

General description

Carbon monoxide (CO) is one of the most common and widely distributed air pollutants. It is a colourless, odourless and tasteless gas that is poorly soluble in water. Carbon monoxide has a slightly lower density than air. In the human body, it reacts readily with haemoglobin to form carboxyhaemoglobin. Small amounts of carbon monoxide are also produced endogenously. Carbon monoxide exposure is still one of the leading causes of unintentional and suicidal poisonings, and it causes a large number of deaths annually both in Europe and in the United States. The scientific literature on carbon monoxide sources, concentrations, and human exposures and health effects in outdoor and indoor environments has been reviewed extensively by the US Environmental Protection Agency (1). Some useful reviews in short form have also been published recently (2–4).

Sources

The annual global emissions of carbon monoxide into the atmosphere have been estimated to be as high as 2600 million tonnes, of which about 60% are from human activities and about 40% from natural processes (1). Anthropogenic emissions of carbon monoxide originate mainly from incomplete combustion of carbonaceous materials. The largest proportion of these emissions are produced as exhausts of internal combustion engines, especially by motor vehicles with petrol engines. Other common sources include various industrial processes, power plants using coal, and waste incinerators. Petroleum-derived emissions have greatly increased during the past few decades (5). Some widespread natural nonbiological and biological sources, such as plants, oceans and oxidation of hydrocarbons, give rise to the background concentrations outside urban areas.

In various indoor environments, space heaters fuelled with oil, gas or kerosene, gas stoves and some other combustion appliances, and tobacco smoking cause significant emissions of carbon monoxide.

Occurrence in air

Global background concentrations of carbon monoxide range between 0.06 and 0.14 mg/m³ (0.05–0.12 ppm). During the early 1980s, there was an annual 1–2% increase in nonurban tropospheric concentrations of carbon monoxide, whereas between 1989 and 1992 concentrations began declining rapidly.

The ambient concentrations measured in urban areas depend greatly on the density of combustion-powered vehicles, and are influenced by topography and weather conditions. In the streets, the carbon monoxide concentration varies greatly according to the distance from the traffic; it is also influenced by topography and weather conditions. In general, the concentration is highest at the leeward side of the “street canyon”, and there is a sharp decline in the concentration from pavement to rooftop level (6).

In the streets of large European cities, 8-hour average carbon monoxide concentrations are generally lower than 20 mg/m³ (17 ppm) with short peaks below 60 mg/m³ (53 ppm). Carbon monoxide levels have a close quantitative and temporal association with the levels of other primary exhaust

pollutants such as nitrogen monoxide and volatile organic compounds (7, 8). In urban traffic environments, the concentrations measured inside motor vehicles are generally higher than those measured in ambient air. The carbon monoxide levels are highest in personal cars, the mean concentrations being 2–5 times the levels measured in streets or inside subway trains (6, 8, 9). Traffic patterns, car model and maintenance, vehicle ventilation conditions and season are factors that affect the carbon monoxide levels inside the cars (10–12). In Southampton in the United Kingdom, commuters using bicycles have been shown to be exposed to mean concentrations of 6.1–20.5 mg/m³ (5.3–17.9 ppm) with short peak values as high as 71 mg/m³ (62 ppm) (13). In the inner city of Amsterdam in the Netherlands, the corresponding mean concentrations in bicycle trips have been much lower: 0.6–4.1 mg/m³ (0.5–3.6 ppm) (14).

Carbon monoxide concentrations measured at fixed-site monitoring stations seem to reflect rather poorly short-term personal exposures of various urban population groups. Cortese & Spengler (15) reported that in a group of commuters living in the Boston metropolitan area in the United States, the 1-hour average personal concentrations measured by portable analysers were 1.3–2.1 times the concentrations measured by fixed-site analysers. Also, in Washington DC and Denver in the United States (16) and in Helsinki in Finland (17) there was no significant association between personal 1-hour exposure levels and the corresponding carbon monoxide concentrations measured at fixed-site monitoring stations. However, the fixed-site monitoring data may reflect population exposures somewhat better at longer averaging times such as 8 hours (15, 16, 18).

