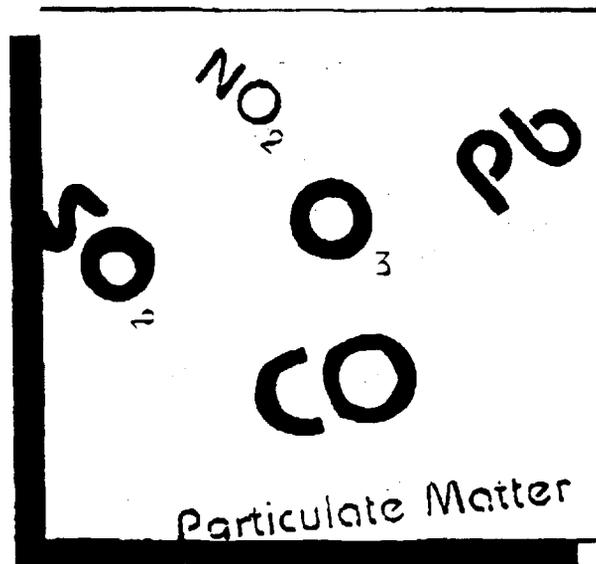


Health Effects of Ambient Air Pollution



Carbon Monoxide

Background

Carbon monoxide (CO) is formed during combustion of any carbon-containing fuel. As mentioned in Chapter 2, a small amount is formed even in the normal metabolic breakdown of natural substances in the human body. Carbon monoxide occurs naturally in the atmosphere, but outdoor exposure levels are usually negligible except in the presence of manmade pollution. Motor vehicles are the most important source of outdoor carbon monoxide pollution, although industrial and domestic sources also contribute. In cities like Los Angeles, monitored ambient concentrations occasionally exceed 20 parts per million (ppm) as a one-hour average. Before cars had catalytic converters, carbon monoxide levels were substantially higher. Even now, concentrations may exceed 40 ppm on streets with very heavy traffic and may exceed 100 ppm in enclosed spaces, such as tunnels or parking garages. People who spend considerable time in such areas may receive much greater carbon monoxide doses than would be predicted from air monitoring data. (Monitoring stations are usually designed to measure the area-wide background level of pollution, not localized excess concentrations.)

Of all the criteria pollutants, carbon monoxide (along with lead) is most widely recognized as a poison, with good reason. Hundreds of people die every year, by accident or suicide, from grossly elevated indoor carbon monoxide concentrations, often in the thousands of ppm. Combustion in a poorly ventilated space—a defective or improperly vented stove or heater, or a car engine running in a closed garage—causes the pollution in these cases. Thus, the potential bad consequences of indoor carbon monoxide pollution cannot be overemphasized. With proper care, such serious risks can be avoided, and indoor carbon monoxide levels need not be much higher than outdoor levels. (Normal cooking and heating still may produce some indoor carbon monoxide, and tobacco smoking also may be an important indoor source.)

The toxicity of carbon monoxide is due to its great affinity for hemoglobin, the oxygen-transporting pigment of red blood cells. Normally, hemoglobin in blood flowing through the capillaries of the lungs will bind chemically with oxygen molecules to form oxyhemoglobin, which eventually releases oxygen to body tissues. But if air in the lungs contains carbon monoxide as well as oxygen, some hemoglobin will combine with carbon monoxide to form carboxyhemoglobin (COHb). Carbon monoxide binds more readily to hemoglobin than does oxygen, so only a small concentration of carbon monoxide in air is required to produce a significant amount of carboxyhemoglobin. Formation of carboxyhemoglobin not only reduces the amount of hemoglobin available to carry oxygen, it also impairs the release of oxygen to body tissues by the remaining oxyhemoglobin. High altitude (low atmospheric pressure) also reduces the body's ability to take up oxygen, so risks from carbon monoxide exposure increase with altitude. Oxygen requirements are most critical in the heart and brain, so most health research on carbon monoxide focuses either on cardiovascular function or on mental performance.

