to CO in Denver were analysed to determine the contribution of three potential CO sources. The data collected during this study supported earlier findings that increased CO exposure is associated with gas cooker operation and with the presence of cigarette smoke and attached garages. In the Denver study it was found that indoor mean exposure (unadjusted for cofactors) was increased by 134% or by 3.0 mg/m³ (2.6 ppm) by gas cooker operation, by 84% or 1.8 mg/m³ (1.6 ppm) by cigarette smoke and by 22% or 0.5 mg/m³ (0.4 ppm) by the presence of an attached garage. Statistical analysis of pairwise comparisons of exposure subgroups in the Washington study indicated no significant difference between personal CO exposure and various domestic cooker types. For all microenvironments, CO exposures in Denver were consistently higher than in Washington DC.

SYNOPSIS

The key findings of studies which have included personal exposure monitoring for CO are presented in Table 2.9.

There is great potential for personal exposure monitoring to produce substantial and relevant data for characterising exposures of a population to CO and to increase the understanding of the causes, extent and variability of exposure. However, to date, the Denver–Washington study is the only large-scale field investigation into population exposure to CO to have been conducted using personal monitoring. Nonetheless, other smaller-scale studies have provided useful and relevant information.
### Table 2.9 Summary table of personal exposure measures to carbon monoxide in mg/m³ (ppm)

<table>
<thead>
<tr>
<th>Study reference &amp; country</th>
<th>Measurement</th>
<th>CO levels</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Alm et al. (1994) Finland</strong></td>
<td>Personal 1-hour mean CO exposure using a passive electrochemical PEM</td>
<td>Mean CO exposure by combustion appliance</td>
<td>Main sources affecting CO exposure: traffic fumes outside and presence of gas stoves, attached garages and cigarette smoke indoors</td>
</tr>
<tr>
<td></td>
<td>55 pre-school children attending two day care centres in Helsinki</td>
<td>Vallila</td>
<td>Presence of gas cooker made a small contribution to CO exposure; this was much greater if the appliance was malfunctioning</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Töölo</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Gas</td>
<td>Mean CO exposure by combustion appliance</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2.0 (1.7)</td>
<td>Vallila</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.9 (1.7)</td>
<td>Töölo</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Electricity</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.9 (0.8)</td>
<td>Vallila</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.0 (0.9)</td>
<td>Töölo</td>
</tr>
<tr>
<td></td>
<td></td>
<td>% Exceedances of 30 mg/m³ Finnish guideline</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Vallila</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Töölo</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Gas</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.7</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>3.0</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Electricity</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.1</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>2.6</td>
<td></td>
</tr>
<tr>
<td><strong>Maroni et al. (1996) Italy</strong></td>
<td>Total daily personal exposure using a passive PEM</td>
<td>Daily personal exposures in different microenvironments</td>
<td>Emphasises that although indoor CO exposure levels tend to be lower than other environments, exposure in the home makes the most significant contribution to overall exposure</td>
</tr>
<tr>
<td></td>
<td>50 office workers in Milan (25 male; 25 female and 33 non-smokers; 17 smokers)</td>
<td>Exposure level</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Office</td>
<td>2.1 (1.8)</td>
<td>32.9</td>
</tr>
<tr>
<td></td>
<td>Home</td>
<td>2.1 (1.8)</td>
<td>50.1</td>
</tr>
<tr>
<td></td>
<td>Commuting - to work</td>
<td>5.2 (4.5)</td>
<td>17</td>
</tr>
<tr>
<td></td>
<td>- to home</td>
<td>3.5 (3.1)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Overall daily</td>
<td>2.2 (1.9)</td>
<td></td>
</tr>
</tbody>
</table>
Table 2.9 (continued)

<table>
<thead>
<tr>
<th>Study reference &amp; country</th>
<th>Measurement</th>
<th>CO levels</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nagda et al. (1983) USA</td>
<td>Total 24-hour personal exposure using an electrochemical PEM</td>
<td>Average exposure according to environment</td>
<td>About 8% of residential exposures were &gt;5.7 mg/m³ (5.0 ppm) with a large number associated with gas stove use</td>
</tr>
<tr>
<td>58 subjects yielding 197 person-days of data</td>
<td>Workplace 2.1 (1.8)</td>
<td>Highest recorded residential exposure was 15.3 mg/m³ (13.4 ppm) over 9 hours. This was associated with the simultaneous use of two kerosene space heaters in the home</td>
<td></td>
</tr>
<tr>
<td>Source</td>
<td>Exposure</td>
<td>% Time</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>1.4</td>
<td>76.7</td>
<td></td>
</tr>
<tr>
<td>Gas stove</td>
<td>2.5</td>
<td>17.4</td>
<td></td>
</tr>
<tr>
<td>Kerosene heater</td>
<td>6.0</td>
<td>3.8</td>
<td></td>
</tr>
<tr>
<td>Wood burner</td>
<td>0.8</td>
<td>2.2</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>1.7</td>
<td>100</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Akland et al. (1985); Jungers et al. (1985) USA</th>
<th>Continuous 24-hour personal exposure measurement</th>
<th>Increase in mean residential exposure due to selected CO sources</th>
<th>% Increase in mean exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td>1000 person-days of data</td>
<td>Gas stove operation 3.0 (2.6)</td>
<td>134</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cigarette smoke 1.8 (1.6)</td>
<td>84</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Attached garage 0.5 (0.4)</td>
<td>22</td>
<td></td>
</tr>
</tbody>
</table>

PEM, personal exposure monitor
Results from the studies described above indicate clearly that personal activity and the presence of indoor CO sources greatly contribute to an individual’s overall exposure. Maroni et al. (1996) observed that exposure in the home contributed around 50% of an individual’s total personal exposure to CO. In the residential setting 24-hour exposures of around 1.7 mg/m³ (1.5 ppm) have been recorded and noticeable contributions of gas cooker operation, environmental tobacco smoke and attached garages have been documented in Finland and in Denver, USA.
2.4 EVALUATION OF THE LITERATURE ON LEVELS OF CARBON MONOXIDE IN UK HOMES

The most relevant data identified in this review come from studies conducted in the UK. All of the UK studies have been undertaken during the last decade or so and are, therefore, likely to reflect current CO levels in the home in the UK. Some investigations conducted in other countries are also of value, particularly when CO levels are assessed in relation to both the factors which determine such levels and the possible health effects. While it is difficult to draw firm conclusions from the limited UK data available, they do provide a useful indication of the typical ranges of CO exposure levels in UK homes.

There are a number of sources of CO in the indoor environment, the most notable of which are gas cooking and certain types of heating systems which burn gas, wood, coal or paraffin. The presence of tobacco smoke, an attached garage or heavily trafficked roads can also be important.

In a recent review on the subject it was suggested that typical indoor concentrations of CO in the UK are in the range of 5–60 mg/m$^3$ (4.4–52.4 ppm) when CO sources are present (Burr, 1995). Based on electrochemical measurements, recorded weekly average CO concentrations typically range from 0.3 to 2.7 mg/m$^3$ (0.3–2.4 ppm) in the kitchen where there is gas cooking and 0.8 to 0.9 mg/m$^3$ (0.7–0.8 ppm) where there is no gas cooking. For homes with gas cookers, levels found in the living room typically range from 0.2 to 2.5 mg/m$^3$ (0.2–2.2 ppm) and in the bedroom from 0.5 to 2.1 mg/m$^3$ (0.4–1.8 ppm; Ross, 1996). Similar results have been obtained in other studies where average indoor readings of CO tend to be below 3.4 mg/m$^3$ (3.0 ppm; Wiech & Raw, 1995).
Environmental tobacco smoke also affects indoor CO levels; concentrations of CO have been reported that range from 2.1 mg/m$^3$ (1.8 ppm) in non-smoking households to 2.6 mg/m$^3$ (2.3 ppm) in homes with smokers (Kirk et al., 1988), although these concentrations were not significantly different.

A marked effect of gas cooking activity on indoor levels of CO has been observed. Peak CO measurements have often been recorded in the kitchen when a gas cooker is in use. These peaks are generally two to three times higher than the normal background levels of CO. Typically, homes with gas cookers exhibit maximum CO concentrations of between 6.0 mg/m$^3$ and 49.3 mg/m$^3$ (5.2–43.1 ppm) for maximum 1-minute averages and 1.9–24.5 mg/m$^3$ (1.7–21.4 ppm) for maximum 1-hour averages, whereas much lower peaks are usually recorded in homes which use electricity only (Ross, 1996). However, much higher levels of up to 183.2 mg/m$^3$ (160 ppm) have been associated with the use of a gas cooker grill (Stevenson, 1985). A possible effect of gas cooker pilot lights on indoor background levels has also been identified (Stevenson, 1985).

Badly installed or malfunctioning appliances are also associated with elevated CO levels. Maximum 1-minute average concentrations of 68.5 mg/m$^3$ (59.8 ppm) in the kitchen and 121.4 mg/m$^3$ (106 ppm) in the living room have been linked with the use of a malfunctioning boiler, for example.

These peak levels suggest that in some UK homes using gas for cooking or certain types of fuel-burning heating systems, CO levels would approach or exceed the WHO 1-hour guideline value of 30 mg/m$^3$ (25 ppm). The presence and use of faulty CO-generating appliances in the home are of particular concern as they can potentially give rise to very high indoor levels of CO.

Long-term average outdoor levels of CO in the UK vary with factors such as the degree of urbanisation and climatic conditions, but are typically below the WHO 1-hour guideline of approximately 30 mg/m$^3$ (25 ppm), and usually within the WHO and EPAQS 8-hour guideline of 11.5 mg/m$^3$ (10 ppm). Short-term peaks (e.g. 1-hour maximum) can reach high levels, particularly in heavily trafficked areas, but currently in the UK these generally do not exceed 29 mg/m$^3$ (EPAQS, 1994). Outdoor levels of CO can influence indoor levels through the influx of outdoor air into the indoor environment, although the limited data generated in the UK suggest that levels of indoor and outdoor CO are generally similar (Field et al., 1992).
3 The role of biomarkers in relating carbon monoxide exposure to health effects
Air quality standards and guidelines for CO tend to be established at concentrations that should protect sensitive individuals from experiencing adverse health effects. However, it can be difficult to relate measured CO exposure levels to predicted health effects. The main toxic mechanism by which CO acts is hypoxia; CO rapidly diffuses across the alveolar membranes and competes with oxygen in binding to haemoglobin, thus forming COHb. The formation of COHb is therefore a useful biomarker of exposure to CO.

The amount of COHb formed, however, is dependent on a range of factors, such as the concentration and duration of CO exposure and the health status and metabolic characteristics of the exposed individual, each of which may vary and thus affect the formation of COHb in an individual. While blood COHb levels represent a useful biological marker of exposure to CO, the predicted relationship between exposure levels and COHb is frequently dependent on a number of assumptions (e.g. activity patterns, exposure duration and pre-existing susceptibilities) and is less precise as an indicator of exposure at low levels of CO. This is especially true when the effects of endogenous production of CO and of smoking are taken into account. Broad predictions about likely health effects can also be made based on COHb levels. However, the use of COHb levels as a health effect marker, to estimate the extent of the risks to health and well-being across a population, is complicated by considerations such as pre-existing susceptibilities and physiological parameters.

Bridging the gap between CO exposure levels and likely health effects is important when data from air quality studies and personal exposure monitoring are used to determine the extent of any risks to health and well-being from exposure to CO. Key factors and considerations in relating CO exposure levels to likely health effects are shown in Figure 3.1.
Figure 3.1 Key factors in relating carbon monoxide exposure measurements to likely health effects

**Susceptible groups**
- Smokers
- People cooking with gas
- People living near roads
- Traffic workers
- Fetuses
- Pregnant women
- People with anaemia and other haematological diseases (including genetically unusual forms of haemoglobin)
- Coronary and pulmonary disease sufferers
- Cerebrovascular disease sufferers
- People with anaemia
- Pregnant women

**Measured by**
- Carbon monoxide (CO) exposure
  - Fixed site monitoring
  - Personal exposure monitoring
  - Activity diaries
- Carboxyhaemoglobin (COHb)
- Coburn–Forster –Kane (CFK) equation
- Hypoxia
- Health effects
- Breath CO
- Blood COHb

**Physiological parameters**
- Neuropsychological tests
- Clinical symptoms
- Subclinical symptoms
3.2 EXPOSURE PHYSIOLOGY:  
THE RELATIONSHIP BETWEEN  
CARBON MONOXIDE LEVELS  
AND BLOOD  
CARBOXYHAEMOGLOBIN

The Coburn–Forster–Kane (CFK) equation, developed to describe the endogenous production of CO, is the foremost model used to explain the relationship between CO concentration and blood COHb levels (Coburn et al., 1965). Work prior to this concentrated on the effects of inspiring high CO concentrations. Coburn et al. (1965) were apparently the first to consider this question at lower or endogenous CO concentrations. The model is still used, owing to its robustness and easy adaptation to more specialised applications. It is still, according to the EPA, the “best all-round model for COHb prediction” (EPA, 1991). In its non-linear form it may be used to predict COHb levels at high CO exposures; in linear form it is applicable to typical air pollution situations (EPA, 1991).

Coburn et al. (1965) set out the physiological parameters for their equation as:

- the rate of CO production (endogenous);
- alveolar ventilation;
- diffusing capacity of the lung;
mean oxygen tension in the alveolar capillaries; and

concentration of CO in inspired air.

The CFK equation assumes a constant CO uptake and elimination rate, which is rarely true. Also, inter-individual variations will give rise to differing COHb levels in the exposed population (EPA, 1991). The toxicity of CO is governed by these factors and by exposure duration, respiratory minute volume, cardiac output, tissue oxygen demand and blood haemoglobin concentration (Klaasen, 1985). The rate at which arterial blood reaches equilibrium with the inspired concentration of CO is affected by the diffusion capacity of the lungs and alveolar ventilation (each also affected by exertion of the exposed person), and the duration and concentration of exposure (Stewart, 1976; Smith, 1980; see also Section 4.2)

At a CO concentration of 34.4 mg/m$^3$ (30 ppm), a state of equilibrium of about 5% COHb is reached after approximately 8 hours. At 114.5 mg/m$^3$ (100 ppm), COHb in the blood reaches 4% after 1 hour and 14% after 8 hours (Ström et al., 1995). The WHO (1994) set a 15-minute CO guideline value of 100 mg/m$^3$ (90 ppm), the aim of which is to prevent COHb levels rising above 2.5%.

The relationship between exposure concentration and blood levels of COHb was studied in 14 non-smoking hockey players, with a mean age of 32.6 years, exposed to CO at four different concentrations (from 0–87.2 mg/m$^3$; 0–76.2 ppm) in skating arenas during strenuous exercise (Levesque et al., 1991). Levels of COHb were based on alveolar breath samples (see Section 3.3). For each 11.5 mg/m$^3$ (10 ppm) of CO in the air, the COHb level of the 14 subjects rose by an average of 0.76%. It should be noted that the rate of CO uptake is greater during exercise than when at rest (Amdur, 1980). Furthermore, the elderly, the very young, pregnant women and other sectors of the population may show different exposure–COHb relationships (sensitive populations are discussed in greater detail in Section 4.3)

Whilst the relative affinity of CO and oxygen for haemoglobin (the affinity constant, also called the Haldane coefficient) is important, another fact to consider is that the rates of association and dissociation differ. The rate of association of CO and haemoglobin is one fifth lower than that of oxygen and the rate of dissociation is one order of magnitude lower. The dissociation of CO from the body as a whole is somewhat less well understood, although it is known that the elimination of CO from the blood and other body stores is initially very rapid.
and subsequently slower. The half life of CO elimination from blood shows considerable inter-individual variation with a reported range of 2 to 6.5 hours (EPA, 1991).

The relationship between concentration of CO, exposure period, level of activity and resulting COHb level is summarised in Table 3.1 and presented diagrammatically in Figures 3.2 and 3.3. The effect of physical activity is clearly shown; greater physical exertion leads to faster CO uptake. The equilibrium level of COHb is largely unaffected, but the time taken to reach that level is shortened.
Table 3.1 Carboxyhaemoglobin levels (% total haemoglobin) in the blood of exposed workers as a function of time and at various atmospheric concentrations of carbon monoxide

<table>
<thead>
<tr>
<th>Time</th>
<th>5 ppm (5.7 mg/m³)</th>
<th>10 ppm (11.5 mg/m³)</th>
<th>25 ppm (28.6 mg/m³)</th>
<th>35 ppm (40.1 mg/m³)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>S</td>
<td>L</td>
<td>H</td>
<td>S</td>
</tr>
<tr>
<td>15 min</td>
<td>0.52</td>
<td>0.54</td>
<td>0.56</td>
<td>0.55</td>
</tr>
<tr>
<td>30 min</td>
<td>0.54</td>
<td>0.57</td>
<td>0.60</td>
<td>0.61</td>
</tr>
<tr>
<td>45 min</td>
<td>0.56</td>
<td>0.61</td>
<td>0.64</td>
<td>0.66</td>
</tr>
<tr>
<td>60 min</td>
<td>0.58</td>
<td>0.63</td>
<td>0.68</td>
<td>0.71</td>
</tr>
<tr>
<td>90 min</td>
<td>0.62</td>
<td>0.69</td>
<td>0.74</td>
<td>0.80</td>
</tr>
<tr>
<td>2 h</td>
<td>0.66</td>
<td>0.73</td>
<td>0.78</td>
<td>0.89</td>
</tr>
<tr>
<td>4 h</td>
<td>0.77</td>
<td>0.84</td>
<td>0.86</td>
<td>1.20</td>
</tr>
<tr>
<td>6 h</td>
<td>0.85</td>
<td>0.83</td>
<td>0.88</td>
<td>1.40</td>
</tr>
<tr>
<td>8 h</td>
<td>0.91</td>
<td>0.91</td>
<td>0.89</td>
<td>1.50</td>
</tr>
<tr>
<td>24 h</td>
<td>1.05</td>
<td>0.93</td>
<td>0.89</td>
<td>1.90</td>
</tr>
<tr>
<td>∞</td>
<td>1.06</td>
<td>0.93</td>
<td>0.80</td>
<td>1.90</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Time</th>
<th>50 ppm (57.3 mg/m³)</th>
<th>75 ppm (85.9 mg/m³)</th>
<th>100 ppm (114.5 mg/m³)</th>
<th>200 ppm (229.0 mg/m³)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>S</td>
<td>L</td>
<td>H</td>
<td>S</td>
</tr>
<tr>
<td>15 min</td>
<td>0.82</td>
<td>1.20</td>
<td>1.60</td>
<td>1.00</td>
</tr>
<tr>
<td>30 min</td>
<td>1.10</td>
<td>1.90</td>
<td>2.60</td>
<td>1.50</td>
</tr>
<tr>
<td>45 min</td>
<td>1.40</td>
<td>2.50</td>
<td>3.40</td>
<td>1.90</td>
</tr>
<tr>
<td>60 min</td>
<td>1.70</td>
<td>3.00</td>
<td>4.10</td>
<td>2.30</td>
</tr>
<tr>
<td>90 min</td>
<td>2.20</td>
<td>4.00</td>
<td>5.20</td>
<td>3.10</td>
</tr>
<tr>
<td>2 h</td>
<td>2.70</td>
<td>4.70</td>
<td>6.10</td>
<td>3.90</td>
</tr>
<tr>
<td>4 h</td>
<td>4.40</td>
<td>6.90</td>
<td>7.70</td>
<td>6.30</td>
</tr>
<tr>
<td>6 h</td>
<td>5.50</td>
<td>7.60</td>
<td>8.20</td>
<td>8.10</td>
</tr>
<tr>
<td>8 h</td>
<td>6.40</td>
<td>8.00</td>
<td>8.30</td>
<td>9.40</td>
</tr>
<tr>
<td>24 h</td>
<td>8.40</td>
<td>8.40</td>
<td>8.30</td>
<td>12.40</td>
</tr>
<tr>
<td>∞</td>
<td>8.50</td>
<td>8.40</td>
<td>8.30</td>
<td>12.70</td>
</tr>
</tbody>
</table>

Adapted from WHO (1979)

H, heavy physical work; L, light physical work; S, sedentary subjects
**Figure 3.2 Uptake of carbon monoxide by blood**

Each of the curves represents the time course of the increase in blood COHb with continuing exposure to a given concentration of CO. Individual activity levels and inter-individual differences mean these COHb levels will differ considerably between different people.

Adapted from EPAQS (1994)
Figure 3.3 Carboxyhaemoglobin level (%) over time at different levels of carbon monoxide and activity

Data from WHO (1979)
Figure 3.3 (continued) Carboxyhaemoglobin level (%) over time at different levels of carbon monoxide and activity.

Data from WHO (1979)
Figure 3. (continued) Carboxyhaemoglobin level (%) over time at different levels of carbon monoxide and activity.

Data from WHO (1979)
3.3 METHODS FOR MEASURING THE LEVEL OF CARBON MONOXIDE IN THOSE EXPOSED

In assessing the health effects of CO exposure, in either clinical investigations or in controlled chamber studies, it is important to determine a subject’s COHb level. This can be achieved either directly from blood samples or indirectly by measuring CO levels in expired breath. It is important to note that COHb is a very useful and direct marker of an individual’s exposure but is less reliable as an indicator of health effect or symptom severity. The relationship between COHb and health effect, is discussed in greater detail in Section 3.5.

ESTIMATING CARBOXYHAEMOGLOBIN LEVELS FROM BREATH SAMPLES

The level of CO in an individual’s blood may be determined from the level of CO in their breath. This relies on an equilibrium relationship for CO between the blood and gas phase whereby the partial pressure of CO in the arterial blood will reach a steady state relative to the partial pressure of CO in the alveolar gas. From the concentration of CO in the breath it is possible to estimate the blood COHb level. The COHb level determined by breath analysis can only be used as an estimate because the Haldane relationship, on which it is based, assumes attainment of equilibrium, which does not occur under physiological conditions (EPA, 1991).
Of the techniques available for the determination of COHb from breath samples, the most common involves a subject holding their breath for a period of time, usually 20 seconds, to allow the alveolar CO concentration to approach maximum. Other techniques include re-breathing, where a subject breathes a set volume of oxygen for 2–3 minutes while expired CO₂ is removed. The final technique applies the Bohr equation to the level of CO measured in mixed expired air, from which the alveolar CO concentration is calculated (EPA, 1991).

The accuracy of any breath sampling method is variable and highly sensitive to ventilation rate and capillary blood volume. It may also be sensitive to other breath gases. In a study assessing the interference of hydrogen with breath CO measurements, Vreman et al. (1993) used various techniques to measure blood COHb and breath CO levels. These included the use of CO-oximeters (Ciba Corning Diagnostics models CCD 2500 and CCD 270) to measure COHb, an electrochemical breath CO detector of the authors’ design, and gas chromatography measurement of both blood and breath CO levels (see below). The authors reported no correlation between COHb measured with CO-oximeter CCD 270 and breath CO measured with electrochemical detection (n = 30, r² = 0.03, Spearman rank correlation coefficient (ρ) = 0.37). However, the gas chromatography measurement of breath CO was highly correlated with COHb (n = 30, r² = 0.79, ρ = 0.89). Furthermore, there was no correlation between electrochemical detection and gas chromatography measurement of breath CO (n = 30, r² = 0.13, ρ = 0.37); the electrochemical detection methods tended to overestimate the CO level. The interference of hydrogen in electrochemical detection measurement of CO was strongly indicated by a correlation between hydrogen concentrations measured by gas chromatography and detector response using the electrochemical detection method.

Although electrochemical detection may not correlate well with blood COHb levels as measured by CO-oximeter, other methods (in addition to gas chromatography) may do so. Lee et al. (1994) used a tunable diode laser spectrometry method and found correlation coefficients of 0.999 for subject means, and 0.945 for individual data points. However, using tunable diode lasers may be less practical in field situations.

The distinct advantage of the breath sample method is that it is non-invasive and quick (although the re-breathing technique is somewhat more time consuming than the breath-hold). But there are other factors that make the breath

* The Bohr equation is used to determine the physiological deadspace (EPA, 1991)
measurement technique less advantageous: people suffering from pulmonary diseases show a different relationship between alveolar and blood CO levels; older people tend to have higher COHb levels than predicted by the alveolar CO concentration; and smokers have an abnormal relationship between alveolar CO and blood CO (EPA, 1991).

Breath samples have been used in a number of investigations assessing individuals’ COHb levels. Cox and Whichelow (1985) used a portable, battery powered Ecolyzer; Wallace (1983) used a General Electric Model SPE CO-detector. Both detectors are of the electrochemical type.

DETERMINING CARBOXYHAEMOGLOBIN LEVELS FROM BLOOD SAMPLES

As COHb is a blood protein, it should be more accurate and appropriate to determine the level of COHb directly from blood samples. Many methods for assessing COHb levels were developed for forensic situations in which the expected COHb levels are much higher, resulting from fires and suicides for example, than those of interest in studies of low-level, long-term exposures to CO. These forensic methods are insufficiently accurate for the range of COHb levels of less than 10%, relevant to the assessment of the (non-fatal) health effects of CO.

There are two main methods employed for measuring low levels of COHb. The first, which is a non-destructive method, involves observing changes in the blood’s light absorption spectrum — the spectrophotometric method. The equipment used is often termed a CO-oximeter. The accuracy of this method is limited to about 1% COHb but the reproducibility is high (i.e. a given sample of blood will provide the same COHb level across many analyses). Calibration of CO-oximeters is achieved using dye solutions of known light absorption. Calibration may be a daily requirement or may only be required every 90 days, depending on the exact make and type of meter (Mahoney et al., 1993).

The second method uses gas chromatography to measure the concentration of CO in the blood. It is more sensitive and time consuming than the spectrophotometry method and involves releasing CO bound to the haemoglobin into the gas phase; the gas phase is then separated using the gas chromatograph, and the concentration of CO is measured (EPA, 1991). Calibration is achieved using standard gas samples of known composition. The gas chromatography method is seen by many as the reference method for COHb analysis.
Within CO-oximetry and gas chromatography there are numerous techniques and makes of equipment used. As will become clear in the controlled chamber studies presented below, there is little agreement on which of the two methods to use. Some investigators use CO-oximetry for quick analyses and support them with gas chromatography analysis on selected samples.

The advantages of the CO-oximeter method, speed and ease of use, must be weighed against its inaccuracy relative to the gas chromatography method. Studies have shown CO-oximetry-derived COHb levels to be 0.7 to 1.0% higher than duplicate analysis by gas chromatography (Chaitman et al., 1992). A comparison of COHb levels derived from five types of CO-oximeter and from the gas chromatography method was made by Mahoney et al. (1993). Excess blood from routine blood gas analyses of 100 patients’ samples was used; 40 of these samples were spiked with CO to increase their COHb level. Five CO-oximeters were used, namely a Radiometer OSM3 Hemoximeter, an AVL Scientific Corp. 912 CO-Oxylite™, Models 2500 and 270 CO-oximeters from Ciba Corning Diagnostics (CCD), and an Instrumentation Laboratory IL 482 CO-Oximeter™. The difference between COHb levels derived from CO-oximeter and gas chromatography was used as the comparison. All CO-oximeters gave COHb levels that differed from those from the gas chromatography method (p<0.03 to <0.0001) by 2.5% or less. Statistical differences between the methods decreased as COHb level increased. This confirmed a general inaccuracy for CO-oximeter-determined COHb levels of about 1.0%. At low COHb levels the CO-oximeters tended to overestimate the COHb level compared with gas chromatography; at high levels the opposite was true (Mahoney et al., 1993; Table 3.2).

The study of hydrogen interference in breath analyses of CO levels outlined above (Vreman et al., 1993), also showed disparities between CO-oximetry-derived and gas chromatography-derived COHb levels at low COHb levels (~1%). The CO-oximeters gave mean readings of between 1.0 ± 0.3% and 1.3 ± 0.2%, compared with a gas chromatography-derived level of 0.56 ± 0.11%. [In this study the samples were not spiked to give a range of COHb levels and comparison between the two methods at higher COHb levels was not possible.]

The divergence between the CO-oximeter (spectrophotometric) and gas chromatography methodologies means that direct comparison between studies is sometimes difficult. For example, whereas Allred et al. (1989; 1991) report low, pre-exposure control COHb values of 0.6% using a gas chromatography method, control measurements of COHb by Hinderliter et al. (1989) and Sheps et al. (1990), using spectrophotometers, were three times higher, at approximately 1.8%.
Because of this, the comparability of the work of Allred and colleagues to other studies has been questioned (Mennear, 1993).

It should also be noted that in clinical reports of CO poisonings, the patient has often received oxygen therapy before a blood or breath sample is taken. As administration of oxygen decreases the half-life of CO in the body, COHb levels measured after such treatment may not accurately reflect the patient’s maximum COHb level (Piantadosi, 1990). Also, the findings of Vreman et al. (1993) may suggest that individual dietary habits have an effect on the COHb level, especially when measuring background or endogenous levels of COHb. This is because certain diets lead to increased production of hydrogen by gut bacteria.

