CARBON MONOXIDE IN HOUSES AND VEHICLES*

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Carbon monoxide is a colorless, odorless gas, the product of combustion and biological oxidation of carbonaceous materials. It is a pollutant to which mankind has been exposed from earliest time and once was a favored method of suicide. It binds to ferrous (+2) iron in heme proteins, hemoglobin and cytochrome P450 among them. Binding is not covalent but results from electronic interactive forces. Carbon monoxide is bound 240 times more tightly than oxygen and may be displaced by it. This is the basis for antidotal treatment of acute carbon monoxide intoxication. In the present, with our concern for environmental pollution, environmental carbon monoxide release is better controlled than in the past. Since automobiles are or have been the main source of environmental carbon monoxide release, the continuing energy crisis which has reduced the driving habits of a large number of Americans has led to the expectation that carbon monoxide emissions from such sources would be reduced still further than the expected reduction due to catalytic mufflers alone. The present economic downturn may also significantly contribute to the reduction of environmental carbon monoxide. Decreased availability of fuel with its attendant increase in price has resulted in substantial "improvements" in the degree to which our homes and offices have been weatherproofed against the loss of now more valuable BTUs. This improvement in energy conservation has led to serious deterioration in indoor air quality from entrapment of a larger fraction of the products of

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combustion. The realization of an increasingly polluted indoor environment is, in large part, the reason for this symposium.

Concentrations of carbon monoxide found by Longo[1] in a variety of indoor and outdoor environments are shown in Table I. Urban environments and smoke-filled rooms may at times be equivalent in their carbon monoxide concentration. Automobile exhaust fumes, most likely gasoline rather than diesel engine exhaust, are as concentrated in carbon monoxide as the smoke found in the mainstream of cigarettes. Presumably, the same analogy might apply to pipe and cigar smoke. Thus, the exhaust gases of that common polluter, the smoker, contain concentrations of carbon monoxide which might be intolerable in the workplace under present workplace standards.

Carbon monoxide is a biologic end product which results from the metabolism of protoporphyrin yielding bilirubin and carbon monoxide.[1] The rates of endogenous production of CO in male and female humans are similar (about 6 to 10 μl./hr./kg.). The rate of production varies because of prevailing hormonal state as well as pregnancy and a fivefold increase in carbon monoxide production may occur after delivery. Similar changes would also be expected as a result of hemolytic rises. Any increase in endogenous production will increase CO-HB concentration and increase carbon monoxide exhalation.

Occupational exposure and exhaust emissions are the main source of carbon monoxide intoxication. After this, carbon monoxide exposure attendant to tobacco smoking follows. Toward this end, cigarettes are now labeled with their tar and nicotine content and a recently enacted rule of the Federal Trade Commission will rank cigarettes according to their output of carbon monoxide.

The expired air of all individuals contains carbon monoxide as an excretory product and this may be an indicator of heme metabolism. Concentrations of 1 to 5 ppm. are not unusual in the exhaled air of both abstaining smokers and nonsmokers. In a clearly dose-responsive manner, carbon monoxide concentration in the expired air of smokers increases with number and temporal proximity to cigarettes smoked.[3]

Cigarette smoking[2] results in a gradual increase in CO-HB to levels of 4% with a decline during the nocturnal period when sleep effectively limits a smoker's ability to burn tobacco and inhale its products. The increase in CO-HB concentration associated with cigarette smoking rises further to 6% when the smoker is also exposed to conditions where envi-

TABLE I

CARBON MONOXIDE CONCENTRATIONS IN AIR FROM VARIOUS SOURCES

Source	*CO Concentration (ppm.)**
Fresh sea air	0.06-0.5
Urban air	1-30
Street corner	5-50
Major interchange	50-100
Automobile exhaust	30,000-80,000
Cigarette smoke	20,000-60,000
Alveolar concentration in smoker	300-400
Smoke-filled room	25-100

* Parts per million by volume

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ronmental levels of carbon monoxide are significant (20 ppm.). The carbon monoxide concentration compares to the concentrations found in some work environments. A similar pattern of daily rise and fall of blood carbon monoxide concentration[2] occurs among nonsmokers whose work results in exposure to carbon monoxide.

Of greatest public health concern is not the self-exposure of consenting adults to carbon monoxide but the unwitting and unnecessary exposure of the fetus *in utero* to carbon monoxide as a result of both environmental pollution and maternal smoking. Data in Table II indicate that the maternal to fetal carboxyhemoglobin ratio varies around one (0.7-1.8) and the concentration of fetal CO-HB in the fetus has been measured as high as 7.6%. The data were taken around the time of delivery with all of the difficulty that such an event entails.