The body burden of carbon monoxide at any given time can be measured by determining the percentage of carboxyhemoglobin in a sample of blood. A rough

estimate can be obtained by measuring the carbon monoxide concentration in exhaled air, after holding the breath for twenty to thirty seconds to equalize carbon monoxide levels between the lung alveoli and the circulating blood. At low levels, each additional 1 percent of carboxyhemoglobin in blood adds about 5 or 6 ppm to the carbon monoxide concentration in breath. From the opposite viewpoint, we might expect that each additional 5 or 6 ppm of carbon monoxide in polluted air would raise the blood carboxyhemoglobin concentration another 1 percent. The actual situation is more complicated, but the approximate carboxyhemoglobin level resulting from any particular carbon monoxide exposure can be calculated (Coburn et al. 1964; Environmental Protection Agency [U.S. EPA] 1979). Often in toxicologic studies, the exposure is described in terms of percent carboxyhemoglobin produced, rather than in terms of carbon monoxide concentration and time. At any given concentration of carbon monoxide in air, up to about ten hours of exposure will be required to "load" the blood hemoglobin to the calculated maximum carboxy-hemoglobin concentration. Loading time will be shortened by exercise, which speeds up respiration and circulation. The body requires a slightly longer time in clean air to fully "blow off" previously acquired carbon monoxide. A healthy nonsmoker residing in clean air will have roughly 0.5 percent carboxyhemoglobin, produced by normal metabolism. Some diseases that increase the breakdown rate of red blood cells will cause higher carboxyhemoglobin levels. Light smokers typically have 2-3 percent carboxyhemoglobin from the carbon monoxide in tobacco smoke, and heavy smokers may have 5 percent or more. If the blood carboxyhemoglobin level is already high from smoking or some other personal cause, ambient pollution exposure will have little effect except to prolong the elevated carboxyhemoglobin level.

The EPA (U.S. EPA 1979, 1984) has reviewed the known health effects of carbon monoxide exposure in criteria documents. Other useful reviews have been published (see, for example, Goldsmith and Landaw 1968; National Academy of Sciences 1977; Gutierrez 1982; McGrath 1982; and Shephard 1983).

Animal Toxicology

After reviewing numerous studies of behavior and functioning of the brain/central nervous system, the EPA (1979) concluded that behavioral changes or impairment of learning might occur in laboratory animals at carbon monoxide-exposure concentrations as low as 100 to 150 ppm. Some effects were observed in single short-term exposures (for example, for two hours) as well as long-term exposures. Findings in different studies were often inconsistent.

Abnormalities of heart function as determined by electrocardiograms have been observed fairly consistently after long-term intermittent exposures at carbon monoxide concentrations of 100 ppm or more, producing 8 to 13 percent carboxyhemoglobin. In a few cases, effects have been reported at carbon monoxide concentrations near 50 ppm, producing carboxyhemoglobin levels of 4 to 7 percent. Scarring or degeneration of the heart muscle was observed in some cases, at least at

the higher carboxyhemoglobin levels. Disturbances of the normal heart rhythm (which might indicate increased risk of a life-threatening heart attack) were reported in some studies but were not found in a later investigation specifically intended to model human heart disease. One research group, working with dogs whose coronary arteries were partly blocked, measured the effect of carbon monoxide exposure on myocardial ischemia (oxygen starvation in the heart muscle). They found evidence of increased ischemia, and thus disturbed heart function, at carboxyhemoglobin concentrations down to 5 percent. Similar effects may be important in humans with diseased coronary arteries, as indicated below. Some researchers have observed enlargement of the heart and/or increases in the number of red blood cells after long-term carbon monoxide exposure. These are typical effects of chronic oxygen shortage, sometimes observable at high altitude, for example.