In underground and multistorey car parks, road tunnels and various other partially or completely enclosed microenvironments with insufficient ventilation, the levels of exhaust pollutants from combustion engines may be much higher than the common ambient levels in street canyons. Indoor ice arenas and indoor motor shows seem to be public places where very high carbon monoxide concentrations occur rather frequently. Intermittent ice resurfacing with a petrol-fuelled or malfunctioning propane-fuelled resurfacer has produced average values for ice-hockey games (averaging time 1.5–2 hours) of between 2 and 152 mg/m³ (2–132 ppm), the mean values of several arenas being 40–46 mg/m³ (35–40 ppm) in each study (19–21). In association with acute epidemic poisonings in ice arenas, the carbon monoxide concentrations have been as high as 170 and 405 mg/m³ (148–354 ppm) (22, 23).

Relatively high carbon monoxide levels have been measured inside homes with faulty or unvented combustion appliances, particularly if the appliances have been used in poorly ventilated rooms. In the kitchen, short peak concentrations have sometimes exceeded 115 mg/m³ (100 ppm), whereas in other rooms concentrations have usually been much lower (1). In Finland, Alm et al. (17) recently reported carbon monoxide peak concentrations of up to 60 mg/m³ (53 ppm) in homes with stoves operating on town gas.

Environmental tobacco smoke in dwellings, offices, vehicles and restaurants can raise the 8-hour average carbon monoxide concentration by up to 23–46 mg/m³ (20–40 ppm) (1).

Conversion factors

1 ppm	= 1.145 mg/m ³
1 mg/m ³	= 0.873 ppm

Analytical methods

The usual reference method for the measurement of carbon monoxide concentration in air is based on the absorption of infrared radiation by the gas in a non-dispersive photometer. This method is suitable for stable installations at fixed-site monitoring stations. More recently, portable carbon monoxide analysers with automated data-logging have become available for personal exposure monitoring. These measurements are based on the electrochemical reactions between carbon monoxide and deionized water, which are detected by specially designed sensors. Nowadays the resolution, stability and sensitivity of the electrochemical analysers are within the specifications of the reference method and, together with the data-logging systems, they fit into a small rucksack or even a pocket (24, 25). A sensitive passive sampler with a solid adsorbent for microenvironmental and personal monitoring of carbon monoxide concentrations has recently been developed (26). Breath analysis of carbon monoxide by specially designed electrochemical analysers is also possible in various occupational and emergency settings (27).

Routes of exposure

Because carbon monoxide is a rather stable gas in the atmosphere, the lungs are practically the only significant route for environmental exposures. Dermal and gastrointestinal absorptions are expected to be negligible. Carbon monoxide binds readily with haemoglobin to form carboxyhaemoglobin (COHb) which can be measured in a blood sample by specific spectrophotometric or gas chromatographic methods. As a biomarker of carbon monoxide exposure, COHb is specific and closely related to the mechanisms of toxicity.

In population groups with relatively high exposures, there are people who are continuously exposed to exhaust from combustion engines at their work. Among these people are car, bus and taxi drivers, policemen, traffic wardens, and garage and tunnel workers. In addition, workers in metal industries and in petroleum, gas and chemical plants as well as firemen may have high exposures. Current smokers clearly have higher exposures than non-smokers, and high levels of environmental tobacco smoke in dwellings, offices, vehicles and restaurants can also increase personal exposures significantly (1). Ice-hockey players and skaters, and others who train in polluted indoor environments have relatively high exposures because of high personal minute ventilations associated with exercise levels during the sports activity (19, 21).