<table>
<thead>
<tr>
<th>Instrument</th>
<th>COHb level</th>
<th>≤2.5</th>
<th>&gt;2.5 ≤5.0</th>
<th>&gt;5.0 ≤10.0</th>
<th>&gt;10.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL 482</td>
<td></td>
<td>0.3±0.4</td>
<td>-0.1±0.4</td>
<td>-0.9±0.5</td>
<td>1.1±1.0</td>
</tr>
<tr>
<td>CCD 2500</td>
<td></td>
<td>0.9±0.4</td>
<td>0.4±0.4</td>
<td>-0.8±0.5</td>
<td>-0.3±0.9</td>
</tr>
<tr>
<td>R OSM3</td>
<td></td>
<td>0.3±0.3</td>
<td>-0.5±0.4</td>
<td>-1.2±0.5</td>
<td>-2.0±0.9</td>
</tr>
<tr>
<td>CCD 270</td>
<td></td>
<td>-0.4±0.7</td>
<td>-1.6±1.3</td>
<td>-1.8±0.6</td>
<td>-2.2±1.0</td>
</tr>
<tr>
<td>AVL 912</td>
<td></td>
<td>0.9±0.4</td>
<td>-0.3±1.0</td>
<td>-0.8±0.9</td>
<td>-1.7±0.8</td>
</tr>
</tbody>
</table>

From Mahoney et al. (1993)

α-β p <0.05 when compared with IL 482, CCD 2500, R OSM3, CCD 270

This bias changed to 0.2 ± 0.4% COHb (p <0.05 compared with the bias for all models) when negative values were converted to a zero value

This bias changed to 1.2 ± 0.7% COHb (p <0.05 compared with AVL 912, CCD 2500, and the IL 482 biases) when negative values were converted to a zero value

Because of this, the comparability of the work of Allred and colleagues to other studies has been questioned (Mennear, 1993).

It should also be noted that in clinical reports of CO poisonings, the patient has often received oxygen therapy before a blood or breath sample is taken. As administration of oxygen decreases the half-life of CO in the body, COHb levels measured after such treatment may not accurately reflect the patient’s maximum COHb level (Piantadosi, 1990). Also, the findings of Vreman et al. (1993) may suggest that individual dietary habits have an effect on the COHb level, especially when measuring background or endogenous levels of COHb. This is because certain diets lead to increased production of hydrogen by gut bacteria.

**SMOKERS, NON-SMOKERS AND NORMAL CARBOXYHAEMOGLOBIN LEVELS**

For individuals who smoke, tobacco smoke is the single most important contributor to CO exposure. Because of their intermittent exposure to very high concentrations of CO in tobacco smoke, smokers generally have a COHb level of between 4% for a light smoker and 15% for a heavy smoker. In contrast, a non-smoker has a COHb level generally less than 3% (Stewart et al. 1974; Lowe-Ponsford & Henry, 1989; EPA, 1991). In healthy individuals living away from large conurbations and otherwise not exposed to CO, a COHb level of between 0.4% and 1.0% can be expected (Stewart et al. 1974; Lowe-Ponsford & Henry, 1989; Burr, 1995), owing to production of CO in the body (Sjöstrand, 1949; Coburn et al., 1966).
A study of COHb levels in US blood donors between 1969 and 1972 (Stewart et al., 1974) revealed that people living in urban areas of the USA with high traffic densities consistently had COHb levels greater than those living in areas of low traffic density, and that 45% of all non-smoking blood donors tested had COHb levels of 1.5% or more. For comparison, a baseline COHb level of 0.45%, from endogenous CO production, was determined based on a group of four adults breathing CO-free air. Tobacco smoking was found to be the single most important factor in determining COHb levels (p<0.01). The other chief factors were geographical location, occupation and current meteorological conditions. Race, sex, height and weight were not important variables.

In non-smokers, the ambient CO concentration is the primary variable determining their COHb level. Ambient levels of CO also affect COHb in smokers, although the relative importance is less. Stewart et al. (1974) found that the relative difference between smokers’ and non-smokers’ COHb levels remained comparatively constant across geographical areas. If ambient levels had no effect on the COHb levels of smokers, their COHb levels would be expected to remain relatively constant across geographical areas and be governed largely by their tobacco smoke intake.

Cox and Whichelow (1985) measured CO levels in the breath of smokers and non-smokers (see Section 2 for full details). They found 74% of smokers had a breath CO level of 11.5 mg/m³ (10 ppm; range for all smokers 3.4–114.5 mg/m³, 3–100 ppm) or greater, whilst 79% of non-smokers had breath CO levels less than 6.9 mg/m³ (6 ppm; range for all non-smokers 2.3–68.7 mg/m³, 2–60 ppm).

**SYNOPSIS**

Various methods exist for measuring CO exposure, although two are most often employed — CO-oximeter (spectrophotometry) to determine blood COHb and gas chromatography to determine blood and breath CO levels. The gas chromatography method is a more accurate, if more time consuming, than the spectrophotometer method. In particular, the latter has been shown to be less accurate in measuring the low levels of COHb encountered in long-term and medium-term exposures to low CO concentrations.

Smokers’ COHb levels tend to be appreciably greater than those of non-smokers. This arises from their intermittent exposure to high concentrations of CO in tobacco smoke.
3.4 PROJECTED CARBOXYHAEMOGLOBIN CONCENTRATIONS ARISING FROM EXPOSURE TO CARBON MONOXIDE IN UK HOMES

This section provides a projection of COHb concentrations arising from exposure to CO in the domestic environment where combustion appliances are functioning normally. Data used for this analysis relate to Home B in the Ross 1996 study, described in detail in Section 2.

From the daily CO monitoring data derived from the 14-home study (Ross, 1996), data have been abstracted for one house (Home B, Table 2.3), which had, with the exception of the house with a faulty boiler, the highest CO levels recorded over one of the 24-hour periods. The data were reduced to 30-minute averages of CO concentrations, and calculations were performed of predicted CO uptake and COHb concentrations using the CFK equation (Coburn et al., 1965; Peterson & Stewart, 1975) for exposures at the actual CO levels measured. The calculations were for a 70 kg man at various levels of respiratory minute volume (associated with different levels of physical activity). Figure 3.4 shows measured CO levels and predicted %COHb calculated from the CFK equation. The 30-minute average CO levels for the kitchen throughout a 24-hour period are shown; they indicate that CO concentrations show a number of brief excursions up to 2.3–5.7 mg/m$^3$ (2–5 ppm) from a background of less than 1.1 mg/m$^3$ (1 ppm). These small rises are followed by a greater increase to a brief peak concentration of 19.5 mg/m$^3$ (17 ppm) at 20:00 h. The predicted COHb concentrations are presented for a
respiratory minute volume of 25 l/min (consistent with light physical activity; walking at 6.4 km/h). It is assumed that the background COHb concentration would be 0.5%. The maximum predicted COHb concentration is 1% between 20:00 and 22:00 h. The concentration is predicted to remain at the background 0.5% during the remainder of the day, barely rising to 0.6% COHb for a short period at 12:00 h.

The home chosen for this analysis had the highest recorded background and peak CO levels of the 14 homes studied (Home I omitted). Even assuming a high level of activity, the COHb concentration for a 70 kg man is predicted not to exceed 1% COHb for any longer than a period of about 2 hours. In practice, it is unlikely that such high levels of physical activity would be maintained in a domestic environment, although children at lower levels of work would show comparable rates of uptake. In order to achieve a blood concentration of 2% COHb, a possible level of concern with regard to angina sufferers (see

Figure 3.4 Measured carbon monoxide levels (30-minute averages over 24 hours) and predicted % carboxyhaemoglobin concentrations calculated* from the Coburn-Forster-Kane equation for a UK home

Data analysis by the Building Research Establishment

*Blood COHb levels were calculated at 25 l/min respiratory minute volume for a 70 kg man

respiratory minute volume of 25 l/min (consistent with light physical activity; walking at 6.4 km/h). It is assumed that the background COHb concentration would be 0.5%. The maximum predicted COHb concentration is 1% between 20:00 and 22:00 h. The concentration is predicted to remain at the background 0.5% during the remainder of the day, barely rising to 0.6% COHb for a short period at 12:00 h.

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Section 4.5.1), it would be necessary to maintain a CO exposure concentration in excess of 11.5 mg/m³ (10 ppm) for several hours or 28.6 mg/m³ (25 ppm) for more than 1 hour.

Based upon these preliminary findings, it is considered very unlikely that a non-smoking individual could achieve COHb concentrations of concern in the domestic environment, providing the cooking and heating appliances were functioning normally. However, much higher COHb concentrations are likely to occur as a result of a malfunctioning appliance.
3.5 Carboxyhaemoglobin: A Biomarker for Carbon Monoxide Exposure and Health Effects

The physiology of CO uptake is well understood. The ease with which models such as the CFK equation can be adapted to various situations allows COHb levels to be predicted at various CO air concentrations, exposure durations and activity levels. As already noted, COHb also results from the endogenous production of CO, which occurs through the breakdown of haemoglobin and other haemoproteins (Coburn et al., 1966; discussed in greater detail in Section 4.2.1).

Whilst the link between CO exposure and COHb level is straightforward, the use of COHb level as a biomarker to predict both the type and severity of health effect is open to question. This uncertainty and the lack of clear correlation between COHb level and health effect may be due to a number of factors:

- the possible effect of toxic mechanisms other than pure hypoxia;
- inter-individual differences in subjective reporting of symptom type and severity; and
- differences in individual sensitivities to CO exposure, for example, smokers who may develop adaptive responses to prolonged CO exposures, or sufferers from diseases that limit oxygen transport.

Table 3.3 summarises the reported health effects associated with particular COHb ranges (EPAQS, 1994).
Table 3.3 Reported health effects associated with levels of carboxyhaemoglobin

<table>
<thead>
<tr>
<th>Blood COHb levels (%)</th>
<th>Observed or reported health effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.5–4.0</td>
<td>Decreased short-term maximal exercise duration in young healthy men</td>
</tr>
<tr>
<td>2.7–5.1</td>
<td>Decreased exercise duration due to increased chest pain (angina) in patients with ischaemic heart disease</td>
</tr>
<tr>
<td>2.0–20.0</td>
<td>Equivocal effects on visual perception, audition, motor and sensorimotor performance, vigilance, and other measures of neuropsychological performance</td>
</tr>
<tr>
<td>4.0–33.0</td>
<td>Decreased maximal oxygen consumption with short-term strenuous exercise in young healthy men</td>
</tr>
<tr>
<td>20–30</td>
<td>Throbbing headache</td>
</tr>
<tr>
<td>30–50</td>
<td>Dizziness, nausea, weakness, collapse</td>
</tr>
<tr>
<td>&gt;50</td>
<td>Unconsciousness and death</td>
</tr>
</tbody>
</table>

From EPAQS (1994)
4 Review of the health effects of carbon monoxide
4.1 INTRODUCTION

This section describes the reported health effects arising from exposure to CO in the domestic environment. Where relevant, studies of occupational or outdoor ambient exposure are also presented. The toxicology of CO is addressed first, including effects on the heart, brain and central nervous system, followed by a discussion of human adaptation to CO exposure, and the effect of CO on atherosclerosis, eyesight and hearing. Susceptible subpopulations are then considered. This is followed by information on clinical investigations of CO exposure, including discussion of immediate and delayed neurological sequelae and the problem of missed or misdiagnosis of CO intoxication. Finally, controlled human exposure studies are examined, with an emphasis on the effect of CO on exercising muscle, the heart and brain. The role of CO as a potential neurotransmitter, in immunological functions and in other areas of physiology is also briefly discussed.
4.2 GENERAL TOXICOLOGY

Section 3 provides a discussion of the physiology of CO exposure, with specific reference to the CFK equation (Coburn et al., 1965), and the relationship between exposure concentration, exposure duration and resulting COHb levels. This section presents an outline of the toxicology of CO.

The human body has compensatory reflexes with which to combat the effects of CO intoxication. The tissues most sensitive to increased COHb are those with high oxygen needs, for example the heart, brain and exercising muscle. Much research has focused on measuring effects of CO in subjects with diseases that make these organs vulnerable to changes in oxygen supply (Samet et al., 1987).

4.2.1 MECHANISMS OF TOXICITY

Carbon monoxide is classified as a chemical asphyxiant whose primary toxic action results from hypoxia (Stewart, 1976). It rapidly diffuses across the alveolar membrane and competes with oxygen in binding to haemoglobin. The affinity of haemoglobin for CO relative to its affinity for oxygen (the Haldane coefficient) has been reported at between 200 and 250 (Stewart, 1976). At a blood pH of 7.4, the Haldane coefficient has a value of 220 (Smith, 1980).

The binding of CO to haemoglobin is slowly reversible, and removal from the exposure source will lead to eventual expulsion of the gas from the exposed individual. Carbon monoxide will also bind to and inhibit other haemoproteins, such as myoglobin, although this normally only accounts for approximately 10% to 15% of the total CO binding in humans. Myoglobin is thought to play a role as a temporary store of oxygen in the heart and skeletal muscle and facilitate oxygen diffusion between haemoglobin and tissues (EPA, 1991). The affinity constant of myoglobin for CO is 40 times greater than that for oxygen (Myers et al., 1979). A combination of this greater affinity and a lower dissociation rate leads to retention of CO in muscular tissue (EPA, 1991). This is partly addressed in Section 4.5. The binding of CO to other haem proteins is discussed below.
REVIEW OF HEALTH EFFECTS

There are two well established mechanisms by which CO exposure results in hypoxia. First, by combining with haemoglobin to form COHb, CO reduces the percentage of haemoglobin available to carry oxygen in the blood. Second, by altering oxyhaemoglobin dissociation such that with increasing CO levels oxygen partial pressures must fall to lower levels for release of a given volume of oxygen (i.e. the oxyhaemoglobin dissociation curve is shifted to the left), CO inhibits the release of oxygen to the tissues from the already reduced amount of oxyhaemoglobin in the blood. A co-operative mechanism exists for the release of oxygen from haemoglobin. As each molecule is released from the haemoglobin, so the oxygen partial pressure required for release of the next molecule is reduced. In the presence of CO, the co-operativity mechanism does not come into play. Essentially, the remaining unbound haemoglobin’s affinity for oxygen is increased so that the haemoglobin gives up its oxygen less freely (Brody & Coburn, 1970; Smith, 1980). An analogy is sometimes made between anaemia and CO induced anaemia, carboxyhaemoglobinemia, in that both reduce the amount of haemoglobin available for oxygen transport, although strictly this is not correct. In a person with 50% carboxyhaemoglobinemia (where half of the haemoglobin is saturated with CO), the oxygen partial pressure must change by 85 mm Hg to deliver 5 ml oxygen per 100 ml blood; in 50% anaemia oxygen partial pressure must change by 75 mm Hg to deliver the same volume of oxygen (Smith, 1980).

A third, potentially serious mechanism is also postulated whereby CO inhibits tissue respiration by binding with the cytochromes a/a₃ (cytochrome c oxidase) and P450. The problem in studying any related health effects is determining the ratio of CO and oxygen within tissues in vivo (EPA, 1991).

Piantadosi (1990) reviewed the physiology of CO intoxication. Intracellular compounds containing copper or iron will bind to CO. As intracellular oxygen partial pressure falls, during tissue hypoxia or hypoperfusion, CO redistributes from the vascular space to extravascular tissue. Extravascular CO binds in vivo to myoglobin in skeletal muscle and the heart and may interfere with normal oxygen diffusion mechanisms. In the case of the cytochromes, CO may inhibit cell processes by binding to cytochrome oxidase (the terminal enzyme complex of the intramitochondrial electron transfer system that reduces oxygen to water in the respiration process). It is by binding to these enzymes that CO inhibits normal cellular function.

The health impact of intracellular uptake of CO at low concentrations is not well understood. The US EPA states that two crucial unknowns remain: the fraction of intracellular binding sites in discrete tissues inhibited by CO at any level of
COHb saturation; and the critical fraction of inhibited sites necessary to amplify or initiate a deleterious physiological effect, or trigger biochemical responses with chronic health effects (EPA, 1991).

Using dogs to study mechanisms of CO toxicity, Goldblaum et al. (1975) found that whereas normal dogs died after 15 minutes to 1 hour of exposure to CO by inhalation, during which COHb levels reached 54% to 90%, transfusion of blood with 80% COHb into anaemic dogs to produce COHb levels of 57% to 64% or intraperitoneal injection of 100% CO in dogs to raise COHb levels to around 60% (Goldblaum et al., 1977) caused no toxic effect. The author suggested (as also reviewed by Balraj, 1984) that the difference in toxic effect was due to the effect of dissolved CO in blood and that this is more important for CO toxicity than COHb since for toxicity to occur it is necessary for CO to be present in the blood and cross into tissues and interfere with tissue respiration. Because of the high CO tension in alveolar air, relatively high levels of CO in blood will occur following inhalation exposure and will persist as the blood is transported to organs such as the heart and brain (since the combination of CO with haemoglobin is not rapid). In contrast, after intraperitoneal exposure CO will be removed from the blood by passage through the lungs, and similarly, following transfusion of blood with elevated COHb, blood CO will be relatively low, owing to the high affinity of CO for haemoglobin.

However, Piantadosi (1990) questions whether sufficient evidence exists to support the premise of Goldblaum et al. (1975, 1977) that intracellular uptake of CO, though well-documented, may be a cause of death in CO intoxications. In the review of CO toxicity by Piantadosi (1990) animal studies are cited that indicate animals can survive very high tissue concentrations of CO.

Haemoglobin does not distinguish between oxygen and CO and, theoretically, a stress is caused by each molecule of CO binding to haemoglobin reducing the oxygen carrying capacity of the blood by a small but finite amount. Therefore, theoretically, there can be no dose without some effect (Stewart, 1976). The question of defining a threshold of effect is complicated by the variability in effect between different tissues and between individuals; CO may therefore be regarded as a multi-threshold toxicant.

Several conditions may make individuals more susceptible to adverse effects from CO exposure. These individuals can be classified into two main groups: those more sensitive because of an illness or other physiological condition, such as anaemia, chronic lung disease and occlusive vascular disease (Allred et al., 1991);
and more vulnerable individuals such as those who, for whatever reason, are more exposed to CO than average (for example, the elderly who spend a proportionately longer time in the home environment than younger and more active individuals or individuals who spend a greater time in the kitchen). In people with limited compensatory responses, such as those suffering coronary artery disease, more severe health effects may result (Benowitz, 1992). Susceptible groups are discussed in greater detail in Section 4.3.

Although exogenous sources of CO are paramount, the endogenous formation of COHb is also important. Humans normally produce CO endogenously as a byproduct of the catabolism of haemoglobin (and probably of other haemoproteins). This process involves the degradation of haemoglobin and other haem proteins liberating CO and occurs in the liver, spleen and erythropoietic system. In certain pathological conditions, such as haemolytic anaemia, the endogenous production of CO can increase by between two and eight times (Sjöstrand, 1949; Coburn et al., 1966). Also, neonates and pregnant women show a significantly greater endogenous CO production than other healthy individuals (EPA, 1991; see Section 4.3.1).

It should be noted that elevated levels of COHb can also result from exposures to methylene chloride (dichloromethane) and other organic solvents (Hamilton & Hardy, 1974), but this is not considered further here.

CARBON MONOXIDE EXPOSURE, HYPOXIA AND THE HEART

The respiratory processes taking place in the myocardium require comparatively large amounts of oxygen, between 8 ml and 10 ml of oxygen per minute for a man at rest (Tusl et al., 1987). Approximately 25% of the oxygen present in arterial blood is extracted by peripheral tissues, the remaining 75% acts as a reserve supply. Total oxygen uptake can be raised by increasing the amount of oxygen extracted from the blood or by increasing blood flow. Resting myocardial oxygen exchange results in 75% of available oxygen being extracted, leaving only 25% in reserve. Increasing the extraction of oxygen from coronary blood supplies would result in dangerously low coronary venous and myocardial oxygen tensions (Balraj, 1984). Therefore, in the myocardial system oxygen uptake is increased by raising the blood flow rate. Ayres et al. (1969) found that among individuals whose COHb levels had been raised to approximately 9% by breathing 5% CO for between 30 and 120 seconds, coronary blood flow increased significantly in those
free from coronary heart disease, but not in those with coronary heart disease. Pirnay et al. (1971) also found compensatory responses in a controlled chamber study of healthy individuals (see Section 4.5.1)

At the point where myocardial blood flow cannot meet oxygen demand, the myocardium becomes ischaemic. This in turn results in the development of chest pain and/or characteristic electrocardiogram (ECG) changes (Allred et al., 1991). The significance of this is discussed in Section 4.5 in which the effect of CO on coronary artery disease sufferers is reviewed. Ayres et al. (1969) also showed that raising COHb to 9% decreased mixed venous and presumably cellular oxygen tension by 20%. Since certain cells and their mitochondria are located at a critical distance from a capillary source of oxygen, a 20% decrease in oxygen tension may inactivate certain oxidative enzyme systems and decrease the energy production of the cell or lead to necrosis (Balraj, 1984).

In healthy individuals, a decrease in the delivery of oxygen to tissues, such as would result from CO exposure, causes an increase in the blood flow and cardiac output to meet the metabolic needs of the heart. Healthy individuals would be able to carry on working at normal levels although their maximum exercise capacity would decrease. Normal individuals do not usually suffer adverse effects from low doses of CO that would lead to COHb levels of less than 5%.

**Carbon monoxide exposure, hypoxia and the brain and central nervous system**

Carbon monoxide is also known to have detrimental effects on the brain. Compensatory mechanisms act in the brain, as in the heart, to ensure a constant delivery of oxygen. Benignus et al. (1992) performed two experiments studying the increase in brain blood flow after exposure to CO. The first experiment involved 14 men aged 18.8 to 33.6 years (mean 25.1, SD = 4.52) exposed to CO in air (0 mg/m³, n = 5; 5725 mg/m³ (6000 ppm), n = 4; 10 992 mg/m³ (9600 ppm), n = 5) from a 30 litre Douglas bag. Brain blood flow was measured before exposure and between 4.55 and 8.47 minutes after exposure. Individual COHb levels were determined by CO-oximeter within 2 minutes of emptying the Douglas bag; estimated changes in COHb ranged from 0% to 18% [original data presented only in a graph]. Relative brain blood flow (a measure of the % change in brain blood flow with respect to baseline) increased with increasing COHb (r = 0.62, p<0.019). There was substantial scatter around the regression line, implying that there might be differences among subjects in the brain blood flow response to COHb. A
second experiment was conducted to test the hypothesis that brain blood flow response to sustained COHb levels would also show inter-individual variation. The study group comprised 12 men (mean age 25.2, SD = 4.6, range 20.1–34.7 years). Baseline COHb levels, behavioural performance and brain blood flow were measured before CO exposure. A blood sample was taken after exposure to 10 992 mg/m$^3$ (9600 ppm) CO from a Douglas bag, and based on this enough CO was injected into an exposure chamber to maintain similar COHb levels for the remainder of the 4-hour experiment. The resulting COHb levels ranged from 10.8% to 18.4%. Although for a given individual there was little variation in brain blood flow response with time there was a significant difference in response between subjects (p<0.01). The results suggest a range of population sensitivities owing to individual variations in ability to compensate for rises in COHb level and the blood’s consequently reduced oxygen carrying capacity.

Respiration and circulation are the primary factors determining the effects of any hypoxia on the brain. The normal human brain receives approximately 15% of the cardiac output even though it accounts for only 2.5% of the body weight (Graham, 1992). A system of auto-regulation maintains a relatively constant blood flow in the face of perfusion pressure changes; in the case of exposure to CO and elevated COHb levels this auto-regulation involves vasodilation to maintain a constant delivery of oxygen (per unit volume; Benignus et al., 1992). When compensatory vasodilation is maximal, auto-regulation fails and cerebral blood flow decreases, oxygen extraction may be increased to maintain oxygen metabolism. Once maximal oxygen extraction is reached, a further decrease in cerebral blood flow will disrupt normal cellular metabolism and function. Oxygen supply may also be impaired by compromised heart function, by stenosis of supplying vessels and by any rise in central venous pressure (Graham, 1992).

The main types of damage to the brain resulting from reduction in the supply or utilisation of oxygen and substrate are selective neuronal necrosis and, after more severe episodes, cerebral infarction. Neuronal necrosis may be delayed for a period following the hypoxic episode. Different sections of the brain are more or less vulnerable to hypoxic insult. For example, the pallidum may be damaged in all hypoxias; the supraoptic, paraventricular and lateral nuclei of the hypothalamus are rarely affected (Graham, 1992).
Graham (1992) has presented the main categories of brain hypoxia, as outlined below.

- Ischaemic hypoxia — either a certain area or the whole of the brain is deprived of blood.

- Oligaemic hypoxia — blood supply is reduced, again either locally (which may lead to infarction of grey and white matter) or generally (in which case the effect will depend on the oxygenation of the haemoglobin). Neuropathological changes may be found along the arterial boundary zones of the cerebral cortex and cerebellum; they may be generalised in the cortex of the cerebrum and cerebellum, severe in the thalami, and minor or absent in the hippocampi.

- Anoxic hypoxia — the blood leaving the lungs is completely devoid of oxygen. In this instance a combination of circulatory failure and hypoxia results in brain damage.

- Hypoxic hypoxia — the oxygen tension of the arterial blood is reduced either as a result of lower oxygen levels in the air or because of impaired pulmonary function.

- Anaemic hypoxia — the type of hypoxia caused by CO exposure. The neurological and psychiatric symptoms cannot be regarded as related purely to CO as other situations (cardiac arrest, hypoglycaemia, closed head injuries among others) can lead to the same symptoms.

Severe CO intoxications frequently cause brain haemorrhages, especially in the white matter and corpus callosum. In those individuals surviving less than 24 hours, basal ganglia changes (unless haemorrhagic) are seldom detected. With greater survival periods macroscopic changes become more evident. For example in survivals of greater than 48 hours petechial haemorrhages and necrosis in the globus pallidus and hippocampus may be seen. Necrosis may also be seen in the cerebral cortex and globus pallidus and along arterial boundary zones. In longer-term survivals, patchy infarctions of the myocardium have been seen, indicating that the level of COHb may not be the only factor in brain damage; hypoxaemia or a reduction in brain blood flow (or both) may also play a major role (Graham, 1992).
Overall, white matter alterations are common and conspicuous and take three forms (Graham, 1992):

- discrete foci of myelin destruction throughout the corpus callosum, internal and external capsules and optic tracts, and sometimes also alterations beneath the ependyma;
- generalised destruction of myelinated fibres from frontal, temporal and occipital poles and the corpus callosum; and
- pallor of myelin staining and frank demyelination in the form of plaques that may or may not be confluent.

Roos (1994) presents a review of brain scans and other laboratory investigations of CO intoxications. Overall, computerised tomography scans found changes in the brain to be centred on the globus pallidus and white matter. Occasionally, sufferers of both immediate and delayed sequelae show no abnormalities in computerised tomography scans.

The mechanism of effect is explained in part by the regionality of brain blood flow. Although brain blood flow may increase enormously following CO exposure, the increase is not uniform across the brain (Roos, 1994). There is also great inter-individual variation (Benignus et al., 1992). The cerebral cortex shows the smallest blood flow increase. Damage to the nervous system may be more a result of blood and tissue acidosis than impaired energy metabolism. In acute CO intoxication the damage mechanism may be summarised as follows: a reduced oxygen delivery resulting in hypoxia; general hypotension with a decreased intracerebral metabolism, metabolic acidosis and inhibited intracellular metabolism by binding of CO to mitochondrial enzymes (cytochromes); and stimulation of free radical formation (Roos, 1994).

Zhang and Piantadosi (1992) attempted to determine if there was oxidative stress involving mitochondria after CO exposure in the rat brain, and studied the nature of the partially reduced oxygen species involved. Rats were exposed to 1% CO for 30 minutes and then re-oxygenated in air for 180 minutes. Increased hydrogen peroxide activity was found in the forebrain after re-oxygenation, indicating an intracellular site of hydrogen peroxide production. Two periods of oxidative stress occurred, immediately after CO exposure and 120 minutes after re-oxygenation, indicated by decreases in the ratio of reduced to oxidised glutathione. The authors concluded that their findings suggest a possible explanation for some of the
delayed toxicity of CO poisoning in the brain. They summarised the postulated mechanism, which involves generation of partially reduced oxygen species in excess of the capacity of local antioxidant defences to deal with them, leading to mitochondrial damage by oxidation of enzymes, lipids or mitochondrial DNA. The regional production of hydrogen peroxide detected indicated that a major source of partially reduced oxygen species following CO exposure may be the subcortical regions such as the basal ganglia. This region is known to be vulnerable to injury in CO intoxication (Piantadosi, 1990).

The role of free radicals in CO toxicity has been investigated by Fechter et al. (1997) in a study using guinea pigs. The study looked at the possibility that free radical generation occurs in the cochlea during CO hypoxia and leads to auditory impairment. Two protective agents were employed, phenyl-n-tert-butyl-nitrone (a free-radical scavenger) and allopurinol (a free radical inhibitor). One hour prior to exposure the animals were treated with one of the protective agents or saline solution. Animals were exposed to 35 ml CO per kg by intraperitoneal injection (producing a COHb level of approximately 40%); control animals were exposed to an equal volume of air. Both free-radical protective agents blocked loss of auditory threshold sensitivity produced by CO, suggesting a potentially significant role for CO in the impairment of high frequency auditory sensitivity.

Many clinical controlled chamber studies have been performed to assess the effect of CO on neuropsychological performance. In these studies (Section 4.5.2), the aim has been to assess the performance decrement associated with CO, not to impart ischaemic anoxic or hypoxic damage.