Human Studies

Most human health studies relevant to ambient carbon monoxide exposure have been conducted in laboratories. A few epidemiologic studies have addressed the relationship of carbon monoxide to rates of death from heart attacks, symptoms of heart and lung disease, or death in newborn infants. Confounding factors are numerous, and results have been inconclusive (Goldsmith and Landaw 1968; Kurt et al. 1978; U.S. EPA, 1984). Laboratory exposure studies usually have focused on maximal exercise performance, mental performance, or heart function. Some studies have also explored possible effects of carbon monoxide on the process of blood clotting, but results have been inconclusive (U.S. EPA 1984). A few investigators have exposed volunteers simultaneously to carbon monoxide and to respiratory irritant pollutants such as ozone. So far, carbon monoxide does not seem to enhance the effects of irritants, and vice versa.

When the oxygen-carrying capacity of blood is reduced by the formation of carboxyhemoglobin, the maximum rate of oxygen delivery to body tissues must decrease. Consequently, the maximum rate at which tissues (for example, muscles) can work must decrease. That is, carbon monoxide exposure must reduce maximum exercise capability. A critical question remains: How much carbon monoxide is required to produce a noticeable effect on exercise, that is, what is the exposure-response relationship? Numerous research groups have addressed this question (see, for example, Drinkwater et al. 1974; Horvath et al. 1975; Weiser et al. 1978; Klein et al. 1980). Decreases in volunteers maximum work rate and maximum oxygen consumption have been observed consistently at carboxyhemoglobin concentrations of 5 percent and higher, and sometimes at 3-4 percent carboxyhemoglobin. Often, experimenters employ higher-than-ambient carbon monoxide concentrations and brief exposure times to attain these carboxyhemoglobin levels. However, they also could be attained by several hours exposure to concentrations as low as 30-40 ppm. Less-than-maximum exercise apparently is not affected by moderate elevations of carboxyhemoglobin. However, we should recognize that most exercise studies have been performed in young, healthy adults. Older or chronically ill people, whose exercise capacity is low to begin with, might be affected by comparatively low levels of carbon monoxide.

People with coronary artery disease (fatty deposits inside the blood vessels supplying the heart) are vulnerable to myocardial ischemia, that is, inadequate oxygen supply to the heart muscle, as indicated in the preceding section. These people have characteristic symptoms of angina (pain and pressure in the chest) and their characteristic electrocardiogram abnormalities (technically known as "S-T depression") are thought to result from ischemia. Both these problems usually occur during exercise, when the heart muscle oxygen requirements are greatest. Again, the presence of carboxyhemoglobin undoubtedly impairs oxygen delivery; the important question is, how much carboxyhemoglobin is necessary to produce a medically important increase in ischemia? To help answer this question, researchers study volunteers with heart disease who consistently develop angina and electrocardiogram changes during exercise. The experimental endpoint is the length of time the volunteer can exercise (in a carefully controlled test on a treadmill) before the signs of ischemia show up. If the time of exercise is shorter after carbon monoxide exposure than in a control study with clean air, one may infer that carbon monoxide disturbed the supply of oxygen to the heart.

Some studies of coronary disease patients have indicated a decrease in time to angina after carbon monoxide exposures that raised average carboxyhemoglobin concentrations to the 2-4 percent range; others showed no such effect (Aronow and Isbell 1973; Anderson et al. 1973; Sheps et al. 1987). New research has attempted to resolve the issue by combining the efforts of several laboratories to obtain a large subject population, thus increasing statistical power (HEI 1988). Initial results suggest that there is indeed a greater tendency to ischemia and angina when carboxyhemoglobin rises to 2-3 percent. The effect appears small compared to typical day-to-day and person-to-person variability of the test results, thus it is not surprising that earlier, smaller-scale studies did not show it consistently.

Studies of brain and nervous system function in carbon monoxide-exposed humans have employed numerous endpoints, including vigilance (for example, ability to respond appropriately to irregularly occurring signals), sensory or time discrimination (vision sensitivity in the dark), complex sensory-motor performance tasks (driving simulation), sleep activity, and central nervous system electrical activity (electroencephalograms). The lowest carboxyhemoglobin level at which changes have been demonstrated reliably is 5 percent. Effects at lower levels cannot be ruled out, because lower levels have not been studied extensively (U S EPA 1984).

References

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