In healthy subjects, small amounts of carbon monoxide are formed endogenously from the catabolism of haemoglobin and other haem proteins. At rest and without exogenous exposure, this results in a COHb saturation of 0.4–0.7%. In certain situations, endogenous carbon monoxide production may be abnormally high, which increases the risk of a high total exposure in polluted environments. During pregnancy, increased maternal COHb levels of 0.7–2.5% have been reported, and the fetuses of nonsmoking mothers have also shown elevated levels of 0.4–2.6%. Hypermetabolism, certain drugs and haemolytic anaemia can increase endogenous COHb levels by up to 4–6% (1, 2, 28).

Toxicokinetics

After reaching the lungs, carbon monoxide diffuses rapidly across the alveolar and capillary membranes. It also readily crosses the placental membranes. Carbon monoxide binds reversibly to one of the haem proteins. Approximately 80–90% of the absorbed carbon monoxide binds with

haemoglobin, which causes a reduction in the oxygen-carrying capacity of the blood. The affinity of haemoglobin for carbon monoxide is 200–250 times that for oxygen, while the relative affinities of other haem proteins (e.g. myoglobin), cytochrome oxidase and cytochrome P-450 for carbon monoxide are much lower (1–3).

The absorption and elimination of carbon monoxide have been described in various mathematical models (1, 29). The most important of these models is the Coburn-Foster-Kane exponential equation, which takes into account all known physiological variables affecting carbon monoxide uptake (30). The most important variables determining the COHb level are carbon monoxide concentration in inhaled air, duration of exposure and alveolar ventilation (Fig. 1). During an exposure to a fixed concentration of carbon monoxide, the COHb concentration increases rapidly at the onset of exposure, starts to level off after 3 hours, and reaches a steady state after 6–8 hours. At steady state, the carbon monoxide concentrations in alveolar breath and ambient air become practically equal (31).

Carbon monoxide is eliminated unchanged via the lungs. The decline in COHb concentration depends on the rate of carbon monoxide release from haem proteins, alveolar ventilation, oxygen concentration in inhaled air, duration of carbon monoxide exposure, and the level of COHb saturation. The formation of COHb is a reversible process, but because of the tight binding of carbon monoxide to haemoglobin, the elimination half-life while breathing room air is 2–6.5 hours depending on the initial COHb level. The elimination half-life of COHb is much longer in the fetus than in the pregnant mother (1–3, 28).

Health effects

There is considerable evidence on human environmental and occupational exposures to carbon monoxide, on consequent levels of the specific biomarker COHb in blood, and on dose–effect relationships with regard to the most important health effects. The organs and tissues that are mostly affected include the brain, the cardiovascular system, exercising skeletal muscle and the developing fetus (1–3, 29).

Effects on experimental animals and *in vitro* test systems

Noncarcinogenic toxic effects

Extensive laboratory studies have been conducted in several animal species on the effects of exposure to carbon monoxide. Considerable information has been obtained on its overall toxicity and direct effects on the blood and other tissues, and on the mechanisms of these effects. In many of these studies, however, carbon monoxide exposures have been very high, which may have caused effects that are not relevant to common environmental exposures in humans (1, 29).

Carcinogenic and mutagenic effects

No evidence is available on carcinogenicity or mutagenicity in relation to carbon monoxide exposure (29).

Mechanisms of action

Approximately 80–90% of the absorbed carbon monoxide binds with haemoglobin, which reduces the oxygen-carrying capacity of the blood and impairs the release of oxygen from haemoglobin to

extravascular tissues. These are the main causes of tissue hypoxia produced by exposures to low levels of carbon monoxide. At higher concentrations the rest of the absorbed carbon monoxide binds with other haem proteins such as myoglobin, and with cytochrome oxidase and cytochrome P-450. According to experimental studies, the binding to myoglobin might contribute to the depression of cardiac function and the impairment of skeletal muscle oxygenation, and the binding to cytochrome oxidase might affect the heart and the brain, but it remains uncertain whether these mechanisms are activated in common human exposures (1, 2).