**4.2.2 Adaptation to Carbon Monoxide**

Adaptation to CO is complex and poorly understood and it may or may not be immediately or eventually beneficial. It is generally agreed that continued hypoxia leads to adaptive processes allowing an individual to tolerate lower oxygen carrying capacity and oxygen partial pressures. The clearest example of this is the adaptation of individuals to high altitude. In humans it is hypothesised that increased haemoglobin concentration is the mechanism of adaptation to CO. Stewart et al. (1974) found a positive correlation between the COHb level in
smokers and haemoglobin concentration — those smokers with a higher COHb level tended to have a higher concentration of haemoglobin in their blood. This correlation was also found, less strikingly, in non-smokers with elevated COHb levels. This may indicate an adaptive mechanism increasing the concentration of haemoglobin in relation to COHb levels but the effect of the many other components of ambient air and tobacco smoke may play an important role. Whether such mechanisms operate in long-term exposures to CO is unresolved (EPA, 1991).

Bartlett (1968) suggested that smokers may be less susceptible to low concentrations of CO found in the environment since their COHb concentrations are already elevated, relative to non-smokers, thus a person with a COHb level of 5% from smoking would not absorb more CO from the environment unless the atmospheric concentration was greater than 34.5 mg/m³ (30 ppm). However, Stewart et al. (1974) respond to this by stressing the much higher CO concentrations in tobacco smoke of approximately 229 mg/m³ (200 ppm). Intermittent exposure to 200 ppm superimposed on a lower ambient CO concentration would further increase the CO body burden (Stewart et al., 1974), though possible adaptation to high CO-levels must be considered.

Acclimatisation to CO has been studied in dogs (Wilks et al., 1959) given a daily 6–8-hour exposure to CO levels of 916 mg/m³ to 1145 mg/m³ (0.08–0.10%; 800–1000 ppm) for 36 weeks. Their tolerance to CO was compared with that of normal dogs, altitude-acclimatised dogs, and normal dogs transfused with blood from normal dogs. In both CO-acclimatised and altitude-acclimatised dogs there was an observed increased tolerance to CO which the authors attributed to an increased concentration of haemoglobin in the blood.

An indirect effect of CO on the cardiovascular system may be an increase in blood viscosity due to CO-induced increases in red blood cell count, blood haemoglobin content or haematocrit (Weir & Fabiano, 1982). However, in a study by Kjeldsen and Damgaard (1968) no significant changes in the haematocrit values were noted. The effect of CO and altitude induced hypoxia on the composition of blood and urine was investigated in eight volunteers. Over 8 days they were intermittently exposed to CO leading to an average COHb level of 13%. There was a moderate increase in reticulocytes on days 3, 6 and 7. In their review of the role of CO in cardiovascular diseases, Weir and Fabiano (1982) concluded that the level and duration of exposure required to induce adaptive changes are such that acute effects would necessitate removal of a person from the exposure source before adaptation and any associated problems could develop.
4.2.3 Health Effects of Carbon Monoxide Caused by Mechanisms Other Than Hypoxia

In Section 4.2.1 the general toxicology of CO and physiological functions and effects other than purely hypoxia-related responses were discussed. This section summarises one of the main effects that cannot be wholly or partly attributed to hypoxic toxicity — atherosclerosis — and also presents recent research on the role of CO in immunological function and other areas.

Atherosclerosis

Atherosclerosis is an accumulation of lipid in the intima of large elastic arteries and medium-sized muscular arteries. Its clinical manifestation is coronary artery disease (Smith & Steichen, 1993). The effect of CO on sufferers from coronary artery disease is one of the main areas of research on CO toxicity, and the role of CO in pathogenesis or exacerbation of atherosclerosis has also been widely researched, although it is an unresolved area.

Benowitz (1992) suggested that CO might contribute to atherosclerosis by altering lipid metabolism and/or increasing the permeation of lipids into blood vessel walls, and perhaps by enhancing platelet aggregation. Although in hypercholesterolemic animals CO may accelerate atherosclerosis, the EPA (1991) has stated that the evidence for CO-induced atherogenesis in animals is contradictory and that any effect must be subtle at most. Penney and Howley (1991), in a review, related CO exposure to hypertension and, based on a careful examination of available animal studies, found no conclusive evidence that CO exposure in normocholesterolemic subjects increased the risk of atherosclerotic disease. Only when serum cholesterol was artificially and greatly increased by dietary supplementation did CO appear to enhance atherosclerosis. Furthermore, in their review of CO and atherosclerosis (including the early studies by Astrup, see below), Smith and Steichen (1993) found no atherogenesis following CO exposure in several animal species when they were fed on normal or high cholesterol diets.
Wald et al. (1973) studied the relative levels of COHb in smokers and the incidence of atherosclerosis. From a total of 1085 volunteers, of whom 180 were non-smokers, from companies (including three tobacco companies) in Copenhagen, 1083 blood samples were taken; 133 subjects were excluded from the analysis. Those smokers in whom COHb levels were greater than 5% were 21 times more likely to develop atherosclerosis than were those smokers in whom COHb was less than 3% (95% confidence limits 3.3, 734.3). The magnitude of the risk did not vary significantly for different types of tobacco, age or sex. The risk was similar for ischaemic heart disease and intermittent claudication*. However, it is not possible to say that CO was the cause of the atherosclerosis. These data only show that the level of COHb is an indicator of likelihood of occurrence of the disease, not that CO has an atherogenic effect.

Similarly, Astrup (1972) reported that atherosclerotic smokers have significantly higher average COHb levels (>6% COHb) than non-atherosclerotic smokers (4.6% COHb). While noting that other smoke components may be contributory factors, Astrup supports his conclusion by reporting that, in rabbits, COHb at similar levels to those found in heavy smokers causes severe arterial damage.

However, Smith and Steichen (1993) found no study in humans showing an association between atherosclerotic disease and CO exposure alone. They suggest that findings, such as those of Wald et al. (1973), of atherosclerosis in smokers, probably cannot be attributed to CO alone, although it may play a role in atherogenesis, as there are many other compounds in cigarette smoke that may have an effect.

Occupational exposures have also been investigated; the following study provides some evidence linking long-term exposure to CO and atherosclerosis.

Stern et al. (1988) studied a cohort of traffic control officers working on bridges (n = 4317) and in tunnels (n = 1212) in New York between 1 January 1952 and 10 February, 1981. Historical CO concentration data were obtained from the company running the crossings. Measurements showed peak levels of 458 mg/m³ (400 ppm), and 24-hour average concentrations of 60.7 mg/m³ (53 ppm) falling to 43.9 mg/m³ (38.3 ppm) over time because of improvements in ventilation. Carboxyhaemoglobin levels were also measured in 1970 (before a ventilation system was built into the toll booths) and respective COHb levels averaged

* Intermittent claudication is a clinical manifestation of chronic ischaemia and presents as muscle pain on exercise relieved by rest (Morris, 1990).
2.12 and 3.90% for non-smoking and smoking bridge officers and 2.93 and 5.01% for non-smoking and smoking tunnel officers. A 1981 study by the National Institute for Occupational Safety and Health did not find post-shift COHb levels differed significantly between bridge and tunnel workers (4.9% and 4.5% respectively). The difference between pre- and post-shift levels was 20% in non-smokers and 10% in smokers.

Standardised mortality ratios (SMR) were analysed comparing this cohort with the population of New York. The overall mortality among bridge workers was less than expected — 314 deaths versus 409 expected; for tunnel workers the overall mortality was approximately equal — 160 deaths versus 153 expected (SMR = 0.76 and 1.04 respectively). Heart disease mortality amongst tunnel workers was the only cause of death that was statistically significantly elevated among the entire cohort — 67 observed deaths versus 54 expected (SMR = 1.24, 90% CI 1.01–1.51, p<0.05). A greater excess was noted when deaths due to arteriosclerotic heart disease were analysed — 61 deaths observed versus 45 expected (SMR = 1.35, 90% CI 1.09–1.68, p<0.05). In those tunnel workers employed for more than 10 years the SMR increased to 1.88, with 30 deaths observed compared with 16 expected (90% CI 1.36–2.56, p<0.01). Increasing age also appeared to produce an elevated risk of arteriosclerotic heart disease. The excess risk of arteriosclerotic heart disease in tunnel compared with bridge workers decreased in all age groups after cessation of exposure when individuals left employment. Potential confounding factors considered in the study were smoking, selection bias and socioeconomic status. However, officers’ smoking habits were similar to the general population and therefore unlikely to explain the findings on arteriosclerotic heart disease (lung cancer registrations were also analysed and no excess was found). Selection bias, whereby potentially high risk employees self-select into jobs, was countered by the fact that the employee’s task was unknown until completion of selection procedures. Furthermore, the bridge and tunnel workers were drawn from the same socioeconomic background and therefore unlikely to differ greatly in race, diet, alcohol consumption and physical activity.

THE ROLE OF CARBON MONOXIDE IN PHYSIOLOGICAL FUNCTIONS

In recent years, much research has centred on the role of CO in immunological response and neuronal messenger-related functions.
Marks (1994) reviewed the literature on the role of CO in relation to haem oxygenase and interactions with various metalloporphyrins. It has been suggested that CO plays a biological role similar to nitric oxide (Marks, 1994; VanUffelen et al., 1996). A short review of some of the literature on sources and role of CO in biological systems is also provided by Rodgers et al. (1994). Broillet and Firestein (1996) reviewed the respective roles of gaseous second messengers in vertebrate olfaction, namely nitric oxide and CO. Both CO and nitric oxide activate guanylyl cyclase but with different potencies, half-lives, and distribution of the enzymes producing them. The roles of nitric oxide and CO include inhibition of platelet aggregation and blood vessel relaxation, and activation of soluble guanylyl cyclase leading to production of the second messenger cyclic guanosine monophosphate. There is also evidence that CO acts as a neuronal messenger by depleting cyclic guanosine monophosphate levels in vitro in cultured neurons through haem oxygenase inhibition. It remains to be confirmed that in vivo haem oxygenase has a role in the regulation of cyclic guanosine monophosphate through CO.

Haem oxygenase may be a protein induced by oxidant stress. The production of CO by haem oxygenase breakdown of haem is a rather costly way to produce a signal molecule (Rodgers et al., 1994) but other biological pathways may be found (Broillet & Firestein, 1996). As well as CO, haem oxygenase-mediated breakdown of haem produces bilirubin. In fact, CO and bilirubin are produced in equimolar amounts, so that the level of COHb may be used to determine the level of bilirubin. The relationship between oxidant stress induced production of haem oxygenase and the antioxidant capacity of bilirubin may be physiologically relevant. Also it is possible that cellular response to stress may be mediated through CO production as well as haem depletion (Rodgers et al., 1994).

A study by Giustino et al. (1993) showed reversible immunological changes characterised by an altered splenic macrophage function in rats prenatally exposed to CO. Exposure to 171.8 mg/m³ (150 ppm) CO from day 0 to day 20 of gestation significantly reduced splenic macrophage oxygen release in both 15-day-old (p<0.05) and 21-day-old (p<0.05) male rat pups; 60-day-old rats exposed in utero exhibited no significant change.

In further studies (Giustino et al., 1994), pregnant rats were exposed to CO in air at 0 mg/m³, 85.9 mg/m³ (75 ppm) or 171.8 mg/m³ (150 ppm) from day 0 to day 20 of gestation. The results showed prenatal exposure to 171.8 mg/m³ CO significantly decreases the number of leukocyte common antigen cells in 21-day-old male rats (p<0.001). Other cell populations showed a trend towards reduction.
that was not significant. There were no significant changes following exposure to 85.9 mg/m³ CO in air.

Thom (1993) studied the involvement of leukocytes in the conversion of xanthine dehydrogenase and xanthine oxidase. The CO exposure was to 1145 mg/m³ (1000 ppm) initially, followed by 3435 mg/m³ (3000 ppm) or sufficient CO to render the animal unconscious. A tenfold increase in myeloperoxidase activity was found in brain microvessel segments after exposure to CO, and fluorescence and light microscopic examination found leukocytes in CO exposed animals, but not in control animals. Thom suggests the results indicate that leukocytes are responsible for the biochemical changes in the brain following CO intoxication. This would support the hypothesis that CO mediated brain injury is a type of post-ischaemic reperfusion injury (Thom, 1993).

The breakdown of haem by haem oxygenase produces CO; alveolar macrophages themselves produce haem oxygenase, therefore CO may play a role in alveolar macrophage function, and this has been investigated by Fukushima et al. (1995). Using alveolar macrophages obtained from rat lungs, CO (10 nmol/l to 1 µmol/l) was found to decrease chemiluminescence of alveolar macrophages in a concentration-dependent fashion. At the higher concentration (1 µmol/l), CO also significantly increased intracellular cyclic guanosine monophosphate levels (p<0.01, n = 7).

The role of CO in a signalling system in the regulation of tumour necrosis factor α production was investigated by Arias-Diaz et al. (1995). They found that an increase in intracellular cyclic guanosine monophosphate, secondary to an endogenous production of CO, participates in the release of tumour necrosis factor α by activated human pulmonary macrophages.

### 4.2.4 Summary

The primary mechanism of CO toxicity is hypoxic stress. It binds to haemoglobin far more tenaciously than does oxygen and thereby reduces the oxygen carrying capacity of the blood. This hypoxia is exacerbated by an effect on the dissociation of oxygen from haemoglobin reducing the amount of oxygen reaching the tissues. Mechanisms involving other haem proteins and cytochromes by which cellular respiration is altered are also postulated.
It is thought that smokers and those exposed to CO over long periods may become adapted to their exposure in a similar way to populations living at high altitude adapt to the lower oxygen levels. In the case of CO, the nature of any adaptive mechanism is unresolved.

The evidence that CO effects atherogenesis in animals fed high cholesterol diets is inconclusive. Studies in human smokers have found relationships between COHb level and the risk of developing atherosclerosis, and workers exposed to CO in exhaust fumes showed an excess heart disease mortality rate (including arteriosclerotic heart disease). Nonetheless, the confounding effects of other constituents of smoke and exhaust should be noted; there is no strong evidence for an association between CO-exposure alone and atherosclerosis.

Animal studies of prenatal exposure to CO suggest that it may be implicated in various effects on immunological functions. A neurotransmissive role for CO has also been suggested.
4.3 SUSCEPTIBLE POPULATIONS

In any situation involving exposure to CO, a primary risk factor is an individual’s ability to transport oxygen in the blood; those individuals with a reduced capacity are more sensitive to any sort of hypoxic stress. This reduced capacity can be the result of a less efficient pulmonary or circulatory system, a pathological condition such as anaemia that reduces the amount of circulating haemoglobin or another condition that in some way reduces the oxygen transport capacity. If, for any of these reasons, an individual’s oxygen transporting capacity is reduced, they may be at greater risk of adverse effects arising from CO exposure than normal healthy individuals.

If it can be assumed that there is an average exposure to CO indoors, then people who are exposed more than average may be thought of as more susceptible to CO exposure. For example, in addition to being inherently more sensitive, the elderly may spend proportionately more time indoors than the young and active, and thereby be exposed longer to indoor CO sources. Those individuals spending a greater fraction of their time preparing meals using a gas cooker may also be exposed to greater CO concentrations and for a longer time.

It is also important to note that socioeconomic, lifestyle, and other factors can play a part in determining individual susceptibilities through diet, exercise, income, housing and so on. For example, an individual may spend a greater time indoors because of unemployment, disability or age. Also a diet rich in fats increases the risk of developing heart disease, as does taking too little exercise (Department of Health, 1993). Such factors may lead to an increased sensitivity to any hypoxic stress.

This section summarises the main population groups that are most sensitive to CO exposure and the reasons for their sensitivity. Combinations of sensitivity factors will tend to compound a person’s susceptibility.
4.3.1 The Pregnant Mother, Fetus and Child

The mother and fetus are inherently at increased risk from exposure to CO owing to the mother's increased rate of endogenous production of CO. As well as her own endogenous CO, the mother also receives some CO from the fetus' endogenous CO production, accounting for approximately 3% of the total maternal COHb. The pregnant mother also has a 20% to 30% reduction in oxygen capacity, through a reduction in haemoglobin concentration (Longo, 1977), and an increased ventilation rate, which leads to an increased rate of CO uptake for a given CO exposure (Marx et al., 1990; EPA, 1991). In the fetus, oxygen partial pressures must fall to lower levels than in the adult for release of a given volume of oxygen (that is, the oxygen dissociation curve is to the left of that for the adult; Figure 4.1; Longo, 1977; EPA, 1991; Seger & Welch, 1992). The oxygen partial pressure is already between a third and a fifth that of the mother (approximately 20 to 30 mm Hg in the fetus compared with 100 mm Hg in the adult). Add to this the fact that fetal blood COHb levels are 10 to 15% greater than the mother's (Longo, 1977) and it can be seen that the fetus is highly sensitive to any decrease in oxygen carrying capacity. Should the mother be exposed to CO, the diffusion of oxygen from mother to fetus and from fetal blood to fetal tissues will be impaired. It is possible for the mother to survive CO intoxication with no adverse effects whilst the fetus dies (Myers et al., 1979). Smoking in pregnancy may worsen an already precarious situation and it is smoking that constitutes the commonest source of fetal CO exposure. That CO impairs intracellular respiration may partially explain why smaller babies, premature deliveries or intrauterine fetal death tend to occur more often among smoking mothers (Koren, 1996).

The teratogenic potential of CO is reviewed by Norman and Halton (1990). From 60 case history reports of maternal CO poisoning the authors note that anatomical malformations show a preponderance in cases of exposure during the first 13 weeks of pregnancy. Functional and psychomotor disturbances were not restricted to any particular period of pregnancy. A relationship was found between the severity of maternal symptoms and fetal outcome. Where the mother remained conscious, fetal outcome was generally good; it was generally poor when the mother became unconscious or comatose.
An example of co-related anatomical malformation of the fetus is provided by Hennequin et al. (1993). A pregnant woman suffered headache and dizziness at 10 weeks’ gestation; her first child suffered a period of unconsciousness at the same time. A gas water heater was suspected as the cause of their health effects but was not repaired. Seven months into the mother’s pregnancy, her daughter was found comatose; blood COHb levels were 27.5% for the daughter and 14% for the mother. Her second child was born weighing 2950 g with various abnormalities, including heart malformities that were rapidly fatal. Subsequent investigations found CO levels of 114.5–137.4 mg/m³ (100–120 ppm) after 2 minutes’ use of the water heater.
Astrup (1972) correlated COHb levels in smoking and non-smoking pregnant women (measured approximately once a month) with the birthweight of their babies. The average birthweight was 2999 g for smoking mothers and 3225 g for non-smoking mothers and there was a negative correlation (p = 0.05) between COHb and birthweight. Other substances in the tobacco smoke may be factors. With this in mind, Astrup (1972) exposed pregnant rabbits to CO giving COHb levels of 0%, 8–10% and 16–18% COHb. There was a dramatic increase in the number of stillbirths and deaths within the first 24 hours of life and a decrease in birthweight with increasing COHb.

The susceptibility of newborn infants to CO is also greater because of a comparatively greater oxygen consumption rate and lower oxygen transport capacity for haemoglobin than healthy adults. Therefore, for a given increase in either CO exposure or COHb level, newborn infants will tend to be more susceptible (EPA, 1991).

There is evidence to suggest that children, also, may be more susceptible to CO intoxication than adults and may experience different symptoms at lower COHb levels than adults. For example, Gemelli and Cattani (1985) provided three case histories of children suffering bouts of sickness, abdominal pain, headache, vomiting, diarrhoea and fever, in whom a diagnosis of gastroenteritis was often made. In two cases, a parent of the child showed symptoms which led to their COHb levels being measured. In one, the father’s COHb level was 23% and the child’s was later found to be 16%; in the second case the father’s COHb level was 25% and the child’s 18%.

The sensitivity of children is also demonstrated in a case report by Lacey (1981), in which an 8-year-old girl exposed to CO in the back of a car during a long journey fell unconscious and suffered neuropsychiatric changes (see also Sections 4.4.2 and 4.4.4). The other occupants of the car also experienced effects of CO intoxication — headaches and dizziness — but did not seek medical attention.

4.3.2 THE ELDERLY

As with other sensitive groups, it is a reduction in oxygen carrying capacity that is the cause of sensitivity in the elderly, in whom the pulmonary system may be weak or work submaximally as a result of ageing. The bodyweight and composition,
and level of activity, may also play a role in making the elderly more susceptible. The elderly also tend to have a greater frequency of cardiovascular and cerebrovascular disease (Department of Health, 1993). Even low levels of CO may therefore result in a critical reduction in oxygen delivery (EPA, 1991). However, a controlled chamber study of young and elderly men found that, for a given CO level, the elderly absorbed CO less readily than the young (Harbin et al., 1988), perhaps a result of a less efficient pulmonary system.

The demographic situation in the UK means there will be an increasing proportion of elderly people in the population in the coming decades. To maintain daily metabolic requirements the average person needs about 10 ml/kg/min maximal oxygen uptake. Even average healthy males of about 75 years, and women of 67 years, may be close to this level of maximal oxygen. It is possible that even a low level of CO exposure may push an elderly individual beyond their ability to deliver oxygen to tissues. The greater life expectancy of females means a greater population of elderly women may be at risk than elderly men (EPA, 1991).

Neurological decline is also a factor in ageing. It has been found that CO has some effects on neuropsychological performance. It is possible that, owing to age-related decreasing neurological ability, the elderly are more susceptible to neuropsychological performance decline following CO exposure. For example, the increase in brain blood flow described by Benignus et al. (1992) may be compromised in an elderly individual because of cerebrovascular disease, so that the compensatory responses necessary to protect against adverse effects are inadequate.

### 4.3.3 Sufferers of Coronary, Pulmonary and Vascular Diseases

Section 4.5.1 reports a number of controlled exposure studies in which ischaemic heart disease sufferers were exposed to various concentrations of CO. Many people may have some form of coronary artery disease unknowingly; that is, they are asymptomatic. Even in known coronary artery disease sufferers, the predominant type of myocardial ischaemia is ‘silent’, or asymptomatic. Although
angina sufferers may have occasional ischaemic episodes resulting in chest pain, they may have many more episodes that are asymptomatic. A particularly high risk group are those individuals suffering totally asymptomatic coronary artery disease (EPA, 1991).

Coronary artery disease is a dominant cause of congestive failure. In individuals with congestive heart failure, there is a markedly reduced circulatory capacity. These individuals are therefore more sensitive to a reduced oxygen level in their blood. As a large proportion of congestive heart failure sufferers also have coronary artery disease, these people are perhaps an even more sensitive population (EPA, 1991).

A subpopulation more sensitive to CO because of a reduced circulatory capacity, and often overlapping the group of sufferers of coronary artery disease, are sufferers of peripheral and cerebrovascular diseases. These diseases limit the blood flow to muscle and other organs (EPA, 1991). Little experimental work has been performed on this group.

4.3.4 INDIVIDUALS WITH ANAEMIA AND OTHER HAEMATOLOGICAL DISORDERS

Anaemia, a clinically diagnosed low haemoglobin value, may be asymptomatic if the anaemia is mild or moderate and the person is inactive. The sensitivity of anaemic individuals to a given CO exposure would tend to be greater because of their lower haemoglobin value. As mentioned previously, in discussing endogenous CO production, individuals suffering from haemolytic anaemia have a higher baseline level of COHb than normal healthy individuals (Coburn et al., 1966).

Anaemia is often the result of the presence of abnormal haemoglobin in the blood. There are many hundreds of variants to normal human haemoglobin. An example of the effect such variations is given by the EPA (1991) who reviewed a study by Solanki and co-workers showing greatly reduced lifespan of haemoglobin in sickle cell disease and increased baseline COHb levels (to 4%).
4.3.5 SUMMARY

Many subpopulations display heightened sensitivities to any hypoxic stress, including the stress imparted by exposure to CO. In the case of CO, the most notable of such populations are the pregnant mother, fetus and newborn infant, the elderly, and sufferers from diseases such as coronary artery disease, congestive heart failure and pulmonary diseases. All these groups show a limited ability to compensate for reduced oxygen carrying capacities and are more sensitive than other individuals in whom compensatory responses are intact.
4.4 CLINICAL INVESTIGATIONS AND OTHER STUDIES

4.4.1 BACKGROUND

The health effects resulting from exposure to CO indoors and clinical manifestations of CO intoxication have been extensively reviewed (e.g. Beck et al., 1940; Myers et al., 1979; Samet et al., 1987; Coultas & Lambert, 1991; Gorman & Runciman, 1991; Lambert & Samet, 1994). Section 3 provides an overview of the relationship between CO concentrations and resulting COHb levels.

The majority of studies have focused on CO exposures resulting in either hospitalisation or other clinical investigation of the sufferer. Studies vary in the way exposures are assessed. Most studies present results of COHb analysis to indicate the CO exposure, whereas others employ measurement of the concentration of CO in expired air from the lungs. The main methods used for determination of CO exposure and of COHb level are discussed in Section 3.3.

Most known cases of CO poisoning fail to reach a hospital alive. For example, in England and Wales during 1985, 1365 people died as a result of CO poisoning; in the same period, hospital admissions totalled 475 with only ten deaths recorded (Burr, 1995).

In 1995 there were 1116 deaths in England and Wales due to toxic effects of CO (International Classification of Disease (ICD) code 986; Office of National Statistics, 1997). This total encompasses a wide range of possible causes of death, from fires to exposures to motor vehicle exhausts. The most relevant causes of death in relation to this report were: 16 from exposure to CO from the incomplete
combustion of domestic fuels; 2 due to CO from other sources; and 20 due to unspecified CO sources. Suicides accounted for a far greater proportion (231) of CO-related deaths. Accidental or intentional exposure could not be determined for a further 20 deaths.

In 1992, 79% of the 1520 reported CO-related deaths were self-inflicted, a further 198 (i.e. 13%) were accidental and 7% (103) were not classified as to whether they were accidental or self-inflicted. Assuming the same proportion of accidental versus self-inflicted deaths, about 15 out of the 103 would be accidental. Of the accidental deaths 54% (i.e. 107) were due to fires and 91 due to other causes. (Burr, 1995).

The usual source of indoor exposure to CO is some form of heating appliance. In the UK the majority of enquiries to the National Poisons Information Service between 1977 and 1982 involving accidental exposures to CO concerned domestic gas-fired central heating boilers. Enquiries were more frequent in the winter months and were apparently related to minimum monthly temperature. (Thompson & Henry, 1983). The increase during winter may be because of increased use of combustion heating appliances and reduced ventilation at this time. Estimates of the proportion of CO-related deaths occurring in the home vary from about 50% to 70% (Schaplowsky et al., 1974; Spiller, 1987; Burr, 1995). An extensive review of indoor CO levels and exposures is presented in Section 2.

In discussing the occurrence of fatalities as a result of CO exposure in the home it is useful to mention town (or coal) gas. This gas was used before the advent of natural gas (methane) and contained CO as a main constituent (14%); the other constituents are oxygen (1%), hydrogen (47%), nitrogen (9%), carbon dioxide (2.5%), methane (23.5%) and propane (3.0%). When coal gas was used as a domestic fuel there were 1500 to 2000 CO deaths per year from this source, including suicides (Lowe-Ponsford & Henry, 1989).

Although not an exhaustive review of the clinical manifestations of CO, the following sections identify main symptoms reported and the types of situation in which intoxications occur. The number of cases of unintentional CO intoxication is probably under-estimated owing to the similarity of symptoms between CO poisoning and other common medical conditions. So, although Burr (1995) reported 475 hospital admissions identified as CO poisonings, there may have been many more instances where patients’ symptoms were due to CO exposure, but either they did not seek medical attention or a diagnosis other than CO poisoning was made. The potential problems in diagnosing CO intoxication are discussed later in Section 4.4.3.
4.4.2 Indoor Exposures

Carbon Monoxide Exposure Suspected on Admission to Hospital

In a mass CO poisoning incident, 184 students and teachers at a school in Michigan, USA, were exposed to an estimated concentration of 572.5 mg/m³ (500 ppm) of CO for a mean of 95 minutes and a maximum of 150 minutes (Burney et al., 1982). The cause of the incident was identified as a forced-air heating system operating incorrectly. Exposure ceased when a teacher recognised the symptoms of CO poisoning and activated the fire alarm. Questionnaires were sent to all occupants of the school and to doctors and administrators at the four hospitals where patients were treated. Of the 160 people (87%) who became ill, 96 (60%) were admitted to hospital. Blood samples were taken for COHb analysis from 66 patients, of whom almost half had COHb levels of between 21% and 25%. (The range of COHb levels for all 66 patients was 4% to 28%; the mean level was 18.2 ± 6.4%). Patients’ symptoms and their reported frequency are presented in Table 4.1. No significant difference in type or severity of symptoms was noted between sexes or among age groups. Most symptoms correlated with the duration of exposure: headache, p = 0.0001; dizziness, p = 0.0002; muscle weakness, p = 0.006; trouble with vision, p = 0.007; and trouble with thinking, p = 0.02; though nausea, shortness of breath and loss of consciousness did not (p = 0.15).

[No details are given regarding correlation of symptoms and COHb level.]

The indoor burning of charcoal or wood and its health effects were the subject of a paper by Dahmash et al. (1993). The authors examined the circumstances surrounding 11 patients’ admission to hospital in Riyadh, Saudi Arabia. Each patient was found unresponsive in their small, poorly ventilated home. The domestic heating method used was charcoal or wood-burning clay-type braziers. Exposure commenced between 20:00 h and 22:00 h, when the individuals retired to sleep. All were discovered, unconscious the following morning. Patients were examined on admission, with particular attention paid to the nervous and cardiorespiratory systems. The measured COHb levels ranged from 13.3% to 51.8% with a mean of 28%. None of the patients experienced cardiovascular collapse or pulmonary oedema, but ten were transiently hypotensive. Dahmash et al. (1993) postulated that the hypotension may have been a result of myocardial depression or vasodilation. Ten patients had leucocytosis, eight had
hyperglycaemia, and seven had elevated transaminase levels. One also suffered moderate myoglobinuria without acute renal failure. Mofenson et al. (1984) stated that muscle necrosis leading to myoglobinuria and acute renal failure has been described in adults. The authors observed no correlation between the COHb level and the patient’s clinical status on arrival, except that the patient with the highest COHb level, 51.8%, was the only individual comatose on admission.