Permissible workplace exposures to carbon monoxide have been set for healthy males and published by a variety of organizations, notably the American Conference of Governmental Industrial Hygienists, whose threshold limit value is often quoted. It is generally agreed that these values are applicable to healthy men and equally healthy, but nonpregnant women. Values promulgated by a variety of agencies are shown in Table III. From what we know of the biology and toxicology of carbon monoxide, the exposure concentration permitted should be lower for longer exposure periods and the lowest levels are those associated with exposure of the civilian population to continuous carbon monoxide con-

TABLE II

RELATION OF THE CONCENTRATIONS OF FETAL TO MATERNAL CARBOXYHEMOGLOBIN IN MOTHERS WHO SMOKE DURING PREGNANCY

Fetal carboxyhemoglobin concentration %	*Maternal carboxyhemoglobin concentration %*	*Fetal/maternal carboxyhemoglobin ratio*
7.6(±1.14)(SEM)*	6.2(±0.75)*	1.2(±0.2)*
3.1(±0.84)†	3.6(±1.06)†	0.9(±0.14)
5.0(±0.48)	6.7(±0.61)	0.7(±0.04)
2.4(±0.30)	2.0(±0.31)	1.2(±0.08)
5.3(±0.22)	5.7(±0.24)	0.9(±0.06)
7.3	8.3	0.9
3.6(±0.7)	6.3(±1.7)	0.6(±0.15)
7.5‡	4.1	1.8

* One or more cigarettes 1 hr. or less prior to delivery
† One or more cigarettes 1 to 24 hrs. prior to delivery
‡ Calculated from (HbCOm) and the ratio of (HbCOf) to (HbCOm)

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TABLE III

CURRENT MAXIMUM RECOMMENDED EXPOSURE LEVELS FOR CARBON MONOXIDE

Designation	*Level (ppm. by volume)*
TLV (USA, UK)	50
TLV (USSR)	18
TLV (Czechoslovakia)	30
MPC_{90} (USN, EN; submarines)	25
MPC_{90} (USA; spacecraft)	15
MPC_{100} (USA; spacecraft) civilian population (USA)	15
MPC civilian population (USA)	9 (8 hr. average)
MPC civilian population (FDR)	8 (24 hr. average)
MPC civilian population (USA)	1 (24 hr. average)

TLV = threshold limit value, MPC = maximum permitted concentration

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centration. As noted earlier, many street corners clearly exceed these concentrations. Therefore, we are advised to seek the presumed shelter and safety of the indoor environment.

In this regard, early pioneering work was done for the Environmental Protection Agency by John Yocum and his collaborators at The Research Corporation of New England who studied indoor sources and production rates of carbon monoxide and other pollutants. Their results, published in 1974-1975, showed that carbon monoxide concentrations in homes where gas was used for cooking peaked above concentrations found in air outside the home. At times, indoors was measurably worse than outdoors. Around this time also, it was reported that carbon monoxide was a contaminant in the indoor environment of sports arenas where the strenuous sport of hockey was played.[4]

It is clear that the indoor production of carbon monoxide is associated with unvented internal as well as external combustion devices. We now recognize that the unvented gas stove used for cooking is a major contributor to the deterioration of the indoor environment. It was recently reported[5] that high concentrations of carbon monoxide may be found in apartments where the gas stove is also a supplemental heat source. These authors showed (Figure 1) that gas consumption and temperature during the heating season correlate well against time. The increased fuel consumption is most likely a direct consequence of gas stoves being used for heat because the use of stoves for cooking would presumably be similar in the fall and spring.

These data of Sterling and Kobayashi[5] are derived from buildings in the South Bronx where rent-subsidized public housing and more common tenements without rent supplementation have inconsistent to absent central heat and building maintenance. People living in these buildings are generally poor and experience a degree of carbon monoxide exposure (Figure 2) lower only in dwellings with major structural damage, cracked doors, broken windows, and holes in ceilings and floors. These dwellings are likely to be quite cold. Rent-subsidized dwellings may be more adequately heated but have much higher levels of carbon monoxide than do tenement dwellings. The difference between them may derive from the existence of stoves as supplemental heat sources as well as the decreased infiltration of outside air.