Effects on humans

It is unlikely that carbon monoxide has any direct effects on the lung tissue except at extremely high concentrations. Its toxic effects on humans are due to hypoxia, which becomes evident in organs and tissues with high oxygen consumption such as the brain, the heart, exercising skeletal muscle and the developing fetus.

Neurological and neurobehavioural effects

It is well known that severe hypoxia due to acute carbon monoxide poisoning may cause both reversible, short-lasting neurological deficits and severe, often delayed, neurological damage (2). At a COHb level of about 10%, carbon monoxide is likely to cause headache, and at somewhat higher levels there will be also dizziness, nausea and vomiting. At a COHb level of about 40%, carbon monoxide starts to cause coma and collapse, and at 50–60% the poisonings are often lethal (1).

The dose–effects of low-level carbon monoxide exposures on human behaviour have been critically reviewed by Laties & Merigan (32) and by Benignus (33). There seems to be reasonably good agreement that there is no significant impairment of visual or other behavioural functions in healthy young sedentary subjects at COHb levels below 18%. Early studies suggested, however, that these effects start at the much lower level of 3–5% in some people. One obvious reason for the discrepancy between the different studies is that the early studies showing the highest sensitivity to carbon monoxide were single-blind in design, whereas the more recent studies have been double-blind (34). During exercise there may be errors in behavioural tests at somewhat lower COHb levels than in resting conditions. It is also possible that abnormal cardiovascular function and other disease processes increase the sensitivity of subjects to carbon-monoxide-induced behavioural effects (33).

Psychomotor effects, such as reduced coordination, tracking and driving ability, and impaired vigilance and detection of small environmental changes have been revealed in double-blind studies at COHb levels as low as 5.1–8.2% (3, 35, 36).

The effects of carbon monoxide on cognitive performance have generally been equivocal at COHb levels of 5–20% (32). More recently, Bunnell & Horvath (37) have shown that at COHb levels of 7% and 10% visual tracking performance can be significantly improved in resting conditions, but in contrast it is significantly impaired if the subjects engage in heavy exercise. Moreover, both response patterns seem to be dependent on the COHb concentration in the blood.

Cardiovascular effects

Numerous controlled human studies have been conducted in healthy subjects and in patients with ischaemic heart disease in order to characterize the effects of low-level carbon monoxide exposures on the cardiorespiratory responses to exercise. In these experiments, the subjects have typically been exposed to clean air and carbon monoxide in a chamber or through a face mask. After the exposure,

which has usually been conducted at rest to achieve a predetermined COHb concentration in the blood, the subjects have engaged in an exercise test on a treadmill or cycle ergometer until exhaustion (healthy subjects) or the appearance of angina pectoris or electrocardiographic signs of cardiac ischaemia.

In apparently healthy subjects, the maximal exercise time and the maximal oxygen consumption have decreased at COHb levels as low as 5%. The regression between the percentage decrease in maximal oxygen consumption and the percentage increase in COHb concentration appears to be linear, with approximately a one percentage point fall in oxygen consumption per one percentage point rise in COHb level above 4% (1, 4).

Patients with cardiovascular disease, especially ischaemic heart disease, are expected to be particularly sensitive to carbon monoxide. Atherosclerotic narrowing of the coronary arteries and impaired dilatation mechanisms restrict blood flow to the myocardium and prevent physiological compensation for lowered oxygen delivery caused by elevated levels of COHb. In exercise, these subjects experience myocardial ischaemia, which can impair myocardial contractility, affect cardiac rate and rhythm, and cause angina pectoris (1, 4).