Hampson et al. (1994) identified 79 patients exposed to CO resulting from burning charcoal briquettes indoors in 32 separate incidents between October 1982 and October 1993. More than one person was exposed in 69% of incidents. Their ages ranged from 3 months to 87 years and all were from the state of

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Study authors and frequency of symptom reporting (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>–</td>
</tr>
<tr>
<td>Headache</td>
<td>90</td>
</tr>
<tr>
<td>Trouble thinking</td>
<td>46</td>
</tr>
<tr>
<td>Dizziness</td>
<td>82</td>
</tr>
<tr>
<td>Nausea</td>
<td>46</td>
</tr>
<tr>
<td>Drowsiness</td>
<td>–</td>
</tr>
<tr>
<td>Trouble sleeping</td>
<td>–</td>
</tr>
<tr>
<td>Heart pounding</td>
<td>–</td>
</tr>
<tr>
<td>Shortness of breath</td>
<td>40</td>
</tr>
<tr>
<td>Weakness</td>
<td>53</td>
</tr>
<tr>
<td>Numbness or tingling</td>
<td>–</td>
</tr>
<tr>
<td>Dry mouth</td>
<td>–</td>
</tr>
<tr>
<td>Chest pain</td>
<td>–</td>
</tr>
<tr>
<td>Decreased vision</td>
<td>26</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>–</td>
</tr>
<tr>
<td>Vomiting</td>
<td>–</td>
</tr>
<tr>
<td>Unusual spells</td>
<td>–</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>–</td>
</tr>
<tr>
<td>Loss of consciousness</td>
<td>6</td>
</tr>
</tbody>
</table>

–, not measured
Washington, USA. Carboxyhaemoglobin levels ranged from 3.0% to 45.8%, the average being $21.6 \pm 9.6\%$. Unconsciousness occurred, at least transiently, in 33% of the patients. The symptoms presented in Table 4.1 occurred in more than 25% of patients. Symptoms reported less often were lethargy, abdominal pain, confusion, weakness, dyspnoea, chest pain, ataxia, seizures, euphoria, irritability, and incontinence.

**CARBON MONOXIDE EXPOSURE IDENTIFIED AFTER ADMISSION TO HOSPITAL**

Grace and Platt (1981) presented the case histories of five people in Denver, Colorado, USA, for whom CO poisoning was identified only after hospital admission (occult poisoning — i.e. poisoning not immediately obvious to the diagnostician). A 67-year-old diabetic man presented with light-headedness, vertigo, anterior chest pain that worsened with deep inspiration, dry cough, chills and a mild headache. His wife suffered similar symptoms. He was diagnosed as suffering a viral syndrome, hypokalaemia and diabetes mellitus. Following discharge, the patient returned to hospital twice more over two weeks, collapsing at the hospital on the final visit. A COHb measurement showed 15.6%; his wife’s COHb level was 18.1%. The cause of the poisoning was identified as a faulty gas boiler. Another case involved a 69-year-old man who passed out, and suffered shortness of breath and neuropsychological changes. He was diagnosed as suffering acute inferior myocardial infarction with secondary mild congestive heart failure and chronic obstructive pulmonary disease. Two relatives visited the patient in hospital and later stayed in his mobile home. The following morning they reported to the hospital with headache and vomiting. They were found to have COHb levels of 28% and 32%. A faulty gas water heater was identified as the cause.

Patients presenting with influenza-like symptoms (headache, dizziness, nausea, vomiting, diarrhoea, weakness, general malaise, or shortness of breath) to the triage nurse at the University Hospital, Louisville, Kentucky, USA, were asked to provide blood samples for COHb determination (Dolan et al., 1987). Among the 55 patients (10% of those eligible) enrolled in the study, COHb levels ranged from 0% to 21%; levels of 10% or more were reported in 13 patients (23.6%). Smoking did not significantly increase the likelihood of having an increased COHb. Mean

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* Since the finalisation of this report and the expert workshop and subsequent peer review, a questionnaire-based study on long-term exposure to CO and resultant chronic sequelae has been published (CO Support, 1997, *Carbon Monoxide: Invisible Destroyer of Health and Life*, available from 25 Swarcliffe Road, Leeds LS14 5LE)
COHb for non-smokers was 6.11 ± 4.4% versus 7.32 ± 5.3% for smokers. More patients using wood as a heat source had elevated COHb levels than those using other forms of heating (p<0.05). None of the patients with a COHb level of 10% or more was diagnosed as having subacute CO poisoning by emergency physicians.

Occult CO poisoning in Seattle, USA, was studied by Kirkpatrick (1987). Patients were included in the study if they presented with symptoms of fatigue and headache or with at least two out of a list of other symptoms (trouble thinking, dizziness, nausea, trouble sleeping, heart pounding, shortness of breath, numbness or tingling, chest pain, decreased vision, diarrhoea, unusual spells, abdominal pain and unconsciousness; see Table 4.1). In a total of 26 cases, 15 had been exposed to CO from defective gas furnaces, three from faulty oil furnaces, and eight from vehicle exhausts. Blood samples were taken within 5 hours of suspected CO exposure. Mean COHb levels were 15.8% (range 8.8–36.8%) for patients exposed to faulty furnaces. Kirkpatrick concluded that COHb measurement is limited in its usefulness as it does not correlate well with severity of symptoms, a fact also noted by Dahmash et al. (1993, see above).

Balzan et al. (1994) studied patients admitted to a Maltese coronary care unit with unstable angina. Exposure to CO was not suspected. Sampling blood from 104 patients identified three suffering definite CO intoxication. The first, a 71-year-old man, had a COHb level of 15.2% on admission, related to use of a kerosene heater for 12 hours with insufficient ventilation. The second case, a 55-year-old non-smoker, had also used a kerosene heater until 6 hours before admission; his COHb level was 7.5%. Finally, a 50-year-old non-smoker presented with fresh onset of angina pectoris. The COHb level of this patient, 3 hours after exposure, was 10.1%. The authors estimated the peak COHb levels for each patient reached 20%, 15% and 15% respectively. However, as the authors noted, no control group was used. Assessment of these results is further complicated by the fact that each patient had previously been administered oxygen by emergency services as a treatment for their angina.

Miller et al. (1995) examined 197 cases of potential non-fatal unintentional CO poisonings occurring in Connecticut, USA, between November 1993 and March 1994. The study involved a review of telephone logs of the Connecticut Poison Control Centre to identify the poisoning cases. Of the 61 people who could be contacted, 51 (84%) were considered to have had CO poisoning resulting from exposure to a residential source of CO. Poisoning was defined as two or more symptoms consistent with CO poisoning (i.e. headache, nausea, diarrhoea,
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dizziness, dry mouth, drowsiness, or vomiting), or CO poisoning diagnosed by a physician and a COHb level in excess of 10%. A 32 item questionnaire was administered to one adult from each of the 36 households in which exposures occurred. The most frequently identified source of CO was heating systems (oil heating systems (16 households), gas heating systems (11 households), kerosene heating systems (3 households), and gas appliances and fireplaces (6 households)). A breakdown of the 51 patients’ symptoms and reported frequency of symptoms is presented in Table 4.1.

The initial symptom reported by patients varied as follows: headache (55%); dizziness (16%); nausea (13%); dry mouth (10%); and drowsiness (6%). Of the 51 cases, 32 were able to provide information on the time interval between onset of symptoms and their first consideration of CO as the cause of the symptoms. It took less than 1 hour for ten patients (31%); but more than 7 days for 13 patients (41%) to consider CO exposure as a possible cause of their symptoms.

Carbon Monoxide Exposure in Children

Schaplowsky et al. (1974) presented the results of a national survey of CO levels in the home air and in children’s blood. A total of 25 communities across the USA participated in the study conducted from November 1972 to March 1973. Carboxyhaemoglobin levels were measured in 2299 children soon after they arrived at schools or day centres. Of these, 22.5% had COHb levels of 3% or more with a mean of 4.04%. The highest recorded level was 7.99%. No correlation between COHb and health effects or between CO and COHb was presented. The fact that COHb was measured soon after arrival at school or day centre led the authors to assume that the home environment was the source of CO (Schaplowsky et al., 1974). Exposure to in-vehicle or roadside sources may also have been important.

Ocular and Aural Effects

As well as affecting the heart, brain and skeletal muscle, CO exposure may affect the eyesight and hearing. In the clinical investigations mentioned above, effects on the eyesight of some patients were reported by Kirkpatrick (1987) and Burney et al. (1982). Garland and Pearce (1967) reported four cases of accidental CO poisoning in which two of the patients were apparently deaf, although this improved over 24 hours. Visual failure (of presumed cortical origin) was also reported.
Mild, transient ocular disturbances may develop after long-term exposure to low concentrations of CO. Acute poisonings may cause severe reversible visual disturbances following a period of unconsciousness. After recovery from a coma, the patient may discover immediately that they are blind, or blindness may occur more gradually after the patient has regained consciousness (Grant, 1974).

Twelve people exposed to CO because of blocked furnace flues in three separate incidents were studied by Kelley and Sophocleus (1978). The specific subject of the study was retinal haemorrhage in subacute CO poisoning. Five patients were exposed for more than 12 hours. Retinal haemorrhages in the nerve fibre layer of the retina were found in all five.

After remaining in a coma for 4 days, the 8-year-old girl reported by Lacey (1981; see Sections 4.3.1 and 4.4.4) was found to have absent light perception with intact pupils and normal optic fundi, suggesting a cortical blindness. One month later she complained of blurred vision on lateral gaze.

A 22-year-old man suffered severe bilateral sensorineural hearing loss that only slightly improved over 11 months (Morris, 1968). He reportedly suffered CO poisoning due to a faulty anthracite-burning stove. On admission to hospital his COHb level was found to be 25%. He regained consciousness within 12 hours and neurological signs, other than deafness, returned to normal. Further examination showed a marked concentric contraction of the peripheral field of the left eye to red light. No abnormality was found in the right eye. A review of the patient’s medical history revealed no factors that might have been responsible for the deafness and the author stated that the deafness was likely to have been a result of acute CO poisoning.

SYNOPSIS

The key findings of clinical investigations of CO intoxication are presented in Table 4.2.

It is likely that many more subacute CO intoxications occur than are brought to the attention of medical practitioners. Individuals may be exposed to CO over long periods and suffer definite adverse health effects without either suspecting CO intoxication or seeking medical attention. When medical attention is sought, the reported symptoms are many and varied but headache, dizziness and nausea are the most frequently reported. The level of COHb measured in intoxicated
# Table 4.2 Summary of clinical reports of carbon monoxide poisoning

<table>
<thead>
<tr>
<th>Reference</th>
<th>Source of exposure</th>
<th>Subjects</th>
<th>COHb level (%)</th>
<th>Reported symptoms</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Carbon monoxide exposure suspected on admission</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Burney et al. (1982)</td>
<td>Michigan school students and teachers exposed to CO from malfunctioning forced-air heating system; mean duration 95 min; estimated exposure concentration 572.5 mg/m³ (500 ppm)</td>
<td>184, 9–86 y, Range, 4–28</td>
<td>Average, 18.2 ± 6.4</td>
<td>Headache, dizziness, nausea, confusion/trouble thinking, weakness/fatigue, dyspnoea/shortness of breath, decreased vision, unconsciousness</td>
<td>160 people became ill; 96 admitted to hospital; COHb levels measured in 66 patients</td>
</tr>
<tr>
<td>Dahmash et al. (1993)</td>
<td>Riyadh hospital admittees exposed to CO from wood or charcoal braziers in poorly ventilated home; exposure lasted overnight</td>
<td>11, 15–47 y, Range, 13.3–51.8</td>
<td>Average, 28</td>
<td>Headache, dizziness, vomiting, lethargy/drowsiness, dyspnoea/shortness of breath</td>
<td>All patients found unconscious</td>
</tr>
<tr>
<td>Hampson et al. (1984)</td>
<td>Indoor burning of charcoal briquettes; 32 separate incidents in Washington State</td>
<td>79, 0.25–87 y, Range, 3.0–45.8</td>
<td>Average, 21.6 ± 9.6</td>
<td>Headache, dizziness, nausea, vomiting, lethargy/drowsiness, abdominal pain, confusion/trouble thinking, weakness/fatigue, dyspnoea/shortness of breath, chest pain, ataxia, seizures, euphoria, irritability, incontinence</td>
<td>Unconsciousness, at least transient, in 33% of patients; &gt;1 person exposed in 69% of incidents</td>
</tr>
<tr>
<td><strong>Carbon monoxide exposure identified after admission</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grace &amp; Platt (1981)</td>
<td>Faulty gas boiler or water heater</td>
<td>5</td>
<td>15.6–32</td>
<td>Headache, vomiting, shortness of breath, unconsciousness, cough, chills, neuropsychological changes</td>
<td></td>
</tr>
<tr>
<td>Reference</td>
<td>Source of exposure</td>
<td>Subjects</td>
<td>COHb level (%)</td>
<td>Reported symptoms</td>
<td>Comments</td>
</tr>
<tr>
<td>--------------------</td>
<td>------------------------------------------------------------------------------------</td>
<td>------------------</td>
<td>----------------</td>
<td>-----------------------------------------------------------------------------------</td>
<td>----------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Dolan <em>et al.</em> (1987)</td>
<td>Home heating methods were: gas (5); wood (3); electric (1); other (4)</td>
<td>55, 16–86 y</td>
<td>Range, 0–21</td>
<td>Headache, dizziness, nausea, abdominal pain, weakness/fatigue, dyspnoea/shortness of breath, cough, fever, right upper quadrant pain</td>
<td>Prospective study of patients presenting with flu-like symptoms; 55 blood samples taken; none of 13 patients with COHb levels &gt;10% diagnosed as suffering from CO poisoning by emergency physician</td>
</tr>
<tr>
<td>Kirkpatrick (1987)</td>
<td>Defective gas furnaces (15); faulty oil furnace (3); vehicle exhausts (8)</td>
<td>26, 5–61 y</td>
<td>Range, 8.8–36.8</td>
<td>Headache, dizziness, nausea, abdominal pain, confusion/trouble thinking, weakness/fatigue, dyspnoea/shortness of breath, chest pain, diarrhoea, trouble sleeping, heart pounding, numbness or tingling, decreased vision, unconsciousness</td>
<td>3 patients presented comatose</td>
</tr>
<tr>
<td>Balzan <em>et al.</em> (1994)</td>
<td>All exposed to kerosene heaters</td>
<td>3, 50–71 y</td>
<td>Estimated peak level, 15–20</td>
<td>Angina pectoris</td>
<td>Prospective study of admission to coronary care; 104 patients sampled of whom 3 identified as suffering CO intoxication</td>
</tr>
<tr>
<td>Miller <em>et al.</em> (1995)</td>
<td>197 potential non-fatal unintentional CO poisonings in Connecticut of which 61 were contacted and 51 considered to result from residential CO sources: oil heating systems (10); gas heating systems (11); kerosene heating systems (3); gas appliances and fireplaces (6)</td>
<td>51</td>
<td>None reported although selection criteria stipulated &gt;10% COHb</td>
<td>Headache, dizziness, nausea, vomiting, lethargy/drowsiness, weakness/fatigue, diarrhoea, trouble sleeping</td>
<td></td>
</tr>
</tbody>
</table>
patients varies from only a few percent to over 50%. The exposure situations often involve some form of malfunctioning heating appliance or may result from an ill-advised use of a fuel-burning appliance indoors, as noted by Dahmash et al. (1993) and Hampson et al. (1995). The varied clinical symptoms of acute CO intoxication include frequent mention of decreased vision and hearing deficits. As with neurological sequelae, recovery from ocular and aural effects may be a long process. In the eye, the effect of CO appears to be on the retina, although visual effects of presumed cortical origin have also been reported.

4.4.3 MISDIAGNOSIS OF CARBON MONOXIDE POISONING

The investigations detailed above reveal a very wide and varied group of symptoms associated with exposure to CO. These symptoms may very easily be confused with those of many other ailments. The purpose of this section is to highlight information on the symptoms and potential misdiagnoses of CO poisoning (see Table 4.3). Subacute CO poisoning is most often misdiagnosed as an influenza-like illness. Other examples of misdiagnoses include gastroenteritis, psychiatric disorders, migraine headaches, heart disease, food poisoning, cerebral haemorrhages and vascular accidents, hypoglycaemia, solvent intoxication, alcohol inebriation, cerebral tumour, and ischaemic cerebral diseases (Kelley & Sophocleus, 1978; Barret et al., 1985; Gemelli & Cattani, 1985; Dolan et al., 1987; Kirkpatrick, 1987).

Wherever a group of people presents with similar symptoms, especially headache and vomiting, the possibility of CO intoxication is indicated. Vague symptoms of other types may also be indicative of CO intoxication. People may be exposed together in a home or workplace environment.

Spiller (1987) stressed the difficulties for physicians in diagnosing CO exposure. Exposure generally results in diverse and non-specific clinical findings which may not be diagnosed without a clear history of exposure. Generally, CO does not produce symptoms of respiratory irritation (Grace & Platt, 1981; Piantadosi, 1990). The fact that groups of people are often exposed together and present to a physician with the same or similar symptoms often leads to a diagnosis of food poisoning or influenza.
Table 4.3 Some possible misdiagnoses in patients with carbon monoxide poisoning

<table>
<thead>
<tr>
<th>Symptom caused by CO exposure</th>
<th>Misdiagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Neurological</strong></td>
<td></td>
</tr>
<tr>
<td>Cerebral ischaemic accident</td>
<td>Cerebrovascular accident</td>
</tr>
<tr>
<td>due to CO poisoning</td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>Migraine, tension headache</td>
</tr>
<tr>
<td>Anoxic convulsions</td>
<td>Epilepsy</td>
</tr>
<tr>
<td>Vomiting, headache, bizarre</td>
<td>Meningitis, encephalitis</td>
</tr>
<tr>
<td>neurological symptoms</td>
<td></td>
</tr>
<tr>
<td>Late-onset Parkinsonian</td>
<td>Parkinsonism</td>
</tr>
<tr>
<td>symptoms</td>
<td></td>
</tr>
<tr>
<td><strong>Psychiatric</strong></td>
<td></td>
</tr>
<tr>
<td>Lethargy, somatic symptoms</td>
<td>Depression</td>
</tr>
<tr>
<td>Hyperventilation, headache,</td>
<td>Anxiety state</td>
</tr>
<tr>
<td>malaise</td>
<td></td>
</tr>
<tr>
<td>Hyperventilation</td>
<td>Hyperventilation syndrome</td>
</tr>
<tr>
<td>Confusion, hallucinations</td>
<td>Acute confusional state</td>
</tr>
<tr>
<td><strong>Cardiac</strong></td>
<td></td>
</tr>
<tr>
<td>A critical coronary artery</td>
<td>Myocardial infarction</td>
</tr>
<tr>
<td>lesion decompensated</td>
<td></td>
</tr>
<tr>
<td>through hypoxia</td>
<td>Cardiac arrhythmias</td>
</tr>
<tr>
<td>Conduction system hypoxia</td>
<td></td>
</tr>
<tr>
<td>**Pharmacological and</td>
<td></td>
</tr>
<tr>
<td>toxicological**</td>
<td></td>
</tr>
<tr>
<td>Hypoxic coma, non-traumatic</td>
<td>Drug overdose</td>
</tr>
<tr>
<td>rhabdomyolysis</td>
<td>Ethylene glycol poisoning</td>
</tr>
<tr>
<td>Coma and renal failure</td>
<td></td>
</tr>
<tr>
<td>Vomiting, ataxia, slurred</td>
<td>Ethanol intoxication</td>
</tr>
<tr>
<td>speech, coma</td>
<td></td>
</tr>
<tr>
<td>Agitation, confusion,</td>
<td>Drug abuse</td>
</tr>
<tr>
<td>hallucinations</td>
<td></td>
</tr>
<tr>
<td><strong>Infections</strong></td>
<td></td>
</tr>
<tr>
<td>Muscle aches, tachypnoea,</td>
<td>Influenza and other viral infections</td>
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<td>headache, exhaustion</td>
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<td>Lethargy, myalgia</td>
<td>Post viral syndrome</td>
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<td>Nausea and vomiting</td>
<td>Gastroenteritis and food poisoning</td>
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<td>Dyspnoea, delirium</td>
<td>Pneumonia</td>
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<tr>
<td>Headache, malaise</td>
<td>Sinusitis</td>
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<tr>
<td><strong>Others</strong></td>
<td></td>
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<tr>
<td>Abdominal pain, nausea,</td>
<td>Cholecystitis and other acute abdominal conditions</td>
</tr>
<tr>
<td>vomiting</td>
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Adapted from Lowe-Ponsford & Henry (1989)
Barret et al. (1985) assessed incidences of patient misdiagnosis in a population from the city of Grenoble and the Department of Isère, France. The criteria used for defining a missed CO poisoning diagnosis were:

- evidence before admission of a consultation for symptoms consistent with CO poisoning not followed by appropriate management and investigation;
- at admission, wrong diagnosis mentioned in the family doctor’s letter; and
- errors in management made after admission proving that the diagnosis was overlooked.

Each diagnosis was reassessed. Confirmation came from measurement of the patient’s COHb level [no details are provided of the COHb levels measured]. Misdiagnoses occurred in approximately 30% of patients during 1975 to 1977. The rate of misdiagnosis fell to 12% in 1978 and to 5% in 1980. Examples of misdiagnoses were food poisoning, solvent intoxication, alcohol inebriation, migraine, cerebral tumour, psychiatric diseases, heart diseases, cerebral haemorrhage, and ischaemic cerebral diseases. The authors concluded that the decrease in misdiagnoses may have been attributable to a campaign of public medical information on CO.

The Dolan et al. (1987) study summarised in Section 4.4.2 holds useful information on the problem of misdiagnosis in CO intoxication. This was a prospective study that used the reported symptoms to determine those patients in whom COHb measurements would be made. Symptoms of headache, dizziness, nausea, vomiting, diarrhoea, weakness, general malaise, or shortness of breath were reported by 55 patients (10% of those eligible) who were enrolled in the study. The finding that none of the patients with a COHb level of 10% or more was diagnosed as having subacute CO poisoning by emergency physicians indicates that, whilst the symptoms reported were indicative of CO intoxication, the physicians had little awareness that CO poisoning might be the cause.

In the case-reports described by Grace and Platt (1981), one patient was assessed on three visits and only on the final visit, following a collapse, was CO intoxication diagnosed. His previous diagnoses had included a viral syndrome, hypokalemia and diabetes mellitus (from which he was known to suffer); symptoms were light-headedness, vertigo, anterior chest pain that worsened with deep inspiration, dry cough, chills and a mild headache. His wife suffered similar symptoms. A second misdiagnosis, reported by the same authors, was that of the 69-year-old man
whose symptoms were correctly diagnosed only after two visiting relatives stayed in his mobile home and later reported to the hospital with headache and vomiting.

SYNOPSIS

The broad range of symptoms associated with CO intoxication makes its diagnosis difficult. It is easy for a doctor to mistake the symptoms, such as headache, nausea, dizziness and vomiting, for those of one of many other ailments, such as influenza, food poisoning, gastroenteritis and migraine headaches, among others. Also, the intoxicated individual may not have experience or knowledge of CO intoxication and thus fail to seek medical attention for what appears to be a ‘bug’, influenza or some other apparently minor ailment. The potential benefits of information campaigns, for both the public and medical fraternity, is exemplified in the Barret et al. (1985) study. The possibility exists that many people either suffer CO intoxication without seeking medical attention, or seek attention but the intoxication is not diagnosed. In such cases the benefit of measuring COHb levels is obvious. Measuring alveolar breath levels of CO and estimating COHb levels is normally sufficiently accurate to confirm exposure, but it is very important to make measurements close to the time of exposure.

4.4.4 IMMEDIATE AND DELAYED NEUROLOGICAL SEQUELAE OF CARBON MONOXIDE EXPOSURE

The effects of CO exposure can usually be negated by removing the subject from the CO source. However, neuropsychological sequelae may develop either immediately or some time after intoxication. Some of the symptoms reported in the clinical investigations described above may be neurological in nature. Hampson et al. (1994) reported symptoms of confusion, ataxia, seizures, euphoria, and irritability in some patients. Grace and Platt (1981) reported neuropsychological changes in one of the five patients in their study. Some patients in the Kirkpatrick (1987) and Burney et al. (1982) studies reported trouble thinking and decreased vision. Thus it is apparent that effects on the
In Section 4.2.1 the main categories of brain hypoxia and their effects are summarised. The work of Graham (1992) indicated that neuronal necrosis may be delayed for a period following an hypoxic episode. This delayed effect may account for some of the findings of delayed neuropsychological sequelae mentioned here.

Garland and Pearce (1967) reported four cases of accidental CO poisoning in which two of the patients apparently became deaf, although this improved over 24 hours. Other neuropsychological complications recorded in these four patients were visual failure (of presumed cortical origin), object agnosia, finger agnosia, temporo-spatial disorientation, ideomotor, constructional and dressing apraxia, dysphasia, dysgraphia, transient deafness, Parkinsonism, epilepsy, incontinence, and mental changes ranging from retardation to frank psychosis. All patients had an initial impairment of consciousness, followed by restlessness, confusion, disorientation and amnesia. Two of the patients were considered to have made a full recovery and were discharged only to be re-admitted within 48 hours suffering acute relapse. For three of the patients, exposure lasted 3 hours and for the fourth patient, 15 minutes. Carboxyhaemoglobin levels ranged from 28% to 63%. The clinical findings were different in each patient, but the symptoms of the patient exposed for the shortest period were no less severe than those of the other three patients.

Lacey (1981) presented the case of an 8-year-old girl who developed persistent neuropsychiatric deficits following CO intoxication. The girl had been exposed to CO during a long car journey during which her parents thought she was asleep. The other car occupants experienced headaches and dizziness but were not medically examined. The girl’s COHb level was 60% on admission to hospital. Neurological disturbances, perceptual deficiencies, personality alterations and computerised tomographic evidence of leukoencephalopathy were still apparent one year after exposure.

Whilst the hypoxic stress imparted by CO exposure may explain many symptoms encountered in poisoning episodes, the pathophysiology of delayed neuropsychological sequelae cannot be explained by this alone (Thom et al., 1995) and it may be the case that the binding of haemoglobin with CO is not the only toxic mechanism (Lowe-Ponsford & Henry, 1989). Coma is not always necessary
for delayed neurological sequelae to develop. According to Graham (1992), a combination of damage to white matter in the brain due to local cytotoxic effects and a moderate reduction in blood flow may be responsible for delayed neurological sequelae. In a review of the neurological complications of CO intoxication, Roos (1994) states that the exact cause of the delayed effects of CO is unknown although most damage appears to be in the cerebral white matter in those presenting with neuropsychiatric symptoms after several weeks. In the acute stage, most damage is found in the putamen and globus pallidus. In severe cases, a multifocal or diffuse leukoencephalopathy with demyelination occurs in the centrum semiovale and the periventricular area (Roos, 1994).

Seger and Welch (1992) suggest that the only prognostic indicators for delayed neuropsychological sequelae are extreme age and loss of consciousness. However, not all elderly people who lose consciousness will necessarily experience problems, and neuropsychological sequelae may also occur in the young and in people who remained conscious throughout their exposure. It is also useful to note that not all sequelae may be wholly attributable to the CO exposure. They may in fact be stress-related reactions — anxiety or agitation — resulting from the patient’s hospitalisation or some external stimuli other than CO (Lowe-Ponsford & Henry, 1989).

There are certain prime characteristics of the delayed toxicity of CO:

- the effects occur suddenly after an apparent recovery period of perhaps days to weeks; and
- there may be behavioural changes, confusion, disorientation, fever, ataxia, Parkinsonism, incoordination and weakness.

In a study of 206 patients poisoned by CO reported by Smith and Brandon (1973) only 2.2% of those surviving their poisoning episode had obvious neuropsychiatric deficits on hospital discharge. However, a follow-up of the surviving patients three years later showed 10.8% had gross neuropsychiatric deficits, 28.4% had an obvious personality deterioration and 36.5% had some loss of memory functions. The temporal relationship of the CO poisoning and resulting sequelae was often noted by the patient, but not by the physician. There was a relationship between the level of consciousness on admission and gross neurological sequelae, but defining a relationship between COHb level and sequelae was impossible because too few patients’ COHb levels had been measured.
The main types of effects on the brain resulting from CO exposure are briefly summarised (in Section 4.2.1). In the Smith and Brandon (1973) follow-up study, one patient was found to be suffering parietal lobe damage with dyspraxia and dysphasia, another was suffering basal ganglia damage and Parkinsonism. Severe global deterioration of cognitive function occurred in five cases. In 33.3% of those accidentally exposed and 41.2% of those intentionally exposed, some degree of memory impairment was reported either by the patient or another informant.