Carbon monoxide may also be produced endogenously from exogenous chemical exposure. Stewart and subsequent workers[6,7] showed

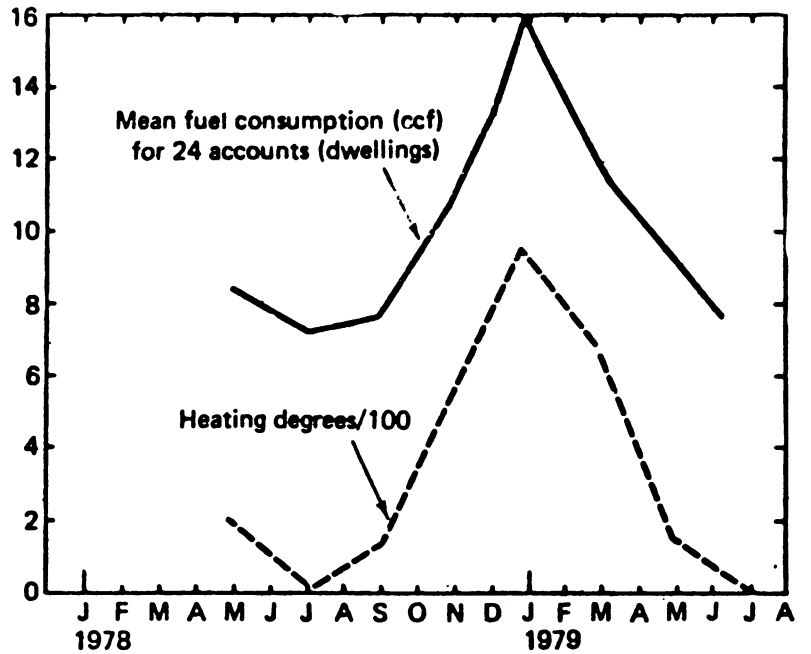

Fig. 1. Metered gas consumption versus temperature. Heating degrees = $\Sigma(65^{\circ}$ average daily temperature). Reproduced by permission from Sterling, T.D. and Kobayashi, D.: Use of gas ranges for cooking and heating in urban dwellings. *J. Air Poll. Control Assoc. 31:* 162-65, 1981.

that methylene chloride, a material common to home paint-stripper formulations, is biotransformed to carbon monoxide and leads to a significant increase in carboxyhemoglobin. Activity as well as dose, i.e., exposure concentration, results in variable concentrations of CO-HB in blood. Thus, methylene chloride used in strenuous home maintenance and even such sedentary hobbies as furniture refinishing may contribute to the passive carbon monoxide exposure of persons within the household environment.

Additional observations on the toxicity of carbon monoxide relate most often to its effects on the transport of oxygen throughout the circulatory system and its interference with the release of oxygen from hemoglobin at low venous oxygen pressure.

Such an effect is shown in Figure 3. This is the basis for the classic observation that a blood concentration of 30% carboxyhemoglobin is significantly worse than 30% anemia. It is clear from the change in the sigmoid oxygen dissociation curve to a more rectangular curve that car-

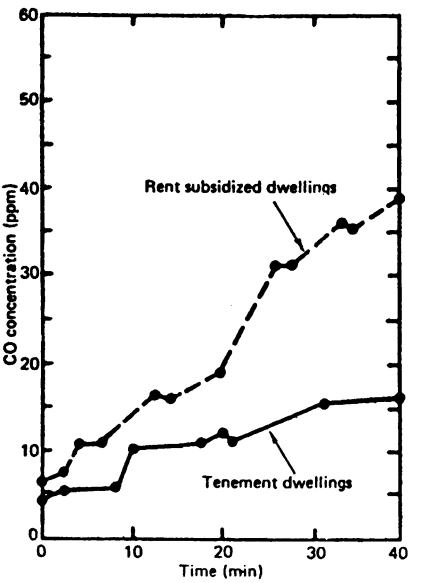

Fig. 2. Comparison of average CO build-up during simulated cooking in four tenement and eight rent-subsidized dwellings. Reproduced by permission from Sterling, T.D. and Kobayashi, D.: Use of gas ranges for cooking and heating in urban dwellings. *J. Air Poll. Control Assoc. 31:* 162-65, 1981.

bon monoxide potently inhibits the cooperative interaction between hemoglobin subunits and will lead to significant tissue hypoxia.

A number of studies have attempted to ascertain the effect of differing levels of activity (sedentary, light versus heavy work) on the time required to achieve various concentrations of CO-HB. These differing levels of activity are significant at high inspired carbon monoxide concentration but their effects are relatively slight at what might be considered indoor environmental levels. As shown in Figure 4, a 30 ppm. concentration of carbon monoxide requires 500 minutes (about eight hours) exposure to achieve a CO-HB concentration of 5% in blood. Such a concentration might be common in a poorly ventilated office.