The early studies of Aronow et al. (38), Aronow & Isbell (39) and Anderson et al. (40) have suggested that low-level carbon monoxide exposures resulting in COHb levels of 2.5–3.0% shorten the time to onset of exercise-induced chest pain in patients with angina pectoris. Although the validity of the studies of Aronow and colleagues has been questioned by the US Environmental Protection Agency, subsequent studies by other investigators have actually given similar results (1, 4). The design and results of the five most important clinical studies (40–44) conducted in patients with ischaemic heart disease are summarized in Table 1. Despite the obvious differences between these studies, they all show a significant shortening in the time to onset of angina at mean post-exposure COHb levels of 2.9–5.9% (post-exercise COHb levels in Table 1 are somewhat lower), which represent mean incremental increases of 1.5–4.4% COHb from the pre-exposure baseline levels (1).

The potential arrhythmogenic effects associated with low-level carbon monoxide exposures have not been fully resolved at COHb levels of $\leq 5\%$ (1, 3). Hinderliter et al. (45) reported no effects at 3.5% and 4.9% COHb levels (post-exercise concentrations) on resting and exercise-induced arrhythmias in ten patients with coronary artery disease and no baseline ectopia. In contrast, Sheps et al. (46) showed in 41 nonsmoking patients with documented coronary artery disease and various levels of baseline ectopia that the frequencies of both single and multiple ventricular depolarizations increased significantly at a mean post-exercise COHb level of 5.0% but not at 3.5%. Dahms et al. (47) found no additional effect of either 3% or 5% COHb over the exercise-induced increases in single or multiple ectopic beats experienced by patients with myocardial ischaemia and baseline ectopia.

According to some epidemiological and clinical data, carbon monoxide from recent smoking and environmental or occupational exposures may contribute to cardiovascular mortality and the early course of myocardial infarction (1). It is not known whether this contribution is due to arrhythmogenic effects or to some longer-term effects, as suggested by some authors. In patients with severe ischaemic heart disease, carbon monoxide poisonings have been lethal at COHb levels of 10–30%, while usual COHb levels in lethal poisonings are around 50–60% (1). Stern et al. (48)

Table 1. A summary of results of the five most important double-blind clinical studies on the effects of low-level carbon monoxide exposures on patients with documented ischaemic heart disease and exercise-induced angina

Reference	Exposure		Exposure duration and activity	Subject characteristics	Effects of CO exposure (symptoms, ECG changes, etc.)
	CO (mg/m ³) ^a	COHb (%) ^b			
Anderson et al. (40)	0 57 115	1.3 2.9 4.5	4-hour exposure at rest, post-exposure exercise on a treadmill	10 males, mean age 49.9 years (5 smokers, 5 nonsmokers), reproducible angina	Time to onset of angina shortened at COHb 2.9% and 4.5% ($P < 0.005$) and duration of angina prolonged at COHb 4.5% ($P < 0.01$). Deeper ST-segment depressions with CO in 5 subjects.
Kleinman et al. (41)	0 115	1.4 2.8	1-hour exposure at rest, post-exposure incremental exercise on a cycle ergometer	24 males, mean age 58.8 years (nonsmokers for at least 6 months), reproducible angina	Time to onset of angina shortened by 5.9% ($P = 0.046$), no significant effect on duration of angina, oxygen uptake at angina reduced by 2.2% ($P = 0.04$). Time to 0.1 mV ST-segment depression shortened by 19.1% ($P = 0.044$) in 8 subjects.
Allred et al. (42)	0 134 290	0.6 2.0 3.9	50- to 70-minute exposure at rest, pre- and post-exposure incremental exercise on a treadmill	63 males, mean age 62 years (nonsmokers), reproducible angina	Time to onset of angina shortened by 4.2% ($P = 0.054$) at COHb 2.0% and by 7.1% ($P = 0.004$) at COHb 3.9%. Time to threshold ischaemic ST-segment changes shortened by 5.1% ($P = 0.02$) at COHb 2.0% and by 12.1% ($P < 0.0001$) at COHb 3.9%. Significant dose relationships in the changes of both the onset of angina ($P = 0.02$) and the onset of ST-segment changes ($P < 0.0001$).