In a study of the beneficial effects of hyperbaric oxygen treatment* compared with ambient pressure oxygen treatment, Thom et al. (1995) looked at the incidence of delayed neurological sequelae in acute CO poisonings. Patients were randomly assigned to one of the treatments. In those patients receiving ambient pressure oxygen, delayed neurological sequelae occurred in 23%; in the hyperbaric oxygen group delayed neurological sequelae did not occur. Their study also found neither clinical history nor COHb to be useful in predicting which patients may develop delayed neurological sequelae. Whilst this study would seem to demonstrate that hyperbaric oxygen is a beneficial treatment in CO intoxication there is considerable debate about its effectiveness (Lowe-Ponsford & Henry, 1989).

Recovery from either immediate or delayed neuropsychological sequelae is difficult to predict. However, the more severe the impairment, the less the likelihood of a full recovery. Whilst age and state of consciousness may indicate whether neurological sequelae are likely to develop, duration of exposure may also be a determining factor (Lowe-Ponsford & Henry, 1989).

The development of neurological sequelae was assessed in the Dahmash et al. (1993) study of 11 patients in Riyadh (Section 4.4.2). Particular attention was paid on admission to the nervous and cardiorespiratory systems, and six patients were followed up for over a year. They showed no nervous system disturbances (such as headache, peripheral neuropathy, aggressiveness or impulsiveness). The other five patients were asymptomatic one month after hospitalisation, but further follow-up was not possible.

* Hyperbaric oxygen is one treatment method for CO intoxication in which the patient is placed in a pressurised oxygen atmosphere to speed the dissociation of CO from haemoglobin.
SYNOPSIS

Symptoms of a neuropsychological nature are often seen in clinical investigations. They may appear immediately after CO exposure or may develop after a period of apparent recovery (termed delayed neurological sequelae). Recovery from delayed neurological sequelae may take months or even years. The prediction of both who is most likely to suffer such sequelae and who will recover is difficult. The level of consciousness associated with the exposure and the individual’s age may be prognostic indicators for development of sequelae but they are by no means certain. Severity of impairment may also indicate the expected level of recovery. The mechanism by which delayed neurological sequelae develop is complex.

4.4.5 OUTDOOR EXPOSURE STUDIES

Whilst the focus of this review is on indoor air quality in the home, it is valid to report the findings of some studies on the health effects of outdoor CO pollution. These studies indicate a possible link between low-level CO exposure and morbidity and mortality, although confounding factors preclude the clear establishment of a causal link.

Burnett et al. (1997) investigated the association between ambient CO levels and hospitalisations for congestive heart failure in the elderly in ten Canadian cities. Daily fluctuations in admissions to 134 hospitals were compared with the daily variations in CO, nitrogen dioxide, sulphur dioxide, ozone, and the coefficient of haze over an 11-year period from 1981 to 1991. Other variables measured were the dew point and temperature. For all pollutants other than CO, daily ‘high-hour’ (daily 1-hour maximum) and daily average concentrations for the day of admission and 1, 2 and 3 days before were calculated; for CO, a daily maximum 8-hour running average replaced the daily average.

The authors found a positive association between the pollutants and daily fluctuations in hospital admissions for congestive heart failure in the elderly that persisted after adjustments for long-term trend, weather, seasonal and other factors known to affect hospital admission rates. Of the air pollutants considered, CO was the strongest predictor of hospitalisation rates and was least sensitive to covariate analysis. The excess number of admissions attributable to a change in concentration from the median to the 95th percentile was estimated for three model specifications (CO alone, CO and nitrogen dioxide controlled for...
REVIEW OF HEALTH EFFECTS

Temperature and dew point, and CO, nitrogen dioxide, sulphur dioxide, and coefficient of haze, controlled for ozone, temperature and dew point. Respective excess hospitalisations were 2.52, 2.60 and 2.79, indicating that changes in CO alone accounted for 90% of the daily excess hospitalisations attributable to the entire pollutant mix. The relative risk for a change from 1.1 mg/m³ (1 ppm) to 3.4 mg/m³ (3 ppm) was 1.065 (95% CI = 1.028–1.104).

The authors presented several reasons for questioning a causal relationship between air pollution and hospitalisations for congestive heart failure. First, there is the possibility that on high pollution days individuals spend more time indoors and are exposed to environmental tobacco smoke and other indoor pollutants. Second, there may be a chance correlation of an epidemic within a population with ambient air pollution, although adjustment of hospital time-series data to remove even sub-seasonal variations in admission rates reduces the risk of this type of bias. Third there are potential errors in individual exposure due to the use of fixed-site monitors to estimate exposure. Carbon monoxide may merely act as a marker for pollutants with which it is highly correlated, such as nitrogen dioxide, and coefficient of haze. Also other environmental controls such as weather variables may have been inadequately controlled (although adjustments were made in the analysis to account for this).

Touloumi et al. (1996) investigated the effects of ‘winter-type’ air pollution (black smoke, sulphur dioxide, and CO) in Athens, Greece for 1826 days between 1 January 1987 and 30 December 1991. Three monitoring stations were used to derive the average daily measurements for each pollutant. For black smoke and sulphur dioxide, 24-hour levels in µg/m³ were calculated; for CO, a maximum 8-hour moving average in mg/m³ was calculated. Pollutant concentrations were as follows: black smoke, mean 84.4 ± SD 48 (range 9–333) µg/m³; sulphur dioxide, 51.3 ± 29.8 (6–361) µg/m³; and CO, 6.6 ± 2.6 (1.4–24.9) mg/m³ (5.8 ± 2.3 (1.2–21.7) ppm). The pollutants showed a clear seasonal variation with higher levels in the late autumn and winter. The relative risk of dying when CO levels increased by 10 mg/m³ (8.7 ppm) was 1.10 (95% CI 1.05–1.15). Mortality data were adjusted for seasonality, long-term cyclical patterns, short-term weather effects and day-of-the-week variations.

Schwartz and Morris (1995) sought to examine the association between air pollution and cardiovascular hospitalisation in Detroit, Michigan, USA. They focused on particulates (PM₁₀), ozone, sulphur dioxide and CO, and gathered pollutant, patient and weather information for the period 1 January 1986 to 31 December 1989. Ischaemic heart disease admissions were associated with CO
(relative risk RR = 1.010, 95% CI 1.001–1.018 (p = 0.022) for an interquartile range (1.47 mg/m³; 1.28 ppm) increase in pollution) although when controlled for PM₁₀ in two-pollutant models, the CO effect became insignificant. Both PM₁₀ and CO were significantly associated with congestive heart failure admissions for an interquartile range increase in pollution in single- and two-pollutant models (for CO: single-pollutant model, RR = 1.022, 95% CI 1.011–1.033; two-pollutant model, RR = 1.022, 95% CI 1.010–1.034).

Three earlier studies looked at air pollution and morbidity in two US cities, Los Angeles and Denver. Cohen et al. (1969) studied survival from myocardial infarction in relation to CO in 35 hospitals in the Los Angeles area in 1958. Based on CO levels, areas within Los Angeles were designated as either ‘low’ (outside the 9.2 mg/m³ (8 ppm) isopleth for 1955) or ‘high’ pollution areas. There was an increased rate of fatalities from myocardial infarction in ‘high’ pollution areas, which was only evident during periods of relative increases in ambient CO.

The second study in Los Angeles (1962–1965) showed a significant association between outdoor ambient CO concentrations and mortality (Hexter & Goldsmith, 1971). Linear regression produced a highly significant coefficient for CO (p<0.002), indicating that it is a constituent of ambient air associated with excess mortality. The estimated contribution to mortality for the highest CO concentration, 23.1 mg/m³ (20.2 ppm), compared with the lowest concentration, 8.4 mg/m³ (7.3 ppm), was 11 deaths for that day (adjusted mean number of total daily deaths, 159), all other factors being equal.

Kurt et al. (1979) studied health impacts of CO pollution during the winter of 1975/76 in Denver, Colorado. Patients presenting with cardiopulmonary complaints — defined as non-traumatic chest pain or an increase in shortness of breath, dyspnoea or wheezing — formed the study cohort. The number of cardiopulmonary complaints was compared with daily 1-hour and 24-hour mean CO concentrations. Excessive numbers of cardiopulmonary complaints were seen when the 24-hour mean CO level was above 5.7 mg/m³ (5 ppm; p<0.05).

All of these studies indicate that a role is played by CO in cardiac morbidity and mortality. However, there are many other risk factors for cardiac illnesses. Identifying CO as the single pollutant of concern is questionable because of the presence of other commonly encountered co-pollutants, especially other automobile emissions in the outdoor environment. The indoor environment also contains a complex mixture of pollutants and risk factors (Walden & Gottlieb, 1990). The lack of personal exposure information prevents clarification.
4.5 CONTROLLED HUMAN EXPOSURE STUDIES

As previously mentioned, certain tissues are more sensitive to CO hypoxia and toxicity, especially the heart and brain. The human body compensates for the effect of CO intoxication through two main mechanisms, increased blood flow and increased oxygen exchange (see Section 4.2.1; Ayres et al., 1969; Benignus et al., 1992); however, these mechanisms may be insufficient to prevent adverse effects. Controlled human exposure studies have been performed on subjects suffering coronary heart disease, angina, intermittent claudication, and other cardiovascular diseases. Healthy subjects have also been studied to assess effects on exercising muscle. Studies of the neuropsychological effects of CO on healthy subjects are also presented here.

Usually a target COHb level of interest is set, to be reached by the end of the exposure period. This level is either reached rapidly using a bolus of CO\(^b\) and maintained using a lower CO exposure level, or reached slowly over the exposure period at a constant CO exposure level.

4.5.1 CARDIOVASCULAR EFFECTS

In their review of the causation and aggravation of cardiovascular diseases, Ström et al. (1995) concluded that myocardial ischaemia is exacerbated by low levels of COHb during graded exercise in subjects with coronary artery disease. Such patients are at an increased risk of adverse health effects because of their

\(^a\) Often referred to as ‘chamber studies’
\(^b\) Studies frequently employ the bolus method in order to reach a sufficiently high target COHb level in a short time. Were the subjects’ COHb levels to be raised slowly, an unacceptably long time might be required (depending on the target COHb level). This is especially so when target COHb levels are greater than 10%.
limited ability to increase coronary blood flow in response to increased myocardial oxygen demand.

Mennear (1993) reviewed the literature on the effect of CO on cardiovascular diseases, with specific regard to the role of CO associated with environmental tobacco smoke, and concluded that although there is little evidence to support a causal role for CO in ischaemic heart disease there is some evidence that exposure to extremely high concentrations of CO may increase the risk of ischaemic heart disease and decrease exercise tolerance among coronary artery disease sufferers. Citing controlled studies by Allred et al. (1989), Hinderliter et al. (1989), Kleinman et al. (1989) and Sheps et al. (1990), Mennear proposed a no effect level for COHb of 2.5%; this level falls below that of the 3.9% COHb found to have no effect on exercise-induced arrhythmias in patients with coronary artery disease (Sheps et al., 1990), and the 2.9% COHb found to decrease exercise tolerance in coronary artery disease patients (Kleinman et al., 1989).

The studies summarised below all follow a generally similar protocol to assess the effect of CO on various physiological parameters pertinent to the cardiovascular and pulmonary systems. The subjects perform exercise either before and after exposure to CO, or only after exposure; the exercise is frequently incremental (i.e. the workload increases over time) and is symptom-limited (i.e. the presence of severe fatigue, dyspnoea, dizziness, ventricular arrhythmias, ECG changes, angina, hypotension or some other exercise limiting factor acts as an end-point). Some or all of a number of parameters are measured in these studies and the effect of CO on them is assessed.

A number of studies on cardiovascular effects by Aronow and co-workers, summarized in this section, have been criticised by the US EPA (EPA, 1984) in an Addendum to their Air Quality Criteria document, and an independent committee's recommendation to the US EPA was not to rely on the Aronow studies. The Aronow studies are, nonetheless, presented here for information; they may be suggestive of an effect of COHb at levels of 2.7% to 3.0%. The criticism levelled at the studies (Aronow & Isbell, 1973; Aronow et al., 1974; Aronow & Cassidy, 1975; Aronow et al., 1977; Aronow, 1981) was that inadequate standardised procedures were used.
STUDIES ON HEALTHY SUBJECTS

In these studies, healthy individuals were exposed to known concentrations of CO and effects on exercise performance recorded.

Pirnay et al. (1971) studied muscular exercise during CO exposure in five men ranging in age from 24 to 35 years (average 27.8 years). The target COHb level employed in this study was 15%. This was reached by the subjects breathing 572.5 mg/m³ (0.05%) CO in air for 5 minutes pre-exercise and throughout a 17–18 minute exercise period. The exercise period involved 15 minutes of moderate exercise followed by 2–3 minutes at the subject’s maximum tolerated level determined in a preliminary control test. The average COHb level attained was 15.4%.

Oxygen consumption during moderate exercise was comparable for both the control and CO exposure tests, however, heart rate rose with increased COHb, from 128.5 beats per minute (bpm) after 15 minutes’ moderate exercise in the control test, to 142.7 bpm after 15 minutes’ exercise in the CO exposure test, thus allowing the aggregate oxygen transport to remain the same. The average maximal oxygen consumption in the last minute of maximal exercise was 15.1% lower (p<0.001) after CO exposure than under control conditions and the maximum heart rate was only slightly higher. This implies that the maximum limit of circulatory adaptation was reached.

Vogel and Gleser (1972) assessed the effect of CO on oxygen transport during exercise. Eight men (aged 20–23 years), including three smokers, were studied at rest and using an upright bicycle ergometer. Exposure was to room air or 257.6 mg/m³ (225 ppm) CO. To reach the target COHb level quickly, subjects first breathed a 40 litre bag of 1.0% to 1.2% CO in air, and were then placed on the maintenance dose of 257.6 mg/m³ CO. After 15 minutes in the room air (control) exposure, and after equilibration of COHb in the CO exposure, resting measurements were taken.

The mean COHb level attained was between 18.6 and 20.0%. Exercise involved two submaximal periods and one maximal period. After a rest of at least 1 hour, or until the subject’s COHb level was below 5%, the second exposure commenced. Submaximal oxygen consumption for a given workload was the same with room air and 18.6% to 20.0% COHb. There was a 23% reduction in maximal oxygen consumption (p<0.001) indicating that the leftward shift in the oxyhaemoglobin dissociation curve accompanying CO exposure is compensated for by a lower
venous oxygen tension. There was no effect of 18.6% to 20.0% COHb on resting heart rate or cardiac output, but at all levels of submaximal exercise, heart rate and cardiac output were higher (p<0.05). Cardiac output and heart rate were the same at maximal exercise levels.

Horvath et al. (1975) noted no significant decreases in maximal aerobic capacity below COHb levels of 4.3%. A group of four healthy male subjects, comprising three non-smokers and a pipe-smoker, was studied. Their ages ranged from 24 to 33 years. Exposures were to filtered air, filtered air with 85.9 mg/m³ (75 ppm) CO and filtered air with 114.5 mg/m³ (100 ppm) CO, in two different exposure protocols, one in which COHb levels were allowed to rise slowly to 3.4% and 4.3%, respectively, in two separate experiments, and a second in which COHb levels were quickly elevated to 3.2% and 4.3%. Baseline COHb levels were 0.3%. The subjects exercised on a treadmill until exhausted and ECG changes were monitored. The parameters measured were COHb, VO₂max*, duration of exercise, heart rate, ventilatory equivalent ratio, and excess carbon dioxide at VO₂max.

Regardless of the mode of CO presentation, the VO₂max was marginally decreased (p<0.10) when subjects’ COHb levels were 4.3% COHb, but no significant differences were noted at approximately 3.3% COHb. Exercise duration was significantly shorter and ventilatory volumes significantly lower at both COHb levels than during air exposure (p<0.05). The difference in exercise duration between the higher and lower COHb levels was significant. No significant difference between COHb levels was noted for heart rate, ventilatory equivalent ratio, or excess carbon dioxide at VO₂max. Oxygen debt was similar under all conditions.

Although the subjects were unaware of the composition of air to which they were exposed, they subjectively reported feeling greater tiredness and cramping in the legs whilst exercising breathing CO. The authors could not determine whether these subjective feelings might have caused the earlier termination of the exercise but felt that the protocol had been adequately explained to the subjects so they would cease exercise only when completely exhausted. This may, however, have led to the noted differences in exercise duration.

Aronow and Cassidy (1975) [see comment on adequacy of study] studied the effect of CO on healthy subjects. They measured decrements in exercise duration following inhalation of CO and monitored ECG changes during the exercise.

* VO₂max is a measure of aerobic fitness referred to as aerobic power or maximal oxygen uptake. It is the greatest rate at which a person can utilise atmospheric oxygen during continuous exercise.
REVIEW OF HEALTH EFFECTS

The electrocardiogram waves are divided into three main sections, the P wave, QRS complex, and T wave. The P and T waves exhibit few variations in shape. The QRS complex displays more readily recognised differences in pattern (Rowlands, 1990). The changes in ST segment are most often used in studies of CO health effects: a normal ST segment does not deviate by more than 1mm above or below the iso-electric line (when no part of the heart is polarised or depolarised).

The subjects were ten healthy, non-smoking adults (nine men and one woman), with a mean age of 50.7 ± 3.8 years (range 45–55 years). On two successive study mornings, subjects first performed a multistage uninterrupted treadmill stress test to exhaustion. After resting for 15 minutes the study exposure commenced, and subjects breathed either 114.5 mg/m³ (100 ppm) CO or compressed, purified air for 1 hour following a double-blind randomised, crossover protocol. The venous COHb level increased to 3.95% after the CO exposure. During exposure to compressed, purified air the mean COHb level decreased from 1.6 to 1.3%.

The effect of 3.95% COHb was a 5% decrease in exercise duration (p<0.001). There was no significant difference between the different study periods in either resting or post-exercise mean systolic blood pressure, diastolic blood pressure, heart rate, or product of systolic blood pressure × heart rate. In the control periods and whilst breathing compressed, purified air, ECG monitoring indicated no ischaemic ST segment* depression in any of the ten subjects, either during or after exercise. However, one of the ten subjects, a 53-year-old, manifested a greater than 1.0 mm ischaemic ST-segment depression after exercise at 3.95% COHb. The authors concluded that 3.95% COHb, commensurate with cigarette smoking or heavy atmospheric CO pollution, impairs exercise performance in normal individuals and that this reduction in exercise duration is probably due to impairment of myocardial oxygen delivery.

A long-term study of six groups of healthy, young men was carried out by Davies and Smith (1980). About half of the 55 subjects were tobacco smokers who were required to abstain from smoking for three days prior to the experiment. With two exceptions, the subjects were aged between 17 and 22 years (the other two subjects were aged 25 and 27). Ten subjects were employed in a pilot study (the results of which are not discussed here). The remaining 45 subjects were split into six groups and spent a total of 18 days in an exposure chamber. During the middle eight days they were exposed continuously to 57.3 mg/m³ (50 ppm; n = 15), 17.2 mg/m³ (15 ppm; n = 15) or 0 mg/m³ (n = 14) CO. There were two experimental runs at each CO concentration with different subjects used in each experiment. Carboxyhaemoglobin was measured, in the first run, using a spectrophotometric technique and alveolar breath samples. Alveolar breath alone was used in the

* The electrocardiogram waves are divided into three main sections, the P wave, QRS complex, and T wave. The P and T waves exhibit few variations in shape. The QRS complex displays more readily recognised differences in pattern (Rowlands, 1990). The changes in ST segment are most often used in studies of CO health effects: a normal ST segment does not deviate by more than 1mm above or below the iso-electric line (when no part of the heart is polarised or depolarised).
second series of exposures to estimate blood COHb. The combined alveolar and blood mean COHb levels were 7.1%, 2.4% and 0.5% respectively for the three different exposures. Electrocardiograms were recorded from each subject. Whereas most other studies use only changes in the ST-segment as an indicator, Davies and Smith (1980) additionally looked at P-wave changes.

Changes in P-waves were noted in 6 of the 15 subjects at 7.1% COHb, in 3 of 16 at 2.4%, and in none of 14 at 0.5%. The authors concluded that P-wave abnormalities were due to a specific toxic effect of CO on atrial pacemaking or conducting tissue. One subject in the study, a heavy smoker, later found to be a sufferer of localised septal hypertrophic myopathy with a small area of permanently ischaemic myocardium, showed marked ST-segment changes after exposure at 17.2 mg/m³ (15 ppm) for 36 hours (COHb 2.6%). This subject had previously taken part in a pilot study involving exposure to 85.9 mg/m³ (75 ppm) CO and had volunteered for the second study. He was removed from the study chamber immediately upon exhibiting these effects.

STUDIES ON SUBJECTS WITH CARDIOVASCULAR AND CARDIOPULMONARY DISEASES

CARDIAC ARRHYTHMIAS

Two related studies were performed on patients with coronary artery disease and various levels of baseline ventricular ectopy (Hinderliter et al., 1989; Sheps et al., 1990). The study group comprised 41 non-smoking patients (36 men and 5 women) with a mean age of 62.8 ± 1.1 years (range 47 to 77 years). Hinderliter et al., (1989) used a subgroup of ten subjects, seven men and three women, with very low baseline levels of ventricular ectopy (0–1 ventricular premature beats per hour) in a randomised, double-blind study of the effects of acute exposure to CO on resting and exercise-induced ventricular arrhythmias. The subgroup’s mean age was 61 ± 5 years. Three patients had a prior history of myocardial infarction and eight had stenosis of at least one major epicardial coronary artery, documented by angiography. The findings from patients with higher baseline arrhythmia frequencies (Sheps et al., 1990) are presented below. Health effects were assessed using cardiac imaging and ambulatory ECG monitoring. Exposure was to pure air, 114.5 mg/m³ (100 ppm) CO or 229.0 mg/m³ (200 ppm) CO for a period sufficient to reach target COHb levels of 4% and 6%. The mean baseline and exposure COHb levels were 1.8%, 4.0% and 5.8% respectively. After exposure
each patient performed an incremental, symptom-limited exercise test whilst breathing room air. Following exercise, COHb levels fell from 4.0% to 3.5% and from 5.8% to 4.9%. The results of this study suggest acute exposure to CO resulting in 4% to 6% COHb does not significantly increase the frequency or severity of ventricular ectopy in patients without significant arrhythmias at baseline. However, the authors have applied certain caveats to their findings: only patients with minimal ventricular ectopy were analysed, therefore the results cannot be generalised to the overall population suffering from coronary artery disease; and all patients were on anti-anginal medication and 70% were on beta-blockers, indicating a potential masking of the effects of CO. However, as most symptomatic ischaemic heart disease sufferers are on medication, the results may indeed be applicable to other patients.

Sheps et al. (1990), studying another subgroup of the same 41 patients, and using a similar exposure protocol, investigated the production of single and multiple arrhythmias in non-smoking patients with coronary artery disease with low (3–50 ventricular premature depolarisations per hour (VPD/h), 11 patients), intermediate (51–200 VPD/h, 11 patients) and high (>200 VPD/h, 9 patients) levels of arrhythmia. Patients’ blood pressure and ECG were recorded and venous COHb analysed. Mean COHb levels were 1.4% at baseline, 3.7% (4% target COHb) and 5.3% (6% target COHb); these values reflect the mean of the pre-exercise and post-exercise COHb levels. After exposure, incremental, symptom-limited exercise was performed in room air.

During exercise, the higher CO exposure (mean, 5.3% COHb) produced a significantly higher frequency of both single (p = 0.03) and multiple (p = 0.02) VPD/h when compared with baseline exposure (mean 1.4% COHb). There were no significant differences between baseline and 5.3% COHb either at rest, or after exercise. There were no significant differences between baseline and 3.7% COHb either at rest, or during or after exercise.

Those patients who developed increased single arrhythmias were significantly older (p = 0.02) than those with no increased arrhythmia; patients exhibiting increased multiple arrhythmias, in addition to being older, exercised longer (p = 0.05) and had a higher peak workload (p = 0.05) during exercise.

The effect of CO on patients with cardiac arrhythmias was assessed by Chaitman et al. (1992). A group of 30 patients, (25 men and 5 women), from 68 non-smoking patients with ischaemic heart disease and chronic ventricular arrhythmias (defined as ≥30 premature ventricular complexes per hour average
over 20 hours) were enrolled in and completed a double-blind, randomised trial. Their average age was 65 years (range 45–77 years). Patients either had angiographic evidence of ischaemic heart disease or were diagnosed on the basis of their medical history. The test protocol included a period of 120 minutes of rest before exposure, 60 minutes of exposure to CO at a concentration sufficient to raise COHb levels to the target levels of approximately 3% and 5%, and a further 90 minutes, during which these levels were maintained for a period of 60 minutes of rest followed by exercise tests and immediate post-exercise rest. The average COHb levels were 0.7% (for room air), 3.2% and 5.1%, measured both by CO-oximeter and by gas chromatography methods. Subjects exercised on a treadmill; the duration of exercise was symptom-limited (3.75 to 18.5 minutes, average 9 minutes). Each subject was monitored prior to and during exposure and for a further 16 hours of routine activity following exposure, using an ambulatory three-channel ECG recorder. There were no significant differences in the number of ventricular ectopic beats per hour at rest, during or after CO exposure at any level. Furthermore, neither level of CO exposure had any impact on the number of exercise-induced ventricular ectopic beats. Thus the authors concluded that exposure to CO leading to 3% or 5% COHb resulted in no proarrhythmic effect during normal daily activity.

The Health Review Committee of the Health Effect Institute (HEI), which commissioned the study, noted the limited power of the study to detect any associations and distinguish between real and chance events due to the small number of subjects, shortness of the exercise period, and variability in measured end-point. They also noted that the proportion of subjects with myocardial ischaemia was higher in the Sheps et al. (1990) study than in the study by Chaitman and co-workers. This may explain the findings of significant effects at 5.3% COHb in the population studied by Sheps and colleagues as they may have been generally more sensitive because of their ischaemia.

MYOCARDIAL ISCHAEMIA

A mean increase in COHb of only 1.6% caused decreased exercise tolerance in people with stable angina pectoris (Anderson et al., 1973). Sitting quietly in a chair, ten adult male patients breathed compressed air, or CO at 57.3 mg/m³ (50 ppm) or 114.5 mg/m³ (100 ppm) for 4 hours in a random, double-blind study. The subjects’ mean age was 49.9 years. Subjects on medication were excluded from the study; this may mean that the subjects in the group were suffering a less severe form of the disease. Furthermore, five of the subjects were smokers, which could
have introduced another confounding factor. Mean COHb levels after exposure were 1.3%, 2.9% and 4.5%. Immediately after exposure the subjects performed incremental exercise, the end-point being patient-reported onset of anginal pain. The duration of exercise before onset of anginal pain was significantly shorter at 4.5% COHb and 2.9% COHb (p<0.005) than after compressed air exposure, but there was no significant difference in exercise duration before anginal pain between the two CO exposures. Compared with air exposure, duration of pain was prolonged at 4.5% COHb (p<0.01), but not at 2.9% COHb. Electrocardiograms recorded during and after exercise generally showed worsening of ST-segment changes. In summary, the men studied presented symptoms of anginal pain after less exercise, and their anginal pain lasted longer, with increasing COHb level.

Aronow and Isbell (1973) [see comment on adequacy of study] undertook a double-blind randomised study of ten non-smoking male subjects aged from 40 to 55 years (mean 49 ± 6 years) with classic exertional angina pectoris. Breathing room air, each subject exercised on a cycle ergometer with a progressive workload until onset of angina. This was used as the control period. Each patient then breathed 57.3 mg/m³ (50 ppm) CO or compressed, purified air for 2 hours on two occasions for each exposure condition, after which the same cycle ergometer test was performed until onset of angina. Mean COHb levels decreased from 1.1% to 0.8% after breathing compressed, purified air; after CO exposure the COHb level increased to 2.7%. All COHb levels were measured using a CO-oximeter. There was no significant difference observed in exercise duration between control and compressed, purified air breathing periods. At 2.7% COHb there was a significant 16% decrease in exercise duration until onset of angina (p<0.001). With the subjects at rest, there was no significant difference in mean systolic and diastolic blood pressure, heart rate, and systolic blood pressure \times heart rate between the control, CO exposure, and compressed, purified air exposure periods. A statistically significant decrease in systolic blood pressure (p<0.001), in heart rate (p<0.001), and a 10% decrease in systolic blood pressure \times heart rate (p<0.001) at onset of exercise-induced angina was observed at 2.7% COHb.

Using a similar protocol Aronow (1981) [see comment on adequacy of study] enrolled 15 patients, 14 men and 1 woman, suffering stable angina pectoris due to angiographically documented coronary artery disease, to evaluate the effect of breathing sufficient CO to raise COHb levels from approximately 1.0% to 2.0%. Their mean age was 59.0 ± 7.2 years. Breathing room air, patients exercised on a bicycle ergometer with a progressive workload until the onset of anginal discomfort (the control period). Each patient then breathed either 57.3 mg/m³
(50 ppm) CO to reach the target COHb level of 2.0%, or compressed, purified air for 1 hour, under double-blind, randomised, crossover conditions. The same bicycle ergometer exercise test was then performed, again until onset of anginal discomfort. The mean baseline COHb levels, measured by CO-oximeter, were 1.0% after breathing compressed, purified air and 2.0% after breathing CO. Eight of the 15 subjects developed a 1.0 mm or more ischaemic ST-segment depression at onset of angina pectoris during the control periods. Breathing CO did not significantly affect the resting (i.e. pre-exercise) product of systolic blood pressure $\times$ heart rate and did not significantly affect the amount of post-exercise ischaemic ST-segment depression at onset of angina pectoris. Breathing CO did not significantly affect the resting (i.e. pre-exercise) product of systolic blood pressure $\times$ heart rate and did not significantly affect the amount of post-exercise ischaemic ST-segment depression at onset of angina pectoris. At onset of angina pectoris (i.e. after exercise), systolic blood pressure $\times$ heart rate was significantly reduced by 8% ($p<0.001$).