Several investigators have attempted to determine whether carbon monoxide is capable of inhibiting the mixed function oxidase system *in vivo.* It has been shown that carbon monoxide binds to cytochrome P-450 *in vitro.* Using rats treated with the fast acting barbituate, hexobarbital, Montgomery and Rubin[8] showed significant prolongation of sleeping time when animals were exposed acutely to carbon monoxide. Subse-

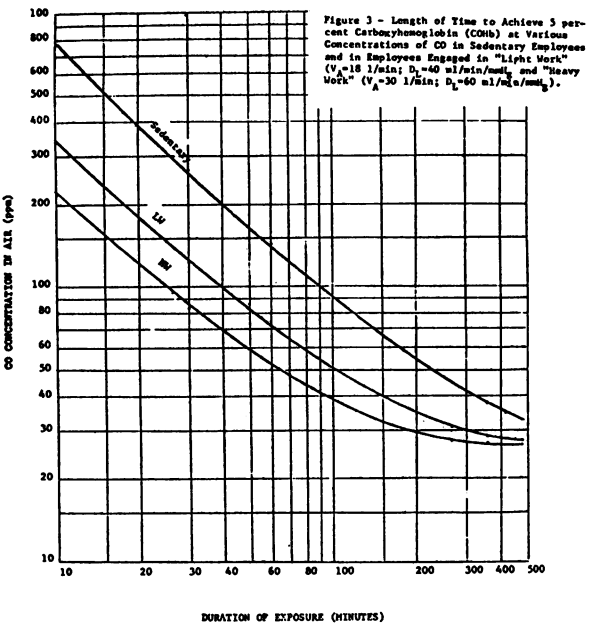

Fig. 3. Length of time to achieve 5% carboxyhemoglobin at various concentrations of carbon monoxide in sedentary employees and in employees engaged in "light work" (V_A=18 l./min.; D_L=40 ml./min./mm.Hg) and "heavy work" (V_A=30 l./min.; D_L=60 ml./min./mm.Hg)

quent work by Roth and Rubin[9] showed that carbon monoxide exposure as used by Montgomery and Rubin decreased arterial and venous saturation of oxygen. A similar decrease was seen when inspired P_{O_2} was 13% or below. Roth and Rubin,[10] using the isolated perfused liver, demonstrated that the effect of carbon monoxide was not on the cytochrome P-450 system but rather that the carbon monoxide produced a degree of *in vivo* anoxia and blood-flow alteration within the liver that interfered with oxidation of the drug.

Still other biochemical effects of carbon monoxide have been demonstrated. Garrett and Jackson[11] found that rats exposed to 60 puffs of cigarette smoke had profoundly decreased hepatic protein synthesis, an effect not modified by the utilization of a Cambridge filter, a charcoal filter, or their combination. These exposures produced high levels of carboxyhemoglobin, and it is presumed that the influence of this very substantial degree of hypoxic anoxia must have resulted in a significant re-

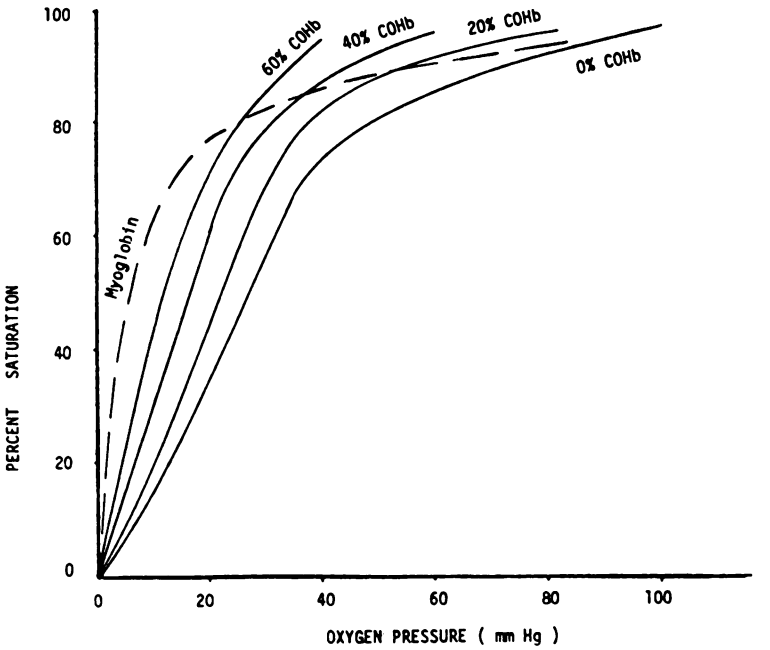

Fig. 4. Oxyhemoglobin dissociation curve[7]

duction in liver ATP concentration and concomitant interference with protein synthesis.