Sheps et al., 1987 (43)	0 115	1.5 3.6	1-hour exposure at rest, post-exposure incre- mental exercise on a cycle ergometer	25 males and 5 females, mean age 58.2 years (nonsmokers for at least 2 months), ischaemia in a screening test	No significant changes in time to onset of angina, duration of angina, maximal exercise time, maximal ST- segment depression, time to significant ST-segment depression, or maximal left ventricular ejection fraction. 3 subjects experienced angina only on CO exposure, actuarial analysis including these subjects showed shortening in time to onset of angina in the study group ($P < 0.05$).
Adams et al. (44)	0 115–229	1.6 5.2	1-hour exposure at rest, postexposure incre- mental exercise on a cycle ergometer	22 males and 8 females, mean age 58 years, non- smokers for at least 2 months, ischaemia in a screening test	Maximal exercise time shortened by 6.5% ($P < 0.05$), level and change in left ventricular ejection fraction at submaximal exercise reduced ($P = 0.05$). Shortening in time to onset of angina ($P < 0.05$) according to actuarial analysis.

^aCarbon monoxide, 1 mg/m³ = 0.873 ppm.

^bCarboxyhaemoglobin concentrations are from venous blood samples taken immediately after exercise; in the study of Anderson et al. (40) samples were taken only immediately after carbon monoxide exposure.

investigated the effects of occupational carbon monoxide exposures on deaths from arteriosclerotic heart disease among 5529 New York City bridge and tunnel officers in the period 1952–1981. Among the more exposed tunnel officers there was a 35% excess risk compared with the New York City population, whereas among the less exposed bridge officers the risk was not elevated. The elevated risk among the tunnel officers declined significantly within five years after cessation of the occupational exposure, and there has also been a significant decline since 1970, when the introduction of new ventilation systems lowered the carbon monoxide levels in tunnels and tunnel booths. The 24-hour average carbon monoxide concentrations inside the tunnels were around 57 mg/m³ (50 ppm) in 1961 and 46 mg/m³ (40 ppm) in 1968. During rush hour traffic in 1968, carbon monoxide concentrations in tunnel toll booths were as high as 74–189 mg/m³ (65–165 ppm) and in 1970 the mean concentration over 38 days was 72 mg/m³ (63 ppm). However, the mean COHb levels measured among smoking and nonsmoking tunnel officers in 1970 and 1981 were generally lower than 5 %.

Current data from epidemiological studies and laboratory animal studies do not suggest that common environmental exposures to carbon monoxide have atherogenic effects on humans (1, 49).

Developmental effects

The pregnant mother, the fetus *in utero* and the newborn infant are at high risk of adverse health effects from atmospheric carbon monoxide exposures. During pregnancy, the endogenous production of carbon monoxide can be elevated as much as 3-fold, the concentration of maternal haemoglobin is often reduced, and the mothers have physiological hyperventilation. As a result of these changes, maternal COHb levels are usually about 20% higher than the nonpregnant values. Carbon monoxide diffuses readily across the placental membranes, and the carbon-monoxide-binding affinity of fetal haemoglobin is higher than that of adult haemoglobin. Moreover, carbon monoxide is cleared much more slowly from fetal blood than from maternal blood. At steady state, fetal COHb levels are up to 10–15% higher than maternal COHb levels (1, 28).

There are theoretical reasons and supporting laboratory animal data to suggest that the fetus and the developing organs are especially vulnerable to carbon monoxide. The developing brain seems to have the highest sensitivity of all organs. There is a well established and probably causal relationship between maternal smoking and low birth weight at fetal COHb levels of 2–10%. In addition, maternal smoking seems to be associated with a dose-dependent increase in perinatal deaths and with behavioural effects in infants and young children. Carbon monoxide is probably one of the most important etiological factors for these effects, although there are numerous other toxic pollutants in tobacco smoke (28).