Mean exercise duration before onset of angina pectoris was unchanged after breathing compressed, purified air but was significantly decreased, by 10%, at 2.0% COHb ($p<0.001$). Ischaemic ST-segment depression of 1.0 mm or more occurred sooner after exercise-induced angina pectoris, after less exertion, and at a lower systolic blood pressure $\times$ heart rate at the onset of angina pectoris. The author concluded that “if there is a safe threshold of CO exposure for patients with angina pectoris due to coronary artery disease, this level would appear to be very low” (Aronow, 1981).

A group of 30 non-smoking patients (25 men, 5 women) aged from 36 to 75 years (mean age 58.2 years) with ischaemic heart disease, manifesting as angina or as a positive stress, was studied to assess the effect of elevated COHb on exercise performance (Sheps et al., 1987). Patients were exposed to air alone and to CO at 114.5 mg/m$^3$ (100 ppm) in air. Exposure duration was determined according to the patient's CO uptake, the target COHb level being 4%. Patients' COHb levels averaged (mean pre- and post-exercise) 1.6% when exposed to air alone, and 3.8% when exposed to CO. No clinically significant effect of 3.8% COHb was found. Patients performed post exposure incremental, symptom-limited exercise on a bicycle ergometer up to maximal workload and a number of parameters were measured.

Peak workload was identical after air and CO exposure. Resting blood pressure was slightly lower at 3.8% COHb compared with air ($p = 0.031$). The maximal blood pressure achieved was identical in both exposure scenarios. There were no significant differences between air and CO exposure states in the following parameters: resting or maximal heart rate after exposure; maximal systolic blood pressure $\times$ heart rate; exercise duration; time to onset of angina; duration of
angina; maximal ST-segment depression; and time to significant ST-segment depression.

Radionuclide angiography showed no significant differences in resting post-exposure left ventricular ejection fraction or maximal ejection fraction between air and CO exposure, however the maximal change in ejection fraction (i.e. the difference between maximal and resting ejection fraction) of 3.5 for air exposure and 2 for CO exposure was reported as approaching significance (p = 0.049). 

Despite further analyses of the data the latter results were difficult to interpret in the light of the lack of significant differences in other variables, although the authors state there may have been a minimal effect of CO exposure on change in ejection fraction.

In a study looking at the effects of short-term exposure to CO on subjects with angina pectoris, Kleinman et al. (1989) reported similar findings to those reported in some studies above. The Kleinman et al. (1989) study was a randomised crossover double-blind experiment using 24 male subjects with stable angina pectoris, in which each subject acted as his own control and maintained his prescribed medication throughout the study. Ages ranged from 49 to 66 years with a mean of 59 ± 1 year, and all subjects had ceased smoking at least 8 months prior to the study. Exposure lasted 1 hour and was to clean filtered air with a CO concentration of 2.3 ± 1.7 mg/m³ (2 ± 1.5 ppm; the baseline exposure) or to CO in air at 114.5 mg/m³ (100 ppm). The levels of COHb were all measured using a CO-oximeter. Levels of COHb after baseline exposure were 0.7% to 2.6% (mean 1.5%) and after elevated CO exposure were 3%. Thus the highest baseline COHb levels were surprisingly high and only 0.4% less than levels following elevated CO exposure. Within 15 minutes of ceasing exposure, each subject began a staged, symptom-limited exercise test while breathing clean filtered air. Exercising in air reduced the COHb level of those exposed to 114.5 mg/m³ (100 ppm) CO from 3.0% to 2.8%. A wide range of exercise times was recorded, from 2 to 12 minutes (mean 6.45 minutes). At 3.0% COHb the time to onset of angina was decreased significantly by 5.9% (p = 0.046), and angina duration decreased, though non-significantly, by 7.9%. The authors concluded that exposure of subjects with stable angina pectoris to low levels of CO resulted in faster onset of anginal pain than exposure to CO-free air alone.

A study by Allred et al. (1989, 1991) also confirmed that low levels of COHb exacerbate myocardial ischaemia during graded exercise in subjects with coronary artery disease. This conclusion was based on a three-centre, double-blind randomised study by the HEI. A group of 63 male, non-smoking patients (mean
age 62.1 ± 8.1 years, range 41 to 75 years) with stable angina pectoris and positive exercise-induced ST-segment changes was employed in the study. Patients had on average 4.6 ± 1.2 anginal episodes per week and continued to receive any required medication throughout the study period. Each subject exercised on a treadmill, before and after exposure to either room air, or CO at two concentrations, in a symptom-limited incremental test. Target levels of COHb were set at 2% and 4% and exposures lasted between 50 and 70 minutes, based on subject uptake rates. These rates were determined during a qualifying visit and monitored during the exposure period. Carboxyhaemoglobin levels were measured using a CO-oximeter for all blood samples and gas chromatography for certain specific blood samples. Patients performed a pre-exposure exercise test, and were then exposed to either air or CO followed by a second, post-exposure, exercise test. Each individual therefore acted as his own control. Statistical analyses used trimmed means, the two largest and two smallest observations being removed. (Using untrimmed means produced only slight differences in result significance.)

Carboxyhaemoglobin levels, measured by gas chromatography, increased from baseline levels of 0.6 ± 0.02% to 2.00 ± 0.05% (2% target level) and 3.87 ± 0.08% (4% target level) after the second, post-exposure exercise test. CO-oximeter measurements were between 0.40% and 0.92% higher than gas chromatography-derived levels.

Taking ECG ST-segment change during the post-exposure exercise test as the end-point, exposures at the 2% and 4% COHb target concentrations produced respective decreases of 5.1% (p = 0.01) and 12.1% (p<0.0001) in the length of time to threshold ST-segment change compared with room air exposure. In patients where the ST-segment change was not reached, the total exercise duration was used instead of time to ST-segment change. The authors noted that the effect of this modification would be to underestimate any changes due to CO. The amplitude of ST change was 11% greater at 2% COHb (p = 0.002), and 17% greater at 4% COHb (p<0.0001) than under room air exposure conditions. No change in duration of ST-segment change was noted. The authors reported an apparent dose–response relationship between COHb level and decrease in time to ST-segment change. For each 1% increase in COHb there was a corresponding 3.9% decrease in time to ST-segment change.

The mean product of systolic blood pressure × heart rate was also determined at the ST-segment change. At 2% COHb, there was no significant change in this product. At 4% COHb, a 4.4% decrease (p = 0.03) in the product was noted compared with room air exposure.
The length of time to onset of angina decreased by 4.2% (p = 0.027) and 7.1% (p = 0.002) at the 2% and 4% COHb target concentrations respectively. At 2% COHb, 38 patients experienced a relative decrease in time to onset of angina and 23 a relative increase; one had no change. At 4% COHb, 45 patients experienced a relative decrease in time to onset of angina and 18 experienced a relative increase. Again, a dose–response relationship was apparent: the average decrease in time to onset of angina appeared to be approximately 1.9% for every 1% increase in COHb. There were no significant differences in the product of systolic blood pressure × heart rate at onset of angina when patients were exposed to room air, or to 2% or 4% COHb.

A significant correlation was shown between the change in length of time to the ST-segment change end-point and the change in time to onset of angina (Spearman's rank-correlation coefficient = 0.49; p ≤ 0.0001; Pearson correlation coefficient = 0.49; p ≤ 0.0001). This strongly suggests a decrease in oxygen availability to the myocardium in patients with coronary blood flow limitation. The authors stated that the most likely mechanism for these changes is a reduction in the oxygen carrying capacity of the blood, although more complex effects of CO on myocardial function cannot be excluded.

There was a 1.7 ± 1.6% decrease in the total exercise duration following exposure at the 2% COHb target concentration (p = 0.29) and a 6.2% decrease at the 4% COHb target concentration (p ≤ 0.0001) compared with room air only.

To test for other factors that might influence the results, covariate analyses were performed. These found the actual COHb level to be the most significant covariate. The only other significant covariate was patient weight (p ≤ 0.05) at the 4% COHb level.

The significance of the results for patients in normal everyday settings was also evaluated. The average patient presented evidence of ischaemia at light to moderate workloads, such as may be reproduced by climbing one or two flights of stairs. According to the authors, the exposure concentrations and resulting COHb levels “appear to be within a realistic range for subsets of the adult, non-smoking, US population that are heavily exposed to traffic or other local sources of CO”. Whilst the actual exposure concentrations used in this study were greater than the US EPA ambient air quality standards (see Table 2.1, Section 2.1), the measured COHb level of 2% was at the upper end of the range of values expected to occur after exposure to 10.3 mg/m³ (9 ppm) over 8 hours or to 40.1 mg/m³ (35 ppm) over 1 hour (the EPA standards).
The quality of life detriments associated with these changes in ST-segment and earlier onset of angina are not fully resolved. It is generally accepted that myocardial ischaemia is detrimental, but it may be difficult to compare the exercise performed in studies such as this with everyday exercise such as walking upstairs. The amount of exercise taken by patients with angina is limited by their disease. However, in silent or asymptomatic ischaemics, there is no pain to act as a warning (Allred et al., 1991), and whether such individuals are suffering ill-effects cannot easily be determined.

OTHER STUDIES

Aronow et al. (1974) [see comment on adequacy of study] conducted a double-blind randomised study of ten men (mean age 51 ± 7 years) with occlusive iliofemoral arterial disease of the calf or thigh but no coronary artery disease or hypertension. Patients who suffered from intermittent claudication exercised for a 17% shorter period (p<0.001) before onset of pain after inhalation of 57.3 mg/m³ (50 ppm) CO for 2 hours (leading to a 2.8% COHb level; pre-exposure level 1.1% COHb) than after a control period of exercise in room air.

Ten male patients, aged 53 to 67 years (59.2 ± 5.3 years), suffering chronic obstructive pulmonary disease were the subjects for a study by Aronow et al. (1977) on the effects of CO exposure [see comment on adequacy of study]. Their chronic obstructive pulmonary disease was documented by pulmonary function tests performed within 1 week of the study. All subjects were ex-smokers and had no history of cardiovascular disease and no ST-segment depression after maximal exercise. Two exposure regimes were employed, either 114.5 mg/m³ (100 ppm) CO or compressed, purified air. Before exposure, each patient exercised on a cycle ergometer until onset of marked dyspnœa (the control period). The exercise duration was recorded. Following 30 minutes’ rest, patients breathed either CO or compressed, purified air for 1 hour and then performed the cycle ergometer test again. Mean resting COHb levels recorded before exercise were 4.1% and 1.4% respectively. The mean exercise duration until marked dyspnœa was significantly reduced after exposure to CO relative to compressed purified air (p<0.001). No significant difference was noted between exercise duration in the control period and after breathing compressed, purified air. The authors concluded, based on other literature, that the impairment of exercise performance in sufferers of chronic obstructive pulmonary disease is probably a cardiovascular rather than respiratory effect.
SYNOPSIS

Tables 4.4 and 4.5 summarise the main findings from the studies on cardiovascular effects discussed above. These important studies on both healthy subjects and patients with cardiovascular and cardiopulmonary disease show equivocal results over a range of CO exposures.

Short-term exposure to low levels of CO resulted in reversible exercise performance decrements in patients with angina pectoris and in healthy subjects at COHb levels as low as 3% (or thereabouts; Anderson et al., 1973; Horvath et al., 1975; Kleinman et al., 1989) and ST-segment changes have been noted, also in patients with angina pectoris, at levels as low as 2% COHb (Allred et al., 1989, 1991). In contrast, another study on patients with ischaemic heart disease found little evidence for adverse effects after exercise at COHb levels of around 4% (Sheps et al., 1987).

Carboxyhaemoglobin levels similar to those reported to cause cardiovascular effects in some studies are not unusual. For example, Stewart et al. (1974) found 45% of non-smoking blood donors tested had COHb levels of 1.5% or more. Carboxyhaemoglobin levels such as these could result from an 8-hour exposure to 22.9 mg/m³ (20 ppm) CO, or shorter exposure to higher CO levels.

The criticisms of the work by Aronow and colleagues make its reliability questionable, but the findings of adverse effects in healthy subjects at 3.95% COHb (Aronow & Cassidy, 1975) and in patients with angina pectoris at 2 and 2.7% COHb (Aronow & Isbell, 1973; Aronow, 1981) lend support to the other studies that found adverse effects at similarly low COHb levels. However, there are many differences between studies in study protocols, the methods used to measure COHb levels, and study populations that make comparison of results difficult. Although the study populations of sufferers from cardiovascular and cardiopulmonary disease can be termed sensitive to CO, there may be many more individuals in whom these diseases are asymptomatic or more severe; such individuals could be assumed to be more sensitive than the subjects studied.

The studies reported also lend some support to the findings of Touloumi et al. (1996), Burnett et al. (1997) and others (see Section 4.4.5) who found associations between CO exposure and various measures of morbidity and mortality.
Table 4.4 Summary of effects of carbon monoxide in healthy subjects

<table>
<thead>
<tr>
<th>Reference</th>
<th>Exposure&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Subjects&lt;sup&gt;b&lt;/sup&gt;</th>
<th>COHb level (%)&lt;sup&gt;c&lt;/sup&gt;</th>
<th>Observed effects</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pirnay et al. (1971)</td>
<td>572.5 mg/m³ (0.05%) for 5 min pre-exercise and during exercise (moderate exercise 15 min, followed by maximum tolerable for 2–3 min)</td>
<td>5 males, 24–35 years</td>
<td>15.4</td>
<td>Increased heart rate but no increase in VO&lt;sub&gt;2&lt;/sub&gt; or ventilation with submaximal exercise; VO&lt;sub&gt;2max&lt;/sub&gt; decreased 15.1% (p&lt;0.001)</td>
<td>Decreased maximal O&lt;sub&gt;2&lt;/sub&gt; consumption</td>
</tr>
<tr>
<td>Vogel &amp; Gleser (1972)</td>
<td>40 l bag of 1.0–1.2% CO in air until equilibrium; 2 submaximal and 1 maximal exercise tests</td>
<td>8 males, 20–23 years (3 smokers)</td>
<td>18.6–20.0</td>
<td>Submaximal heart rate increased (p&lt;0.05); submaximal VO&lt;sub&gt;2&lt;/sub&gt; unchanged; 23% decrease in VO&lt;sub&gt;2max&lt;/sub&gt; (p&lt;0.001)</td>
<td>VO&lt;sub&gt;2max&lt;/sub&gt; decreased at &gt;18.6% COHb</td>
</tr>
<tr>
<td>Horvath et al. (1975)</td>
<td>85.9 and 114.5 mg/m³ (75 and 100 ppm); with either progressive or rapid rise to target COHb level; 15 min treadmill exercise to exhaustion</td>
<td>4 males, 24–33 years (1 smoker)</td>
<td>~3.3 and ~4.3</td>
<td>VO&lt;sub&gt;2max&lt;/sub&gt; decreased at 4.3% COHb (p&lt;0.10); exercise duration significantly lower at both CO exposures (p&lt;0.05)</td>
<td>VO&lt;sub&gt;2max&lt;/sub&gt; decreased at &gt;4.3% COHb</td>
</tr>
<tr>
<td>Aronow &amp; Cassidy (1975)</td>
<td>114.5 mg/m³ (100 ppm) for 1 hour; treadmill exercise until exhaustion</td>
<td>9 males, 1 female, 45–55 years</td>
<td>3.95</td>
<td>Mean exercise time to exhaustion decrease 5% (p&lt;0.001)</td>
<td>Exercise time decreased in middle-aged non-smokers at 3.95% COHb</td>
</tr>
<tr>
<td>Davies &amp; Smith (1980)</td>
<td>0, 17.2 mg/m³ (50 ppm) and 57.3 mg/m³ (30 ppm) continuously for middle 8 of 18 days</td>
<td>45 males, 17–27 years (approx half smokers)</td>
<td>0.5–7.1%</td>
<td>Changes in P waves observed in 6/15 subjects at 7.1% COHb; 3/16 at 2.4%, 0/14 at 0.5%; one subject showed marked ST-segment changes after exposure to 17.2 mg/m³ (15 ppm) for 36 hours</td>
<td>P wave changes in some individuals at &gt;2.4% COHb</td>
</tr>
</tbody>
</table>

Adapted from EPA (1991)

COHb, carboxyhaemoglobin; VO<sub>2</sub>, oxygen uptake; VO<sub>2max</sub>, maximal oxygen uptake

<sup>a</sup> Exposure duration, concentration and activity level
<sup>b</sup> Number, sex and age range of subjects
<sup>c</sup> COHb level at end of exposure
Table 4.5 Summary of effects of carbon monoxide exposure in patients with cardiovascular diseases

<table>
<thead>
<tr>
<th>Reference</th>
<th>Exposurea</th>
<th>Subjectsb</th>
<th>COHb level (%)c</th>
<th>Observed effects</th>
</tr>
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<tbody>
<tr>
<td><strong>Arrhythmia studies</strong></td>
<td></td>
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<tr>
<td>Hinderliter et al.</td>
<td>114.5 mg/m³ (100 ppm) and 229 mg/m³ (200 ppm) for ≥1 hour to reach target COHb level of 4% and 6% respectively; incremental, symptom limited exercise test</td>
<td>7 males, 3 females with baseline levels of ventricular ectopy of 0 to 1 VPD/h, 61 ± 5 years.</td>
<td>4.0; 3.5; 2.2 5.8; 4.9; 4.0</td>
<td>No significant increase in frequency or severity of ventricular ectopy in patients without significant baseline arrhythmias</td>
</tr>
<tr>
<td>Sheps et al.</td>
<td>114.5 mg/m³ (100 ppm) and 229 mg/m³ (200 ppm) for ≥1 hour to reach target COHb level of 4% and 6% respectively; incremental, symptom-limited exercise test</td>
<td>36 male, 5 female non-smokers with low, intermediate and high baseline levels of ventricular ectopy, 62.8 ± 1.1 years (47–77 years)</td>
<td>4.0; 3.5; 2.2 5.9; 5.0; 4.1</td>
<td>No significant difference in VPD/h between control and 4% or 5.9% COHb; significantly higher frequency of single and multiple VPD at 5.9% COHb during exercise; no significant effect of either COHb level on amount of arrhythmia, angina, resting ejection fraction, change in ejection fraction with exercise, or presence and magnitude of ST-segment depression during exercise</td>
</tr>
<tr>
<td>Chaitman et al.</td>
<td>182.1 ± 28.6 mg/m³ (159 ± 25 ppm) and 334.3 ± 35.5 mg/m³ (292 ± 31 ppm) for 60 min; 22.1 ± 0.9 mg/m³ (19.3 ± 0.8 ppm) and 35.4 ± 1.4 mg/m³ (31 ± 1.2 ppm) for further 90 min to reach and maintain target COHb levels of 3% and 5%; symptom-limited treadmill exercise test at maintenance CO concentration</td>
<td>25 male, 5 female non-smokers with angiographic or historical evidence of ischaemic heart disease and chronic ventricular arrhythmias (≥30 VEB/h), 65 years (45–77 years)</td>
<td>3.2; 2.9; 2.5 5.1; 4.7; 4.4</td>
<td>No significant differences in VEB/h at either CO exposure</td>
</tr>
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### Table 4.5 (continued)

<table>
<thead>
<tr>
<th>Reference</th>
<th>Exposurea</th>
<th>Subjectsb</th>
<th>COHb level (%) c</th>
<th>Observed effects</th>
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<tr>
<td><strong>Ischaemia studies</strong></td>
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<tr>
<td>Anderson et al.</td>
<td>57.3 mg/m³ (50 ppm) and 114.5 mg/m³ (100 ppm) for 4 hours; post-exposure incremental, symptom-limited exercise on a treadmill</td>
<td>10 males (5 smokers) with reproducible exercise-induced angina, 49.9 years</td>
<td>2.9; 4.5; 3.2</td>
<td>Significantly decreased exercise duration before onset of angina (p&lt;0.005); angina duration increased significantly at 4.5% COHb (p&lt;0.01) but not at 2.9% COHb</td>
</tr>
<tr>
<td>Aronow &amp; Ishell</td>
<td>57.3 mg/m³ (50 ppm) for 2 hours; symptom-limited exercise test</td>
<td>10 males, non-smokers, with exertional angina pectoris, 49 ± 6 years (40–55 years)</td>
<td>2.7; 1.6</td>
<td>Significant reduction in exercise duration before angina, systolic blood pressure, heart rate, and product of heart rate × systolic blood pressure (p&lt;0.001) at 2.7% COHb</td>
</tr>
<tr>
<td>Aronow</td>
<td>57.3 mg/m³ (50 ppm) for 1 hour; post-exposure, incremental, symptom-limited exercise test</td>
<td>14 male, 1 female, non-smokers with angiographically documented coronary artery disease, 59.0 ± 7.2 years</td>
<td>2.0; 1.0</td>
<td>8 subjects developed ≥1 mm ST-segment depression at onset of angina during control period; mean exercise duration and product of systolic blood pressure × heart rate significantly decreased at 2.0% COHb (p&lt;0.001)</td>
</tr>
<tr>
<td>Sheps et al.</td>
<td>114.5 mg/m³ (100 ppm) for 1 hour; post-exposure incremental exercise</td>
<td>25 male and 5 female non-smokers with evidence of ischaemia manifested as angina and/or positive stress test on at least one day, 58.2 years (36–75 years)</td>
<td>4.1; 3.6; 2.4</td>
<td>No significant difference in time to, or duration of, angina or maximal ejection fraction; no significant difference in maximal exercise time, maximal ST segment depression, or time to significant ST segment depression during exercise; small decreases in blood pressure (p = 0.031) and change in ejection fraction (p = 0.049) during CO exposures require further evaluation</td>
</tr>
<tr>
<td>Reference</td>
<td>Exposurea</td>
<td>Subjectsb</td>
<td>COHb level (%)c</td>
<td>Observed effects</td>
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<tr>
<td>Kleinman et al. (1989)</td>
<td>114.5 mg/m³ (100 ppm) for 1 hour; post-exposure incremental exercise</td>
<td>24 male non-smokers with reproducible exercise-induced angina, 59 ± 1 years (49–66 years)</td>
<td>3.0; 2.8; 1.5</td>
<td>Time to onset of angina decreased 5.9% (p = 0.046); no significant changes in angina duration, heart rate or systolic blood pressure at onset of angina</td>
</tr>
<tr>
<td>Allred et al. (1989; 1991)</td>
<td>48.1 to 231.3 mg/m³ (42–202 ppm) and 163.7 to 408.8 mg/m³ (143–357 ppm) for 50 to 70 min; pre- and post-exposure symptom-limited exercise test</td>
<td>63 male non-smokers with reproducible exercise-induced angina, 62 ± 8.1 years (41–75 years)</td>
<td>2.4; 2.0; 1.8; 4.7; 3.9; 4.1</td>
<td>Earlier onset of myocardial ischaemia found with CO exposure; time to ST end-point decreased 5.1% (p = 0.01) and 12.1% (p&lt;0.001) and time to onset of angina decreased 42% (p = 0.027) and 7.1% (p = 0.002) at 2.0 and 3.9% COHb respectively; changes in performance clinically significant; significant linear dose-response relationship found for ST change for the range of COHb levels; significant correlation between decrease in time to angina and decrease in time to ST-segment change</td>
</tr>
</tbody>
</table>

Other studies

<table>
<thead>
<tr>
<th>Reference</th>
<th>Exposurea</th>
<th>Subjectsb</th>
<th>COHb level (%)c</th>
<th>Observed effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aronow et al. (1974)</td>
<td>57.3 mg/m³ (50 ppm) for 2 hours; symptom limited exercise test</td>
<td>10 males with classic intermittent claudication of calf or thigh, 51 ± 7 years (33–58 years)</td>
<td>2.8; –; 1.7</td>
<td>Significantly reduced exercise duration following CO exposure (p&lt;0.001)</td>
</tr>
<tr>
<td>Aronow et al. (1977)</td>
<td>114.5 mg/m³ (100 ppm) for 1 hour; symptom limited pre- and post-exposure exercise</td>
<td>10 males, ex-smokers with chronic obstructive pulmonary disease, 59.2 ± 5.3 years (53–67 years)</td>
<td>4.1; 4.0; 2.7</td>
<td>Mean exercise duration until marked dyspnoea significantly decreased (p&lt;0.001)</td>
</tr>
</tbody>
</table>

Adapted from EPA (1991)

- –, not measured; VEB, COHb, carboxyhaemoglobin; VPD, ventricular premature depolarisations
- a Exposure duration, concentration and activity level
- b Number, sex, medical state and mean age (age range) of subjects
- c Measured COHb after exposure; after exercise stress test; change in COHb between control and post-exposure
4.5.2 Neuropsychological Effects

In addition to effects on the cardiovascular system, CO may affect an individual's performance in neuropsychological tasks. Using healthy subjects, the studies summarised below have aimed to evaluate the effect of various concentrations of CO on a variety of psychological functions by assessing performance in tasks involving object tracking, visual detection, time discrimination, manual dexterity and reaction time.

In a wider context, neuropsychological evaluation is increasingly being used in the assessment of the effects of occupational and environmental pollution on the central nervous system. The last decade has seen a dramatic growth in publications related to occupational and environmental health hazards (e.g., inorganic lead, organic solvents, pesticides) and the psychological methods employed to detect evidence of neurotoxicity in human populations have been the focal point of numerous scientific papers over the last two decades (Stollery, 1996a; Williamson, 1996). Given that many occupational and environmental pollutants may influence the efficiency of everyday behaviour (i.e. by influencing an individual's memory, attention and reasoning skills), the advantages of neuropsychological methods lie in their unobtrusive nature and the collection of relevant information on an individual's ability to conduct their daily lives. However, and perhaps more importantly, neuropsychological methods are also capable of detecting impairments of central nervous system functioning at concentrations of a toxin which are below the levels required to produce adverse effects on other organ systems. Indeed, impairments in psychological performance can be detected in asymptomatic healthy individuals and, in some cases, can reveal consistent exposure–response relations across the range of occupational exposures that are currently acceptable on general health and safety grounds (Stollery, 1996b). The ultimate utility of psychological methods lies in their ability to link performance decrements to various psychological functions; it is important to note that considerable evolution in these methods has taken place since their initial application to neurotoxicology, and in particular CO exposure, in the 1970s and earlier.

In general terms, it is known that prolonged exposure to CO at high concentrations causes ischaemic damage to the brain, and the areas most sensitive
to such damage appear to be the basal ganglia and subthalamus. Carbon monoxide causes anoxia without primary loss of blood circulation, so glucose is still supplied and metabolic products removed (Norton, 1980). In the various studies reviewed below, short-term CO exposures have been employed and performance decrements have been assessed at given CO exposures and COHb levels. The purpose of such exposures is of course not to damage the participants brain in any way, but rather to seek to establish at what concentrations CO is capable of exerting a detrimental effect on human performance.

Benignus et al. (1990a) recently reviewed and re-analysed published data on the dose–effect functions for COHb and behaviour. The authors focused on the effect of CO on compensatory tracking tasks such as those employed by O’Donnell (1971a), Putz (1979) and Benignus et al. (1990b). They used data from a previous study (Benignus et al., 1990b) to estimate a dose–effect curve for COHb levels and a tracking task, and suggested that for healthy young men at rest, COHb should have little or no behavioural effects at levels below 20%. However, they stressed a number of caveats to this conclusion because most of the data are from healthy young men not simultaneously exposed to other pollutants or drugs, the effects of task variables such as monotony, frequency and number of tasks have not been systematically studied, and the poor replication of research results makes forming solid conclusions difficult. [Furthermore, it is worth noting that early studies used rather idiosyncratic experimental designs and unsophisticated data analysis techniques.]

The effect of CO exposure on time estimation tasks is one of the most controversial areas of neuropsychological research on CO and has been investigated by several authors (Beard & Wertheim, 1967; O’Donnell et al., 1971a,b; Stewart et al., 1973; Otto et al., 1979).

In the initial study by Beard and Wertheim (1967), 18 young [age not specified] non-smoking university students were played two 100 Hz tones and had to decide which tone lasted longer. The first (reference) tone was played for one second and the second (comparison) tone was played 0.5 seconds later. The duration of the comparison tone varied between 0.675 and 1.325 seconds (1 ± 0.325 seconds). Participants were asked to decide whether the comparison tone was longer, shorter or the same length as the reference tone. Carbon monoxide exposures were 0, 57.3, 114.5, 200.4 and 286.3 mg/m³ (0, 50, 100, 175 and 250 ppm respectively) and the intended CO concentration was built up to within 11.5 mg/m³ (10 ppm) of the value within 1 minute. No information is provided on the COHb levels reached during each exposure condition, and the authors stated that
determinations of COHb were inaccurate. However, Benignus et al. (1990a) estimated the COHb levels to be approximately 2.5, 5.0, 8.7 and 12.5% COHb. Each test session lasted 4 hours, with a 6 to 7 minute assessment period and a 13 minute break between assessments. Each subject was observed on at least 15 occasions. The order of exposure conditions was not specified. The analysis used is a series of t-tests whereas analysis of variance may have been more appropriate. O’Donnell et al. (1971a) have also criticised the exposure situation (a small, soundproof audiometric booth) arguing that this limits visual and kinaesthetic input and introduces the factor of boredom. On the basis of their results, Beard and Wertheim (1967) concluded that time discrimination deteriorated after 90 minutes at 57.3 mg/m³ (50 ppm) and at proportionally shorter times at higher concentrations up to 286.3 mg/m³ (250 ppm). The proportion of correct responses diminished and the ‘perceptual’ behaviour of the participants became more erratic. As might be expected, accuracy was poorer for smaller time discriminations (0.125 s) than longer time discriminations (0.325 s) and the slope relating CO concentration to accuracy appears shallower. However, this is likely to be due to baseline effects, given that accuracy at 0 mg/m³ was only about 50% for discriminations of 0.125 s compared with about 95% for discriminations of 0.325 s.