Adaptation and high altitude effects

There is only indirect evidence for short- and long-term compensation to increased COHb levels in blood. According to experimental animal data, the following physiological responses have been proposed: (a) increased coronary blood flow; (b) increased cerebral blood flow; (c) increased haemoglobin through increased haemopoiesis; and (d) increased oxygen consumption in muscle. It is not known, however, whether these responses are evoked in humans, especially at common environmental exposures to carbon monoxide (1).

There have been few studies on the effects of carbon monoxide at high altitude. The results of the short-term studies suggest that the two forms of hypoxia produce at least additive effects on humans. The results of some long-term studies have been inconclusive, but the fetuses of smoking mothers, in particular, may be at a high risk of chronic hypoxia (1).

Evaluation of human health risks

Exposure evaluation

Global background concentrations of carbon monoxide range between 0.06 mg/m³ and 0.14 mg/m³ (0.05–0.12 ppm). In urban traffic environments of large European cities, the 8-hour average carbon monoxide concentrations are generally lower than 20 mg/m³ (17 ppm) with short-lasting peaks below 60 mg/m³ (53 ppm). Carbon monoxide concentrations inside vehicles are generally higher than those measured in ambient outdoor air. The air quality data from fixed-site monitoring stations seem to reflect rather poorly short-term exposures of various urban population groups, but appear to reflect better longer averaging times, such as 8 hours.

In underground and multistorey car parks, road tunnels, enclosed ice arenas and various other indoor microenvironments, in which combustion engines are used under conditions of insufficient ventilation, the mean levels of carbon monoxide can rise above 115 mg/m³ (100 ppm) for several hours, with short-lasting peak values that can be much higher. In homes with gas appliances, peak carbon monoxide concentrations of up to 60–115 mg/m³ (53–100 ppm) have been measured. Environmental tobacco smoke in dwellings, offices, vehicles and restaurants can raise the 8-hour average carbon monoxide concentration to 23–46 mg/m³ (20–40 ppm).

Carbon monoxide diffuses rapidly across alveolar, capillary and placental membranes. Approximately 80–90 % of the absorbed carbon monoxide binds with haemoglobin to form carboxyhaemoglobin (COHb), which is a specific biomarker of exposure in blood. The affinity of haemoglobin for carbon monoxide is 200–250 times that for oxygen. During an exposure to a fixed concentration of carbon monoxide, the COHb concentration increases rapidly at the onset of exposure, starts to level off after 3 hours, and reaches a steady state after 6–8 hours of exposure. The elimination half-life in the fetus is much longer than in the pregnant mother.

In real-life situations, the prediction of individual COHb levels is difficult because of large spatial and temporal variations in both indoor and outdoor carbon monoxide concentrations.

Health risk evaluation

The binding of carbon monoxide with haemoglobin to form COHb reduces the oxygen-carrying capacity of the blood and impairs the release of oxygen from haemoglobin to extravascular tissues. These are the main causes of tissue hypoxia produced by carbon monoxide at low exposure levels. At higher concentrations the rest of the absorbed carbon monoxide binds with other haem proteins such as myoglobin, and with cytochrome oxidase and cytochrome P-450 (1, 2). The toxic effects of carbon monoxide become evident in organs and tissues with high oxygen consumption such as the brain, the heart, exercising skeletal muscle and the developing fetus.

Severe hypoxia due to acute carbon monoxide poisoning may cause both reversible, short-lasting neurological deficits and severe, often delayed neurological damage. The neurobehavioural effects

include impaired coordination, tracking, driving ability, vigilance and cognitive performance at COHb levels as low as 5.1–8.2% (3, 35, 36).

In apparently healthy subjects, maximal exercise performance has decreased at COHb levels as low as 5%. The regression between the percentage decrease in maximal oxygen consumption and the percentage increase in COHb concentration appears to be linear, with a fall in oxygen consumption of approximately one percentage point for each percentage point rise in COHb level above 4% (1, 4).

In controlled human studies involving patients with documented coronary artery disease, mean postexposure COHb levels of 2.9–5.9% (corresponding to postexercise COHb levels of 2.0–5.2%) have been associated with a significant shortening in the time to onset of angina, with increased electrocardiographic changes and with impaired left ventricular function during exercise (40–44). In addition, ventricular arrhythmias may be increased significantly at the higher range of mean postexercise COHb levels (46, 48). Epidemiological and clinical data indicate that carbon monoxide from recent smoking and environmental or occupational exposures may contribute to cardiovascular mortality and the early course of myocardial infarction (1). According to one study there has been a 35% excess risk of death from arteriosclerotic heart disease among smoking and nonsmoking tunnel officers, in whom the long-term mean COHb levels were generally less than 5% (48). Current data from epidemiological studies and experimental animal studies indicate that common environmental exposures to carbon monoxide do not have atherogenic effects on humans (1, 49).

During pregnancy, endogenous production of carbon monoxide is increased so that maternal COHb levels are usually about 20% higher than the non-pregnant values. At steady state, fetal COHb levels are up to 10–15% higher than maternal COHb levels (1, 28). There is a well established and probably causal relationship between maternal smoking and low birth weight at fetal COHb levels of 2–10%. In addition, maternal smoking seems to be associated with a dose-dependent increase in perinatal deaths and with behavioural effects in infants and young children (28).

In contrast with most other man-made air pollutants at very high concentrations (well above ambient levels), carbon monoxide causes a large number of acute accidental and suicidal deaths in the general population.

Guidelines

In healthy subjects, endogenous production of carbon monoxide results in COHb levels of 0.4–0.7%. During pregnancy, elevated maternal COHb levels of 0.7–2.5%, mainly due to increased endogenous production, have been reported. The COHb levels in nonsmoking general populations are usually 0.5–1.5%, owing to endogenous production and environmental exposures. Nonsmokers in certain occupations (car drivers, policemen, traffic wardens, garage and tunnel workers, firemen, etc.) can have long-term COHb levels of up to 5%, and heavy cigarette smokers have COHb levels of up to 10% (1, 2, 28). Well trained subjects engaging in heavy exercise in polluted indoor environments can increase their COHb levels quickly up to 10–20%. In indoor ice arenas, epidemic carbon monoxide poisonings have recently been reported.

In order to protect nonsmoking, middle-aged and elderly population groups with documented or latent coronary artery disease from acute ischaemic heart attacks, and to protect the fetuses of

nonsmoking pregnant women from untoward hypoxic effects, a COHb level of 2.5% should not be exceeded.

The following guidelines are based on the Coburn-Foster-Kane exponential equation, which takes into account all the known physiological variables affecting carbon monoxide uptake (30). The following guideline values (ppm values rounded) and periods of time-weighted average exposures have been determined in such a way that the COHb level of 2.5% is not exceeded, even when a normal subject engages in light or moderate exercise:

- 100 mg/m³ (90 ppm) for 15 minutes
- 60 mg/m³ (50 ppm) for 30 minutes
- 30 mg/m³ (25 ppm) for 1 hour
- 10 mg/m³ (10 ppm) for 8 hours.

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Fig. 1. The relationship between carbon monoxide exposure and carboxyhaemoglobin levels in blood^a

^aThe predicted COHb levels resulting from 1- and 8-hour exposures to carbon monoxide at rest (alveolar ventilation rate of 10 litres/minute) and with light exercise (20 litres/minute) are based on the Coburn-Foster-Kane equation (30) using the following assumed parameters for nonsmoking adults: altitude = 0 metres; initial COHb level = 0.5%; Haldane coefficient = 218; blood volume = 5.5 litres; haemoglobin level = 150 g/litre; lung diffusivity = 30 ml/torr per minute; and endogenous carbon monoxide production = 0.007 ml/minute. Carbon monoxide 1 ppm = 1.145 mg/m³.

Source: US Environmental Protection Agency (1)