Stewart et al. (1973) attempted to replicate the Beard and Wertheim (1967) study using a group of 27 healthy graduate students and medical faculty members (22–43 years; 24 men, 3 women), studied in a double-blind randomised trial. Only three of the group were smokers, although they were requested to abstain from smoking for the duration of the study. This was confirmed by pre-exposure COHb measurement. Exposure took place in an air-conditioned chamber with ‘pleasant lighting, comfortable chairs, and a study desk’. Carbon monoxide exposures were <2.3, 57.3, 114.5, 227 and 572.5 mg/m³ (<2, 50, 100, 200 and 500 ppm) for up to 5 hours, designed so that the maximum COHb level attained would not exceed 20%. No information on COHb levels in relation to the respective CO concentrations and durations was provided, only a range of COHb levels was given — 0.4% to 20% COHb. The methods used for COHb determination included gas chromatography analysis of blood samples and alveolar breath samples. The results from three time perception tasks were presented. These included a replication of the time discrimination task used by Beard and Wertheim (1967), with the exception that the interval between tones was 1.5 seconds rather than 0.5 seconds, a task requiring the estimation of presentation time of lights and tones presented for 1, 3 and 5 seconds, and a task requiring the individual to estimate the duration of 10- and 30-second empty intervals. Exposures were for up to 5 hours, with testing occurring every hour. The
authors reported no relationship between COHb levels and performance in any of the tasks, and concluded that short-term exposure of healthy adults to concentrations of CO up to 572.5 mg/m³ (500 ppm), which result in COHb levels as great as 20%, has no detrimental effect on sense of time.

Otto et al. (1979) attempted to follow more closely the experimental design of Beard and Wertheim (1967) using 13 male volunteers (19 to 30 years), but also failed to replicate their results. The three main differences between the two studies were that test session duration was 3 rather than 4 hours, the activity of the volunteers between work periods was more closely controlled to ensure similar behaviour, and electroencephalogram data were recorded through scalp electrodes. Exposures to CO lasted 2.33 hours and were to 0, 85.9 and 171.8 g/m³ (0, 75 and 150 ppm); COHb levels were 0.16%, 3.77% and 7.81% respectively and were measured spectrophotometrically. The sequence of tones, durations and inter-test intervals were exactly the same as those of Beard and Wertheim (1967). There was no evidence of impairment on the time discrimination task nor any trends in performance change over time.

O’Donnell et al. (1971a) tested four air force pilots to assess the effects of CO exposure on human sleep (using electroencephalogram measures) and psychological performance as assessed in a number of different tasks. Performance was assessed using tasks of critical flicker fusion, mental arithmetic, a compensatory tracking task under moderate and high workloads, a 10-second and a 30-second time estimation task, and a time discrimination task using tones in a manner similar to that of Beard and Wertheim (1967). Each pilot was assessed at 0, 85.9 and 171.8 mg/m³ (0, 75 and 150 ppm) CO, the latter two conditions producing COHb levels of 5.9% and 12.7%, as assessed by a modified gas chromatography technique. Estimates of ‘empty’ time periods tended to be overestimated, but there were no differences due to CO exposure. No exposure effects were observed in any of the other tasks, including the time discrimination task. Finally, for the sleep measures, there was no dramatic whole-night effect of CO, although the authors drew attention to the possibility that during CO exposure there was a tendency for volunteers to have more deep sleep (stages 3 + 4) and less light sleep (stages 1 + 2), but there was no evidence that CO affected the number of times that volunteers moved from one stage of sleep to another (stage mobility), and no evidence that they spent less time in a particular sleep stage once they had entered it. The authors noted that, based on these data, it might be concluded that CO exposure tends to reduce central nervous system activation, but that this is insufficient to lead to changes in the overall rhythm of the sleep pattern and has no demonstrable effects on performance.
O’Donnell et al. (1971b) assessed time estimation and performance in a critical instability tracking task among nine non-smoking male university students (19 to 22 years), exposed to CO levels of 0, 57.3 and 143.1 mg/m³ (0, 50 and 125 ppm), producing COHb levels of 1%, 3% and 6.6% as measured by a modified gas chromatography technique. In the time estimation task volunteers were required to estimate an ‘empty time’ interval of 10 seconds during exposure for 3 hours on three occasions, one at each CO level, using a double-blind counterbalanced design. Under all conditions volunteers tended to overestimate the 10-second interval and the accuracy of the estimates tended to improve during the 3-hour session. The only performance variation occurred between 135 and 150 minutes, where time estimations at 57.35 mg/m³ (50 ppm) CO exposure were longer than under the control condition (p<0.05). This difference corresponded to improved accuracy for the control condition rather than a decline in accuracy for the exposure condition. In the critical instability tracking task volunteers had to keep a needle from going off a display dial by manipulating a control stick. As time on the task continued the difficulty of the task was made progressively greater until ultimately control was no longer possible; the difficulty level at which volunteers failed to maintain the needle on the dial was recorded. The data showed a tendency for performance to improve over time in all conditions, but none of these changes was significant. Inspection of the data for the three exposure levels over time suggests that the difficulty level attained during the exposed condition was lower than that during the control condition. However, the only comparison to achieve significance was that between the control and exposure conditions at 135 to 150 minutes at 57.25 mg/m³ (50 ppm). Again this was due to improved performance in the control condition. This effect was not seen during the 143.1 mg/m³ (125 ppm) exposure and was not present at either concentration between 165 and 180 minutes of exposure. Based on additional analyses, the authors suggested that performance under the control condition tends to improve and then decline during the 3-hour session (quadratic component), whereas performance under the exposure conditions tends to show somewhat flatter linear improvements. [There were some limitations in the data analysis and the appropriate two-factor analysis of variation, with time and exposure level as the two factors, was not undertaken] The Pensacola Ataxia Battery, which provides a measure of the volunteers’ dynamic equilibrium, showed no differences between the three exposure conditions, and in general the study failed to find any convincing evidence of decrements in performance due to CO exposure.

Harbin et al. (1988) studied the effects of low-level CO exposure in 33 young men (mean age 22.8 years) and 22 older men (mean age 68.7 years) using two versions of a visual oddball task (non-semantic and semantic) and a reaction time task
where the number of choices was varied between one and eight. In the visual oddball task, volunteers had to monitor a series of 600 stimuli. Frequent stimuli were presented on 75% of the trials and the task was to detect, keep track of, and report the number of presentations of the rarer (25%) stimuli. The non-semantic condition used the letters A and B, and the semantic condition used stimuli which were members of the categories of vegetables and animals. In the non-semantic condition, B was the rare stimulus; in the semantic conditions, vegetables were the rare stimuli. The order of semantic and non-semantic conditions was random. Performance was assessed by measuring the amplitude of the late evoked response (also referred to as P300 or P3). Volunteers were exposed to either air alone or CO in air at 229 mg/m³ (200 ppm) for the first hour followed by CO in air at 57.3 mg/m³ (50 ppm) for a further 2 hours, the aim being to raise COHb levels to 5% to 6%. There was no significant correlation between COHb level and either late evoked response or reaction time. The only significant correlations were between age and the late evoked response in the visual oddball task (p = 0.00198) and in the reaction time task (p<0.0002) and between age and reaction time (p<0.0001). Finally, there was evidence that the older adults absorbed CO less readily than the young adults. The authors considered the possibility that natural variability might have obscured a genuine CO effect, but power analyses indicated that this was unlikely. The other possibility is that the parameters assessed are not sensitive to CO. However, one important implication of this result is that whereas the elderly are sometimes seen as a sensitive group, the results show no evidence of this in terms of performance and there seems to be some compensatory mechanism operating which reduces the amount of CO absorbed by the elderly.

Stewart et al. (1970) examined 18 healthy male graduate students and medical school faculty members (age range 24 to 43 years), in a series of 25 experimental exposures, to known concentrations of CO designed to imitate those that may be encountered in urban and industrial settings. The three smokers were asked to abstain from smoking during the study. The mean CO concentrations ranged from less than 1.1 to 684.7 mg/m³ (<1 to 598 ppm) and exposure durations varied between 1 and 24 hours. Pre-exposure blood samples were analysed for COHb levels and a battery of other blood tests was performed. Volunteers exposed to CO concentrations in excess of 114.5 mg/m³ (100 ppm) were required to demonstrate a normal exercise ECG prior to exposure. Subjective and objective responses were recorded during each waking hour of exposure and any untoward subjective responses were also recorded in the first 24 hours post-exposure. Performance was assessed on a series of time estimation (1, 3 and 5 seconds), reaction time (driving simulation task), hand steadiness and manual dexterity tasks. No untoward subjective or objective signs of illness were noted during, or in the 24 hours following, any of the experimental exposures.
following, exposure to 28.6, 57.3, or 114.5 mg/m³ (25, 50 or 100 ppm) CO. The only significant relationship was a decrease in manual dexterity with CO concentrations in the Crawford collar and pin test; this was regarded by the authors as spurious for two reasons. First, no paired t-test approached significance and second, the very similar Crawford screw test exhibited no correlations with CO concentration. Neither time estimation or reaction time was significantly impaired by any CO exposure level. A number of volunteers reported headaches at concentrations of 229 mg/m³ (200 ppm) to 684.7 mg/m³ (598.0 ppm). A final experiment involved a steadily rising concentration of CO to a peak of 1145 mg/m³ (1000 ppm), maintained for 30 minutes with a mean COHb level of 31.8% at the end of exposure. Dramatic impairment of manual dexterity was noted in this experiment when the COHb saturation was 28%, 2¼ hours into the exposure. At 22% COHb in the same experiment, manual dexterity appeared normal.

Benignus et al. (1990b) assessed the effects of CO on a compensatory tracking task in which the participant was required to keep a moving spot on an oscilloscope screen centred by the manipulation of a joystick. Blocks of performance were of 64 seconds duration, during which the spot movement was either fast or slow. A group of 74 men (mean age 23.4 years) was randomly divided into five subgroups with target COHb levels of endogenous* [i.e. no CO exposure], 5%, 12% and 17%. There were two 5% groups, a fast COHb formation and a slow COHb formation group; both the 12% and 17% groups were fast COHb formation. Blood COHb was measured using a CO-oximeter. The exposure duration was 4 hours. Although evidence was found that mean tracking error scores increased as a function of COHb, the effects were not statistically significant and there were no differences between the slow and fast COHb formation groups.

A very early study by Hanks (1970) also found no effects on a tracking task attributable to CO exposure from 0 to 114.5 mg/m³ (0–100 ppm) for 4.5 hours.

Work by Putz (1979) among 30 adult (age range 18 to 26 years), non-smoking, students subjects randomly assigned to one of three exposure groups in a double-blind procedure, did find a significant effect of CO on tracking task performance undertaken in a dual-task situation. Exposure was to ambient CO levels (5.7 mg/m³; 5 ppm) and CO in air at 40.1 mg/m³ (35 ppm) and 80.15 mg/m³ (70 ppm) for 4 hours; the resulting COHb levels after the third hour of exposure were 1, 3 and 5% respectively. Carboxyhaemoglobin was measured by

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* As described in Section 4.2, humans produce CO endogenously through haem oxygenase-mediated breakdown of haem proteins
spectrophotometer and estimated from alveolar breath samples. A visual manual tracking and a peripheral monitoring (peripheral light-intensity-change) task were administered each hour during the exposure period. The tracking task required the volunteer to maintain a spot of light in the centre of a ring by applying pressure on a control to off-set the effect of a vertical forcing function and was conducted at both low and high frequency. The peripheral monitoring task was performed using bright and dim stimuli. Both tasks were performed concurrently with the tracking task designated as the primary task. At COHb levels of 5.1% there was a 30% performance impairment in the visual tracking task (increase in tracking errors) compared with performance at 1% (p<0.01) and 3% COHb in the high frequency condition only. Response times for the peripheral monitoring task increased at different rates as a function of the CO level (p<0.05). However, the main source of this effect was a significant increase in response time (p<0.01) between the second and fourth hour in the 5% COHb group. There was no significant difference between the three groups (1%, 3% and 5% COHb) at the end of the exposure period. The authors concluded that when COHb levels increased to 5% during peripheral monitoring, the subjects lost vigilance more rapidly than at the lower COHb levels.

It is significant that this study examined tracking performance in a dual-task, rather than single-task, situation. Dual-task arrangements decrease the amount of attentional capacity available to perform tasks, and this appeared to impair the ability to track the target successfully and increased the time required to make decisions about stimulus intensity. The authors argue that dual-task demand characteristics can serve to exacerbate conditions of toxic stress and are likely to be a useful technique in assessing exposure effects.

McFarland et al. (1944) studied the effect of CO exposure and altitude on visual thresholds after dark adaptation, with the aim of assessing the combined effects, primarily in pilots. Exposure to CO alone (two experiments on one pilot) resulted in a rise in visual thresholds, indicating a decline in visual sensitivity. Estimated COHb levels were between approximately 4% and 19%. This effect was reported to be replicated in a similar experiment on a further three volunteers.

A more recent study by Hudnell and Benignus (1989) also studied the effects of COHb levels on human visual detection thresholds in 21 male volunteers (mean age 23.25 ± 3.7 years, range 18.5–33.8 years) in a double-blind experiment. Participants were randomly assigned to either a control or exposure group; the target COHb levels were endogenous for the control group and 19% for the exposure group. To reach the target COHb level, volunteers were initially exposed
to a mixture of CO and air with an average CO concentration of 13 246.3 mg/m$^3$ (11 568.8 ppm) for 4 to 5 minutes and thereafter to CO at 162.1 mg/m$^3$ (141.6 ppm) for a total exposure time of 2 hours. The control group's mean COHb was between 0.7% and 0.8%; the exposure group's mean COHb rose to 17.1% as determined by a CO-oximeter. A battery of visual tests was used to assess the effect of CO on scotopic and photopic vision, pattern detection and motion detection processes, both before and after exposure. No significant effects were found, indicating that the visual functioning of young healthy volunteers was not affected by COHb levels of about 17% maintained over 2 hours.

Bunnell and Horvath (1988) studied 18 adults (11 men, 7 women; age range 18–29 years) on a series of cognitive tasks under three different workloads (resting, 35% VO$_{2\text{max}}$, and 60% VO$_{2\text{max}}$) and three CO exposures (ambient CO, 51.5 mg/m$^3$ (45 ppm) and 74.4 mg/m$^3$ (65 ppm)). Final COHb levels across the three exercise conditions were: 0.7, 0.8 and 0.7% at ambient CO; 6.7, 7.2 and 7.4% at 51.5 mg/m$^3$ exposure; and 9.3, 10.0 and 10.2% at 74.4 mg/m$^3$. Levels of COHb were measured by both CO-oximetry and gas chromatography analysis of randomly selected samples. The levels of COHb tended to be higher following exercise owing to an increased ventilation rate. The cognitive tasks included a task of spatial reasoning (Manikin task), a short-term memory scanning task (Sternberg task), a Stroop colour–word interference task, a visual search task, a visual tracking task and a multiplication task. These last two tasks were also required to be attempted concurrently in a dual-task arrangement (divided attention task). No effects of CO exposure were seen on the spatial reasoning task, the memory scanning task, tracking task or divided attention task. The colour–word interference component of the Stroop task showed a significant CO effect, with the 7% and 10% conditions both showing greater interference than the 0% condition. The CO effect was only observed on the time required to name the colour of printed words (which is typically taken as the ability to ignore the name of the colour word when responding to its colour). However, the authors suggested that the effect was due to a form of negative transfer which renders the transfer of one set of response rules to another set of response rules more difficult. For the visual search task there was an interaction between workload and COHb levels: at rest, search rates were faster in the 10% COHb condition than in the 0% COHb condition, whereas for the 60% workload the search rate was slower in the 10% condition than in the 0% condition. This effect was interpreted in terms of the Yerkes–Dodson law, with CO exposure acting as a mild stressor, increasing arousal at low workloads. This was the only instance when CO and exercise were seen to interact and affect performance. The authors concluded that their data suggest that people are able to tolerate COHb levels as high as 10%,
with accompanying physical work, displaying little increase in physical or psychological discomfort and only mild decrements (about 10%) in specific areas of cognitive performance.

Schulte (1963) enrolled 49 volunteers (smokers and non-smokers) from the Cincinnati Fire Department (mean age 37.5 years) in a study to determine whether alterations in some functions of the higher centres of the central nervous system occurred at COHb levels lower than those necessary to evoke subjective symptoms or alterations in the physiological functions of other tissues. In addition to COHb determinations, the study included a number of tests including pulse and respiratory rates and blood pressure, neurologic reflexes, muscle persistence, static steadiness, time of onset of subjective symptoms, colour stimulus response test, letter stimulus response test, plural noun underlining, t crossing test and arithmetic test. None of the tests are described in any detail in the paper.

Performance on the tasks was evaluated during four consecutive testing cycles [duration not given], with volunteers divided into 11 groups [numbers not given] and exposure to CO [duration not given] occurring during none, some and all four of the testing cycles. Exposures were to room air or to approximately 114.5 mg/m³ (100 ppm) CO in air. The time and amount of CO exposure were varied [exposure conditions not given], producing a range of COHb levels from 0% to 20.4%. [The reliability of the analytical methods used can be questioned on the basis of the work by Stewart et al. (1970) who noted that 20.4% COHb is a high level for an exposure to 114.5 mg/m³ CO. Exposure to 100 ppm CO produces an equilibrium COHb level of 14%, well below the 20.4% cited by Schulte (see Figure 3.2)]. One volunteer reported developing a headache at which point his measured COHb level was 20.4%. No significant correlations were found between COHb levels and any of the physiological activities or reaction time in the simple response task. However, statistically significant relationships between COHb and all other psychological tasks, with the exception of errors in the plural noun underlining test, were found, and the author concluded that impairment was detectable at COHb levels of 5%. However, the lack of detail on the tests, procedures and statistical analysis makes the findings questionable and hard to evaluate. Furthermore, the unusually high COHb levels reported, the fact that volunteers were firemen (a group occupationally exposed to very high CO concentrations), and the fact that some were smokers, may also limit the strength of the author's conclusions.

Odour sensitivity and the interaction of CO and alcohol were reported by Engen (1986), who studied volunteers (6 men and 1 woman; age range 20–24 years). All were occasional social drinkers and none were smokers. Four experimental
conditions were employed (CO only, air only, CO plus alcohol and air plus alcohol) in a randomised order over four consecutive days. Each subject was studied under all four conditions. The CO exposure was designed to replicate that expected of a heavy smoker, giving rise to a COHb level of about 7%; alcohol consumption was not above the legal limit for the USA. Blood COHb levels were measured by CO-oximeter and blood alcohol levels were 71 µg/dl at the end of the exposure sessions. Odour sensitivity was assessed on 200 trials over a 50-minute period using an odour described as ‘smoky’ or ‘burnt’. While none of the experimental conditions influenced the hit and false alarm rates, there was an effect on $d'$, which is derived from the number of hits and false alarms and provides a bias-free measure of sensitivity. Measures of response bias were not analysed. Statistical analysis showed that, compared with the air only condition, sensitivity tended to be higher in the alcohol only and the CO only treatment conditions; the combination of alcohol and CO produced lower sensitivities. The authors suggested that there may be a synergistic relationship between CO and alcohol.

Table 4.6 presents the key findings of studies assessing the sensory effects of CO exposure.

SYNOPSIS

The effect of CO exposure on human sensory and psychological functions is perhaps the least well resolved area of CO toxicity. In general, many of the earlier studies are of questionable value because of the low numbers of subjects studied, poor details concerning the nature of the tasks used and the statistical analysis conducted, the use of non-standard experimental designs, and the nature of the sample populations. There are also considerable variations in the methods used to assess COHb levels. Perhaps more importantly, from a psychological viewpoint, the tasks administered bear little relation to current cognitive models of performance. The recent review by Benignus et al. (1990a) covers much of the research conducted on dose-effect functions on human performance; the authors conclude, based mainly on compensatory tracking task studies, that COHb below 20% should have little or no behavioural effect on healthy young males. They go on to say that the state of knowledge is poor, particularly in the field of mechanism(s) by which CO affects the nervous system, and that the diversity among research results makes conclusions difficult to reach. Some of the data from dual-task studies suggest that impairments may be seen below 20% COHb.
### Table 4.6 Summary of sensory effects of carbon monoxide exposure

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<th>Reference</th>
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<th>Subjectsb</th>
<th>COHb level (%)c</th>
<th>Observed effects and comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>O'Donnell et al. (1971a)</td>
<td>85.9, 171.8 mg/m³ (70, 150 ppm) for 540 min</td>
<td>4 airforce pilots</td>
<td>5.9 and 12.7</td>
<td>Critical flicker fusion, mental arithmetic ability, compensatory tracking, and time discriminations — no statistically significant differences between control and CO exposure periods</td>
</tr>
<tr>
<td>O'Donnell et al. (1971b)</td>
<td>57.3, 143.1 mg/m³ (50, 125 ppm) for 3 hours</td>
<td>9 males, 9-20 years</td>
<td>1.0-6.6</td>
<td>Time discrimination, object tracking, balance — no significant effects</td>
</tr>
<tr>
<td>Benignus et al. (1990b)</td>
<td>Bolus of 2977–10 992 mg/m³ (2600–9600 ppm) followed by maintenance dose of 37–171 mg/m³ (32–149 ppm) for 240 min</td>
<td>74 males, 18.16–35.66 years</td>
<td>5.6–16.6</td>
<td>Compensatory tracking — no significant effect</td>
</tr>
<tr>
<td>Putz (1979)</td>
<td>40.1 and 80.2 mg/m³ (35 and 70 ppm) for 4 hours</td>
<td>30 males, 18–26 years</td>
<td>3.0–5.1</td>
<td>Dual task under two workloads (low or high frequency): compensatory tracking and peripheral light stimuli — 30% performance impairment in high frequency tracking at 5% COHb; no effect at low frequency or 3% COHb; increased response time to peripheral light stimuli at 5% COHb between 2nd and 4th hours of exposure</td>
</tr>
<tr>
<td>McFarland et al. (1944)</td>
<td>No levels reported</td>
<td>4 males</td>
<td>~4–19</td>
<td>Absolute visual threshold — COHb-ordinal decreased visual sensitivity; conclusion based on typical data from 1 subject only</td>
</tr>
</tbody>
</table>
### Table 4.6 (continued)

<table>
<thead>
<tr>
<th>Reference</th>
<th>Exposurea</th>
<th>Subjectsb</th>
<th>COHb level (%)c</th>
<th>Observed effects and comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hudnell &amp; Benignus (1989)</td>
<td>Bolus of 13 246.3 mg/m³ (11 568.8 ppm) for 4–5 min then 162.1 mg/m³ (141.6 ppm) for 2 hours approx.</td>
<td>21 healthy males, 23.25 ± 3.7 years (18.5–33.8 years)</td>
<td>17</td>
<td>Various visual tests—no effect noted on scotopic or photopic vision, pattern or motion detection</td>
</tr>
<tr>
<td>Bunnell &amp; Horvath (1988)</td>
<td>Bolus then 51.5, 74.4 mg/m³ (45, 65 ppm) for 50 min</td>
<td>11 males, 7 females, 20.3 years (18–29 years)</td>
<td>7 and 10</td>
<td>Various cognitive tasks performed under three physical workloads—no significant effects of either 7 or 10% COHb</td>
</tr>
</tbody>
</table>

Adapted from EPA (1991)

--: not measured, COHb, carboxyhaemoglobin

* Exposure duration, concentration

b Number, and mean age (age range) of subjects

c Measured COHb range
4.6 EVALUATION OF THE LITERATURE ON HEALTH EFFECTS OF CARBON MONOXIDE

The primary toxic action of CO is hypoxia. By combining with haemoglobin to form COHb, CO reduces the oxygen carrying capacity of the blood. It also inhibits the dissociation of oxygen from haemoglobin, thereby reducing the amount of oxygen reaching the tissues. An additional toxic mechanism postulated involves binding of CO to other haem proteins and cytochromes, interfering with cellular function.

There is some debate as to the role of CO in atherogenesis. Some experimental studies have shown an enhancing effect of CO exposure on atherogenesis in animals fed high cholesterol diets and the study of Stern et al. (1988) appears to show an increased risk of atherosclerotic disease mortality in tunnel workers occupationally exposed to CO.

Some groups are more sensitive to hypoxic stress and hence exposure to CO; the pregnant mother and fetus are two of the most important. The fetus is inherently close to an anoxic state, as its oxygen partial pressure is between a fifth and a third that of the mother. Studies have shown anatomical malformation of the fetus following acute intoxication of the mother, although not all intoxications lead to such effects. The mother is also somewhat compromised during CO exposure because of lower haemoglobin levels, an increased ventilation rate and an inherently higher endogenous COHb level.
Other sensitive groups are the elderly and people suffering coronary, pulmonary, haematological or other diseases that in some way affect either oxygen uptake or transport in the body.

In assessing the health effects of indoor exposure to CO the greatest reliance has been placed on reports of CO poisonings and other studies where clinical investigations have been made. There is a strong consistency in both the type and reported frequency of symptoms. Headache is among the most frequently reported symptoms; dizziness, vomiting, and diarrhoea are also often reported.

However, a problem exists because the reported symptoms may be associated with a number of different causes, possibly leading to a misdiagnosis of CO poisoning. If CO poisoning is the cause and is not diagnosed, the patient may return to the exposure source and thus be returned to a hazardous situation. Frequently, it is found that the cause of the CO exposure is a combustion-type heating system of some kind. This includes water heaters as well as space heaters. Other exposures are reported in which unflued fuel-burning appliances such as barbecues and kerosene heaters are identified as the CO source.

The severity of the reported symptoms has generally been shown to correlate with the duration of exposure (Burney et al., 1982). However, the level of COHb in the patient’s blood does not correlate well with symptom severity (Kirkpatrick, 1987; Dahmash et al., 1993). While COHb level is a meaningful and useful physiological marker of the internal CO dose at a given time, the lack of correlation between COHb and symptom severity may indicate that a toxic effect other than hypoxia is involved in some at least of the reported health effects of CO. It is also important that the level of COHb is related to the last known time of exposure. Between feeling ill and reaching medical attention the individual will have either removed themselves or been removed from the exposure situation. Also, oxygen therapy may have been administered so that, when the patient receives medical attention, the COHb level measured in a hospital may not reflect the peak level of CO exposure.

Epidemiological studies on ambient outdoor levels of CO and heart-disease morbidity, such as those by Schwartz and Morris (1995), Touloumi et al. (1996) and Burnett et al. (1997), and earlier studies by Cohen et al. (1969) and Hexter and Goldsmith (1971), indicate that CO may play a role. However, confounding factors in these studies makes application of their findings to indoor exposures difficult.
Studies on cardiovascular and neuropsychological effects have produced sometimes contradictory results. Samet et al. (1987) concluded that whilst evidence was once considered to indicate that adverse health effects result from low levels of CO exposure, some controversy exists over the effect of levels of CO generally encountered in indoor environments. This is especially true in the area of neuropsychological effects. However, the multi-centre controlled exposure study of Allred et al. (1989, 1991) has provided strong indications of an effect on myocardial ischaemia from COHb levels as low as 2%.

In chamber studies of both cardiovascular and neuropsychological effects, comparison between studies is difficult for a number of reasons. Across both study areas, the methods used for measurement of COHb differ between researchers, some using spectrophotometers or CO-oximetry, others using gas chromatography analysis, and others, perhaps correctly, using a combination of the two methods. The point in time at which the COHb level is measured is also important but it is not performed at a consistent point across studies. Furthermore, if, as described above, COHb levels do not necessarily correlate with severity of symptoms, the use of bolus-type exposures in controlled exposure studies could be brought into question. If exposure duration is a more important indicator of symptom severity, then in studies using boluses of CO at very high concentrations there may not be a steady state reached in the exposed subject.

In controlled exposure studies on cardiovascular effects the exercise protocols employed differ from group to group. In many studies the subjects are removed from the exposure situation and perform exercise in room air; their COHb levels can thereby be significantly reduced through natural ventilatory processes. Even between the end of the exposure period and the beginning of exercise a reduction in the COHb level would be expected. Figure 4.2 gives a graphical comparison of COHb level and health effects found in the controlled exposure studies on cardiovascular effects presented in this review.

A further lack of consistency, only of significance in cardiovascular studies, is whether the study subjects continue to receive medication throughout the study period. For example, Anderson et al. (1973) excluded from the study those subjects on medication. This presents a problem in comparing their results with those from other groups such as Allred et al. (1989; 1991) because the patients using no medication may have suffered a less severe form of cardiovascular disease. Testing subjects who are on medication may be justified on medical and ethical grounds but does reduce the likelihood of finding adverse health effects (Chaitman et al., 1992).
There are a limited number of studies assessing the effect of CO on cardiac arrhythmia (Hinderliter et al., 1989; Sheps et al., 1990; Chaitman et al., 1992) and a number of considerations make their relevance difficult to assess, including the inter-individual variation in arrhythmia, the number of ECG measurements and period over which measurements are made, intra-population differences, and whether subjects receive medication.

The study of neuropsychological effects is complex and some of the techniques used may be questioned. Beard and Wertheim (1967) found that decrements in time discrimination were related to COHb at levels estimated to be as low as 2.5%. However, later work (O’Donnell et al., 1971b; Otto et al., 1979) failed to replicate these findings. Hudnell and Benignus (1989) tested visual performance at COHb levels up to 17% and found no significant effect of COHb on task performance.
However, Bunnell and Horvath (1988) found mild decrements in cognitive task performance at around 10% COHb.

Based on the available evidence it is unlikely that, for most individuals, normal levels of CO in the home will have any adverse effect on health. In the case of sensitive groups it is possible that, under certain circumstances, the level of CO in the home may rise sufficiently to cause some health effects, such as those reported by Allred et al. (1991). Whether these individuals actually notice an adverse effect will depend on the degree of limitation their sensitivity imparts. For example, a decrease in time to angina may manifest itself as a decreased ability to perform normal activities in the home such as walking upstairs. In the case of neuropsychological effects, it is unlikely that effects would become apparent unless CO levels were sufficiently high to cause COHb levels greater than 20%. Such levels are very unlikely unless some sort of malfunction occurs in a heating appliance or unflued appliances are used indoors without adequate ventilation. In these instances, it is likely that other health effects (headache, nausea etc.) would become manifest before neuropsychological defects were noted.
5 Exposure risk situations in UK homes and possible health implications
In this section, data are presented about possible CO exposure risk situations in UK homes and resulting health implications. The overall aim is to give an indication of the extent of exposure to CO in the domestic environment at levels which may pose a risk to the health and well-being of the occupants. Important influences on indoor CO levels are combustion appliances for heating and cooking (particularly unflued appliances), environmental tobacco smoke, and the presence of an attached garage or proximity to a heavily trafficked road (see Section 2). As described in Section 4, the presence of malfunctioning or unflued appliances has been shown to be associated with acute health effects in exposed individuals. Data on the number of dwellings and individuals living in domestic environments with different CO sources are, therefore, important for assessing the potential numbers of people at risk and the possibility for risk management strategies in UK homes.

Data presented here are largely drawn from the 1991 English House Condition Survey undertaken by the Department of the Environment (1993, 1996).

Results of the survey were derived from a sample of 25,000 dwellings in England and have been extrapolated to represent national figures. The data are based on two ‘populations’ — dwellings and households. Differences between figures drawn from these two populations are due either to the presence of vacant dwellings or in some cases dwellings occupied by multiple households. It is important to note that the use of a sample survey to draw conclusions about the national stock introduces some uncertainty as each figure is subject to sampling error.

At the end of 1991 there were 19.725 million dwellings, of which 639,000 were unoccupied. A further 224,000 were not available for permanent occupation because they were not used as a main residence. At the time of the survey the population of England stood at 48.1 million, giving an average dwelling occupancy rate of 2.44. The total number of households calculated from the survey results was 19.11 million, giving an average occupancy rate of 2.52 individuals per household.
5.2 EXPOSURE RISK SITUATIONS

HEATING PROVISION IN ENGLISH HOMES

Summary information about heating provision in English homes is presented in Table 5.1. About 31.0 million individuals reside in dwellings with mains gas central heating systems; solid fuel central heating accounts for 2.1 million individuals and oil or tanked gas systems also account for 2.15 million individuals. Thus a total of 35.23 million people live in dwellings with mains gas, solid fuel or oil powered central heating provision. Just under 2% of all households owning a central heating system do not use it. Instead of their central heating, over 43% of these households use a gas fire in their living room and over 36% use a portable heater or no heating source. Important reasons for non-use of a central heating system are ‘running costs’ and that the system needs repair or is too old. For other fixed heating systems, 5.37 million people live in dwellings with mains gas powered systems and 1.1 million with solid fuel systems (of these, 0.88 million individuals reside in dwellings with solid fuel open fires as their main form of space heating). Approximately 0.56 million individuals live in dwellings where portable appliances are the principal source of heating.

WATER HEATING PROVISION IN ENGLISH HOMES

Table 5.2 summarises information on the provision of water heating in English homes, which is chiefly by mains gas central heating (12.67 million dwellings and 30.91 million individuals). Approximately 1.95 million people reside in dwellings where the main form of water heating is by individual gas-fired heaters.
The primary types of cooking appliances used in English homes are shown in Table 5.3. The majority of households in England make use of cooking appliances consisting of a mains gas hob and oven (8.92 million households: 22.48 million individuals). Approximately 1.0 million people reside in dwellings where bottled gas, solid fuel or oil fired hobs and ovens are the main types of cooking appliance.

**OTHER EXPOSURE RISK SITUATIONS**

Approximately 5.69 million people live in dwellings with an integral or attached garage and 7.32 million live in homes which are located near a major road (Figure 2.5 presents a graphical representation of typical CO levels with distance from a road). Both of these considerations may play a role in elevated indoor CO levels as a result of the exchange of indoor and outdoor air. The relationship between indoor and outdoor CO levels is discussed in Section 2.3.4.
Another important consideration is ventilation, as poor ventilation can result in elevated levels of indoor air pollutants, including CO. In the 1991 English House Condition Survey, data were collected on dwellings considered to be ‘unfit’. According to the criteria for the ‘fitness’ standard of the 1989 Local Government and Housing Act, 1.49 million dwellings were classified as unfit. Of these, 0.27 million dwellings (0.66 million individuals) were considered to be unfit for human habitation because of inadequate ventilation [details on the provision of ventilation and specific forms of combustion appliances are not given].

### Table 5.2 Main type of water heating provision in English homes

<table>
<thead>
<tr>
<th>Water heating system</th>
<th>No. of dwellings (millions)</th>
<th>No. of individuals (millions)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Non-electric heating systems</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gas central heating</td>
<td>12.67</td>
<td>30.91</td>
</tr>
<tr>
<td>Solid fuel central heating</td>
<td>0.98</td>
<td>2.39</td>
</tr>
<tr>
<td>Oil central heating</td>
<td>0.61</td>
<td>1.49</td>
</tr>
<tr>
<td>Liquid petroleum gas central heating</td>
<td>0.11</td>
<td>0.27</td>
</tr>
<tr>
<td>Individual gas heater</td>
<td>0.80</td>
<td>1.95</td>
</tr>
<tr>
<td>Total</td>
<td>15.2</td>
<td>37.0</td>
</tr>
<tr>
<td><strong>Electric heating systems</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>On peak electric immersion</td>
<td>2.46</td>
<td>6.00</td>
</tr>
<tr>
<td>Off peak electric immersion</td>
<td>1.10</td>
<td>2.68</td>
</tr>
<tr>
<td>Individual electric heater</td>
<td>0.11</td>
<td>0.27</td>
</tr>
<tr>
<td><strong>Others</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No provision</td>
<td>0.08</td>
<td>0.19</td>
</tr>
<tr>
<td>No information</td>
<td>0.02</td>
<td>0.05</td>
</tr>
</tbody>
</table>

Adapted from Department of the Environment (1993, 1996)
Table 5.3 Main types of cooking appliances in English homes

<table>
<thead>
<tr>
<th>Appliance</th>
<th>No. of households (millions)</th>
<th>No. of individuals (millions)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cooking fuel for hob and oven</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mains gas hob and oven</td>
<td>8.92</td>
<td>22.48</td>
</tr>
<tr>
<td>Bottled gas hob and oven</td>
<td>0.29</td>
<td>0.73</td>
</tr>
<tr>
<td>Solid fuel hob and oven</td>
<td>0.08</td>
<td>0.20</td>
</tr>
<tr>
<td>Oil-fired hob and oven</td>
<td>0.06</td>
<td>0.15</td>
</tr>
<tr>
<td>Mains gas hob and electric oven</td>
<td>2.20</td>
<td>5.54</td>
</tr>
<tr>
<td>Bottled gas hob and electric oven</td>
<td>0.10</td>
<td>0.25</td>
</tr>
<tr>
<td>Electric hob and other oven</td>
<td>0.06</td>
<td>0.15</td>
</tr>
<tr>
<td>Electric hob and electric oven</td>
<td>7.33</td>
<td>18.47</td>
</tr>
<tr>
<td>Other combinations</td>
<td>0.02</td>
<td>0.05</td>
</tr>
<tr>
<td><strong>Cooking fuel for hob</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mains gas</td>
<td>11.12</td>
<td>28.02</td>
</tr>
<tr>
<td>Bottled gas</td>
<td>0.39</td>
<td>0.98</td>
</tr>
<tr>
<td>Solid fuel</td>
<td>0.08</td>
<td>0.20</td>
</tr>
<tr>
<td>Oil-fired</td>
<td>0.06</td>
<td>0.15</td>
</tr>
<tr>
<td>Electric hob</td>
<td>7.39</td>
<td>18.62</td>
</tr>
<tr>
<td>Other</td>
<td>0.02</td>
<td>0.05</td>
</tr>
<tr>
<td><strong>Cooking fuel for oven</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mains gas</td>
<td>8.92</td>
<td>22.48</td>
</tr>
<tr>
<td>Bottled gas</td>
<td>0.29</td>
<td>0.73</td>
</tr>
<tr>
<td>Solid fuel</td>
<td>0.08</td>
<td>0.20</td>
</tr>
<tr>
<td>Oil-fired</td>
<td>0.06</td>
<td>0.15</td>
</tr>
<tr>
<td>Electric</td>
<td>9.63</td>
<td>24.27</td>
</tr>
<tr>
<td>Other</td>
<td>0.08</td>
<td>0.20</td>
</tr>
</tbody>
</table>

Adapted from Department of the Environment (1993, 1996)
5.3 GAS SAFETY STATISTICS

There is a requirement for suppliers of flammable gas to notify the Health and Safety Executive (HSE) of any death or injury which has arisen from the supply and use of flammable gas. Figures produced by the HSE (Health and Safety Commission, 1996) cover incidents in both the workplace and home, and are therefore limited in terms of indicating the likely size of the risk of CO exposure in the domestic environment. Also, the figures are based on reported incidents only and are likely to be under-representative.

In 1994/1995 the total number of reported incidents relating to the supply and use of flammable gas was 146. While this represented an 18% decrease on the previous year, it was slightly higher than the annual average of 139 over the previous eight years. It is important to note that one reported incident may involve a number of individuals.

There were 111 reported incidents involving CO poisoning in 1994/1995. This represented the first fall since 1989/1990 when the number of reported incidents was just under 80. As a result of these incidents there were 30 fatalities (annual average for previous eight years = 36) and 198 non-lethal injuries due to CO poisoning.

Notifications relating to dangerous gas fittings themselves may help to give a clearer insight into the extent of risks associated with CO exposure, with potential implications for health effects. In 1994/1995, 1643 notifications of dangerous gas fittings were recorded. The appliances most commonly involved were boilers and gas fires. The most frequently occurring type of hazard as a proportion of all notifications was the inadequate removal of combustion products, accounting for 32% of all dangerous gas fittings notifications. This is likely to be due to the lack of adequate fixed ventilation for open flued appliances, or the lack of adequate flueing, which accounted for 36% and 25%, respectively, of reported defects for all dangerous gas fitting notifications.
5.4 DETERMINING THE EXTENT OF THE PROBLEM

The data presented above give an indication of the number of individuals living in English homes containing one or more CO sources. However, it is difficult to determine and compare detailed risk situations using these data (e.g. the number of individuals in low risk situations, such as those living in homes with no CO sources, through to high risk situations with individuals in homes with many indoor CO sources, the presence of environmental tobacco smoke and ingress of polluted air from outdoors). It is thus difficult to draw firm conclusions about the extent of any health problems arising from exposure to CO in the UK domestic environment. Nevertheless, this information does provide a useful indication of the potential number of individuals at risk of exposure to CO in a crude sense.

Information relating to the likely numbers of poorly installed or maintained combustion appliances in UK homes along with published failure rates may provide a useful indication of the extent of health risks associated with very high levels of exposure to CO. Notifications of dangerous gas fittings may be of value in determining the potential number of individuals likely to experience acute health effects, but reported incidents cover both the workplace and domestic environment, so the information is of limited value with respect to the scope of this review. The data are also likely to represent an underestimate of the true extent of any problem as they only reflect incidents which actually come to be reported.

Nevertheless, the information presented above clearly indicates that a large proportion of the population lives in dwellings that are likely to have higher background CO levels than people living in homes with no CO source. This may have important health implications as some outdoor studies have demonstrated a possible relationship between increased mortality and morbidity from heart disease and low-level CO exposure among susceptible individuals. Prolonged exposure to slightly elevated levels of CO may also have implications in terms of
subclinical health effects. However, a clear link between health related effects and low CO levels still remains a matter of debate and the level of risk to UK occupants is uncertain.

The presence in the home of certain CO sources (usually unflued appliances), such as gas cookers, has also been clearly linked with the occurrence of elevated peak CO levels during periods of activity such as cooking. Therefore, the data presented above demonstrate the very large numbers of individuals who may potentially be exposed to high short-term levels of CO in the home. Studies have demonstrated directly related health effects among sensitive individuals at CO levels similar to the peak concentrations recorded in UK homes.

Exposure to CO at levels typically found in UK homes is likely to be of most significance to susceptible individuals. Susceptible groups may be characterised as those with an existing physiological sensitivity to hypoxic stress (e.g. coronary artery disease sufferers) and those who are vulnerable because of their exposure patterns (e.g. individuals who spend large amounts of time in the home). Important susceptible groups are the pregnant mother, fetus and child. Their susceptibility to CO is both a result of physiological sensitivity and length of time spent in the home where CO sources are present. Other susceptible groups include the elderly who generally experience a reduction in oxygen carrying capacity, largely as result of the ageing process, and those individuals with coronary, pulmonary and vascular diseases. These groups show a limited ability to compensate for reduced oxygen carrying capacities. Their sensitivities may also be exacerbated as a result of spending large amounts of time in environments where there is a risk of exposure to elevated CO levels.

Finally, from the existing data on CO levels in UK homes it is apparent that CO concentrations in excess of 120 mg/m³ (105 ppm) may be produced where certain CO sources or malfunctioning appliances are present. Even in a small study of 14 homes, one home was affected by an appliance producing CO exposure levels of significance to health. While it is not possible to extrapolate this to the overall dwelling situation in the UK, these data represent an obvious cause for concern and warrant further investigation.
6 Conclusions and recommendations
CONCLUSIONS AND RECOMMENDATIONS

6.1 CONCLUSIONS

There is a large body of literature addressing indoor concentrations and the health effects of CO. However, very few studies have been conducted in the UK to date, and, unfortunately, there is limited information from epidemiological studies on the health effects of CO at the low levels typically found in homes.

Outdoor levels are known to influence indoor levels in areas where outdoor air is polluted, for instance by motor vehicle fumes. However, indoor CO levels are frequently higher than those outside because of the presence of significant sources such as gas cookers, various fuel-burning heating systems and, to a lesser extent, tobacco smoke. The presence of a malfunctioning or poorly installed or ventilated combustion appliance is a significant source and often accounts for very high levels of CO in the home, which may in turn cause fatalities. Risks are greatest in severe winter weather.

Recent UK studies have shown typical 1-week averages to range from 0.3 to 2.7 mg/m³ (0.3–2.4 ppm) in kitchens where there was gas cooking and 0.8 to 0.9 mg/m³ (0.7–0.8 ppm) where there were no fuel-burning appliances. Continuous monitoring has indicated maximum 1-minute averages of up to 49.3 mg/m³ (43.1 ppm) in kitchens with gas cookers and peaks (15-minute average) of around 180 mg/m³ (160 ppm) associated with the use of a gas grill. Maximum 1-hour averages for CO in kitchens with gas cookers typically range from 1.9 to 24.5 mg/m³ (1.7–21.4 ppm). Carbon monoxide levels in the home of up to 121.4 mg/m³ (106 ppm) for a maximum 1-minute average reading, and 57 mg/m³ (49.8 ppm) for a maximum 1-hour average, have been linked to the operation of a malfunctioning boiler.

It is apparent that existing air quality guidelines are likely to be exceeded in a number of UK homes. Even in the small study of 14 homes in the UK, CO levels of relevance to health were recorded. While it is not statistically valid to extrapolate these results to the overall dwelling situation in the UK, these data represent an obvious cause for concern as so many houses have appliances capable of producing elevated indoor CO levels (for example, 58% of English homes use mains gas fuelled hobs for cooking).
Exposure to CO is normally evaluated in terms of percentage of carboxyhaemoglobin (COHb) in the blood, but the validity of using COHb as a biomarker of health effect is open to question. Although hypoxia, arising from preferential binding of CO to haemoglobin, is thought to be the main toxic mechanism by which CO acts, binding of CO to other blood components and enzymes may also play a part in its toxicity. A role in promoting atherosclerosis has been postulated for CO, although conclusive evidence is lacking, and immunological function and neurotransmission have also been investigated as possible targets for CO toxicity.

While many of the published clinical investigations of CO intoxication originate outside the UK, this does not limit their applicability. There may be differences in the types of cooking and heating appliance used but the health effects of CO emitted from them will be broadly the same. Where geographical differences may be important is in the question of confounders.

Numerous and varied observations have been made of the health effects of CO in controlled exposure studies. These indicate that exposure to CO can cause performance decrements in certain neuropsychological tasks and that some people, primarily sufferers of cardiovascular disease, may be more susceptible to low-level exposure to CO producing COHb levels as low as 2%. However, the question of the COHb level at which cardiovascular indices do not differ from the norm has not been satisfactorily answered. Perhaps the most prudent conclusion to draw is that there is no threshold of effect in patients suffering cardiovascular disease. However, these patients will of necessity be more sedentary than normal individuals. Whether their activity levels place them in danger at the CO concentrations found indoors is open to question.

The key considerations relate to individuals with coronary artery disease who may experience a reduced angina threshold at around 2% COHb. More severe symptoms are generally experienced even among normal healthy individuals at about 20% COHb. Between these levels long-term, low-level exposures would be likely to present a health hazard. A great deal of importance would be attached to CO concentrations high enough to produce long- or short-term COHb levels above 10%, especially in sensitive individuals.

Observed reductions in exercise duration in both healthy subjects and sufferers of cardiovascular disease are reversible on removal of the individual from the exposure source. However, few studies measure performance during the recovery period.
Accidental exposures leading to acute health effects are fairly well documented. Overall, the published evidence on health effects of domestic exposure to CO points most to a hazard of acute intoxication from malfunctioning or unflued fuel-burning appliances. However, it is also probable that CO levels may routinely occur and persist in some homes that might possibly give rise to chronic health effects, particularly among sensitive groups. The question must be, therefore, whether for sensitive individuals there is a CO exposure level below which no adverse health effect will be manifest. The problems in answering this are great. It does, however, seem that any risk of adverse health effects from domestic levels of CO currently found in the UK is likely to be low under normal circumstances, particularly for healthy individuals. Air quality guidelines and standards for CO are based on health effects, being set at levels which aim to protect susceptible individuals from experiencing adverse effects. Therefore, even if guideline values are approached, the majority of the population is unlikely to be affected. Nonetheless, it is prudent to continue to encourage measures which minimise CO levels, with particular attention being paid to gas combustion and other fuel-burning, especially unflued, appliances. Sufficient ventilation is necessary for all such appliances. This is especially relevant because of the large number of people potentially exposed, and also because of the uncertainties relating to the extent of health effects caused or exacerbated by long-term, low-level exposures to CO. It may thus be beneficial to encourage appropriate public information campaigns.

The suitability of CO detectors as a means of mitigating chronic or subacute health effects is limited by the relatively high CO levels required to activate them, and the time-dependent manner of activation. In essence this means that CO levels must be high for a long period before the detector will activate. However, to help protect against intoxication, the use of detectors built to British Standards Institute specification would be extremely advisable.

In relation to the medical treatment of CO intoxication, it is essential to increase awareness of the symptomatology of CO intoxication among accident and emergency departments, general practitioners, environmental health departments and other professions to whom the public look for advice and assistance. Leaving a patient in, or returning them to, a situation from which adverse health effects might develop is unacceptable and, with vigilance, need not occur.
6.2 RECOMMENDATIONS FOR FUTURE RESEARCH

6.2.1 INDOOR EXPOSURE TO CARBON MONOXIDE

1. The number of published studies aimed at establishing CO levels in UK homes is small. Frequently the primary purpose of these studies has not been directly related to establishing residential CO levels, and comparability between the studies is limited.

More studies, primarily aimed at evaluating CO levels among representative samples of UK homes, are needed to ascertain the variability of indoor CO levels across the UK and in different types of housing.

2. Existing studies on CO levels in UK homes may not necessarily be representative of the UK dwelling situation as a whole or of particular high risk groups, owing to the small samples of homes studied.

It would be prudent to develop strategies to ensure that representative samples of UK dwellings are included in future indoor air quality research programmes. The development of such strategies would be dependent on the specific objectives of each individual study — for example, whether the research is aimed at determining the distribution of CO levels throughout the UK housing stock or whether it is aimed at targeting groups at high risk because of dwelling type or as a result of particular susceptibilities to CO exposure.
3. The measurement of indoor CO concentrations is not necessarily the same as measuring exposure to the pollutant. For example, during certain activities such as cooking with gas, personal exposure is likely to far exceed ambient concentrations. The evaluation of indoor exposures is, therefore, critical for a realistic assessment of potential health effects. Data on personal exposure to CO are at present derived from very few studies.

*More studies are required to determine the significance of indoor levels to overall personal exposure to CO, and particularly the significance of certain activities which may lead to high exposures. These studies should examine representative samples of the UK population and should employ methods such as relating fixed site monitoring to personal exposure measurements, questionnaire data and activity diaries. It would also be of value to investigate exposure to CO in susceptible populations, such as expectant mothers and those suffering from cardiovascular disease.*

4. The understanding of population exposure distributions to CO in the UK domestic environment is limited.

*Alternative research approaches aimed at utilising new and existing data on CO exposure levels should be encouraged. Monte Carlo simulation modelling may provide a valuable means of improving the understanding of the predicted distribution of CO exposure levels in UK domestic environments.*

5. From the available studies, a number of factors appear to affect indoor levels of CO, especially the presence of combustion appliances, ventilation measures and the physical location of the home. One particularly significant factor related to high CO levels is the presence of a malfunctioning fuel-burning appliance in the home.

*Studies aimed at assessing the relative contributions of various CO sources and confounding factors to indoor CO levels should be encouraged. It would seem appropriate at this stage to attempt a detailed assessment of the prevalence of malfunctioning fuel-burning appliances in relation to high levels of CO in UK homes and to assess the relative costs and benefits of remediating the problem if one is identified.*
6.2.2 THE RELATIONSHIP BETWEEN CARBON MONOXIDE EXPOSURE AND HEALTH EFFECTS

1. Many studies concentrate on either CO exposure or on the health effects of CO exposure. Few investigations have looked in detail at the relationships between the two areas of study.

*Studies are required that combine measurements of indoor CO levels, personal exposure measurements, levels of CO in expired breath samples and related levels of COHb. The use of other, indirect means for determining exposure should also be explored, for example questionnaires, medical histories, biochemical parameters and so on. Comparison of measurement methods (single point CO level versus personal exposure studies versus breath analysis of CO and thereby COHb level) could also be performed.*

2. It is possible, for certain subgroups of the population, that peak levels are more relevant to health than longer-term average levels. However, only limited data are available on peak CO levels in the indoor environment.

*Studies aimed at assessing the extent and level of peak CO concentrations should be encouraged. The development and validation of models relating the magnitude and frequency of peak levels to mean levels and other factors such as CO sources, housing characteristics, ventilation methods and individuals' activity should be undertaken.*

3. For the UK population as a whole, the impact of low-level, long-term exposure to CO may be of greater overall health significance than acute exposure incidents. Owing to the small number of studies, limited data are available on long-term, low levels of CO in the UK domestic environment.

*Further study of long-term, low-level exposure to CO is required. Studies should be encouraged which assess the long-term CO levels typically found in UK homes. It would also be of value if the relative contributions of different CO sources to extended periods of low levels of CO in the home could be evaluated. Data obtained*
CONCLUSIONS AND RECOMMENDATIONS

from such studies could usefully feed into investigations assessing the potential health effects in individuals who spend large amounts of time in the home environment.

4. The normal range of COHb levels in the UK population has not been fully described. Such information would help in defining the background or normal levels of COHb.

Analysis of donors’ blood COHb level, in combination with a simple questionnaire probing smoking history, occupation, basic health status, and seeking limited socioeconomic information, could be performed. This would help define the normal range of COHb levels in the UK population among healthy, adult smokers and non-smokers.

6.2.3 HEALTH EFFECTS

1. The lack of correlation between COHb and severity of symptoms may point to the importance of mechanisms other than hypoxia.

Mechanisms of CO toxicity warrant further study, especially the possible consequences of CO acting as a transmitter substance and its possible involvement in vascular physiology.

2. Exposure duration and the binding of CO to haem proteins other than haemoglobin may play a role in CO toxicity, especially in the effects seen at <5% COHb in sensitive people.

Studies aimed at defining more closely the relationship between COHb, exposure duration and symptom severity are required.

3. The studies assessing effects on the cardiovascular system and neuropsychological effects are difficult to compare because of differences in protocol, COHb measurement methodology, and so on. Also few studies track performance during the recovery phase when COHb levels are returning to normal.
A more structured approach to the controlled chamber assessment of health effects should be adopted in the UK in which variables such as COHb measurement, equipment type, quality assurance procedures, testing procedures and end-points are defined and a set protocol used across study groups. This approach would produce data that could more easily be compared between groups and would help in defining dose–response relationships and thresholds of effect for CO. The recovery period following exposure as COHb levels return to normal also warrants study.

4. Some experimental studies in which animals were fed high cholesterol diets have implicated CO in atherogenesis. Human studies have shown a link between COHb level and atherosclerosis risk, although confounding factors mean conclusive evidence for an atherogenic role for CO in humans is lacking.

*Further studies of the relationship between CO exposure and development of atherosclerosis are required.*

5. The adverse health effects associated with repeated exposures to low levels of CO are poorly understood. Exposures to low levels of CO raise COHb within a range deemed normal in smokers; also, they soon return to their original level when exposure ceases. Certain assumptions have to be made in relating low-level CO exposure and chronic health effects.

*Studies, perhaps involving occupational exposures, which examine repeated exposure to CO at levels similar to those found in UK homes are required. The health effects investigated could be both neuropsychological and cardiovascular in nature.*

6. The neuropsychological effects of CO exposure have been extensively studied although some of the methods employed to assess the effects may be questioned and have lacked focus.

*It is necessary to design neuropsychological studies of CO exposure effects with specific goals in mind. For example, a better understanding is needed of the effect of CO on 1) monitoring and vigilance, 2) divided attention tasks, and 3) more complex information processing tasks. It may be useful to review the neuropsychological effects encountered in acute poisonings and determine from these the types of effects that can arise in CO intoxication.*
6.2.4 GUIDANCE, CONTROL AND MITIGATION OF CARBON MONOXIDE EXPOSURES AND HEALTH EFFECTS

1. Misdiagnosis of CO poisoning is frequent due to the similarity of its symptoms to those of many other ailments.

In order to assess whether CO poisoning is missed or misdiagnosed, a study of patients presenting to general practitioners and accident and emergency departments with non-specific but potentially CO related symptoms is recommended. Samples of breath could serve as a clinical diagnostic tool. (A limitation in such a study is that COHb levels may have fallen between exposure and presenting to a medical practitioner). A relative-risk scoring system could be developed to aid in determining which individuals’ symptoms are more likely to be related to CO exposure.

2. While some recent studies have investigated the use of potential CO reduction strategies such as mechanical ventilation systems, the data available are limited. Currently therefore, it is difficult to draw any firm conclusions about the efficacy of such mitigation measures in reducing exposure to CO in the home.

More systematic studies aimed at investigating CO reducing factors should be undertaken. Examination of the potentially beneficial effects of the use of extractor hoods or fans in the kitchen would be of particular value owing to the link between high CO levels in the kitchen and gas cooking activity.
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Concentrations of carbon monoxide in UK homes with well maintained and properly functioning heating and cooking equipment and adequate ventilation are not likely to present a risk to health. In homes where equipment malfunctions, high levels may be produced and a serious risk of severe illness and death may then occur. In some homes concentrations of carbon monoxide may be such that, even in the absence of levels leading to obvious poisoning, the health of some groups is placed at risk. People falling into these groups include those with coronary artery disease, the elderly, the pregnant woman and the unborn child and some individuals suffering from anaemia. The need for further research into the mechanisms and effects of exposure to low levels of carbon monoxide is clear and this report makes a number of recommendations which we endorse. The case for providing information on possible sources of carbon monoxide in the home, ways of avoiding exposure to undesirable concentrations and on how to recognise the effects of such exposure is clear.

Statement of advice

Carbon monoxide is an invisible and odourless gas produced when a wide range of fuels are burnt. The capacity of even low concentrations of carbon monoxide to damage health, sometimes permanently, means that all appliances capable of producing carbon monoxide must be properly installed and maintained. The early symptoms of exposure include tiredness, drowsiness, headache, pains in the chest and sometimes stomach upsets. Some people, for example those with heart disease, are at increased risk of effects and should take particular care that they are not exposed. Carbon monoxide monitors can play a useful part in ensuring that any excess production of carbon monoxide indoors is recognised, allowing the fault to be rectified. However their value is limited to detecting high concentrations of CO and they may not alert at concentration levels which may produce some chronic or subacute effects, due to their manner of activation.
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LEICESTER, UK, ON 23-24 JUNE 1997

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