Other studies on carbon monoxide toxicity have focused on its potential as a teratogen. Studies done by Schwetz et al.[12] were unable to demonstrate that pregnant mice or rabbits exposed for seven or 24 hours per day to 250 ppm. produced offspring with a sufficient number of gross abnormalities that carbon monoxide could be considered a potential human teratogen. Only minor abnormalities were found, and this study concluded that, rather than being teratogenic, carbon monoxide at these concentrations is clearly embryotoxic. Presumably, this is due to its action to decrease the availability of oxygen to the developing fetus. Because it produces few obvious morphologic or biochemical abnormalities in the offspring of experimental animals, the research for adverse effects of carbon monoxide has taken advantage of the subtle measurement techniques of behavorial toxicology.

Fechter et al.[13] have studied the effects of carbon monoxide at 150 ppm. on pregnant rats and their offspring. Their data show the rate of weight gain of preweenling rats delivered to mothers maternally exposed

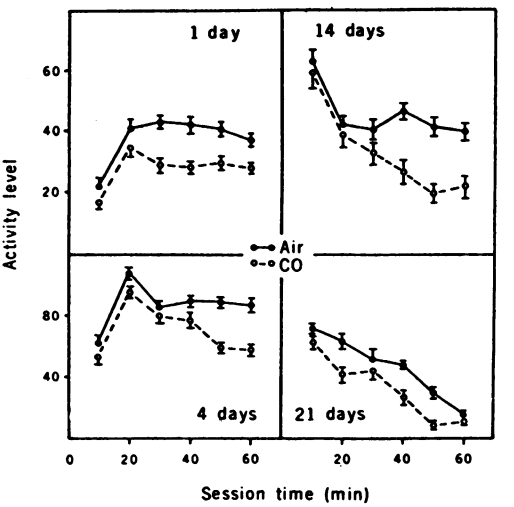

Fig. 5. Open-field activity levels of rats exposed prenatally to CO concentrations of 150 ppm. or to room air. Subjects one and four days old were injected with L-Dopa (100 mg./kg.) at time zero. Subjects 14 and 21 days old were not injected. Activity was averaged across 10-minute intervals for a one-hour period. Reproduced by permission from Fechter, L.D. and Annau, Z.: Toxicity of mild prenatal carbon monoxide exposure. *Science 197:* 680-82, 1977.

to 150 ppm. of carbon monoxide is significantly depressed as early as the fourth day following delivery and lower body weights were recorded at day 10, 14, and 21. These authors reported no difference in the birth weight, in the number of live pups per litter, nor in total number of dead pups.

Their main and most important observation was that the open field activity which occurs as a result of postnatal administration of L-Dopa is significantly lower in animals born to mothers exposed to carbon monoxide during gestation. These data are shown in Figure 5. Other central nervous system indices studied were total brain cathecholamine content (Table IV) as well as brain weight and protein content (Table V). The concentration of brain protein on a milligram-per-gram basis was significantly less in animals exposed to carbon monoxide during the prenatal interval. Following L-Dopa administration, either on day 1 or day 4, it was lower in the offspring from the carbon-monoxide-exposed group.

The same authors[14] showed that cardiac tissue from one-day-old rats exposed prenatally to 150 ppm. of carbon monoxide was much heavier than cardiac tissue from controls. Their work suggested that the increase

TABLE IV

WHOLE BRAIN CATECHOLAMINE LEVELS IN RATS PRENATALLY EXPOSED TO CARBON MONOXIDE (150 ppm.) OR TO AIR

Treatment	*Catecholamine content (μ g./g)*			
	Day 1		*Day 4*	
	DA	NE	DA	NE
Saline				
Air	0.158±0.04	0.072±0.02	0.083±0.02	0.045±0.02
CO	0.108±0.02	0.099±0.02	0.133±0.02	0.071±0.02
L-Dopa (100 mg./kg.)				
Air	5.47±1.62	0.092±0.02	2.96±0.06	0.127±0.02
CO	3.01±0.81*	0.112±0.03	2.23±0.21†	0.123±0.03

Values given are mean ± S.E.M.
*Significantly different from comparable control group at P < .01
†Significantly different from comparable control group at P < .05
DA=dopamine, NE=norepinephrine
Reproduced by permission from Fechter, L.D. and Annau, Z.: Toxicity of mild prenatal carbon monoxide exposure. *Science 197*:680-82. 1977.

TABLE V

WHOLE BRAIN PROTEIN CONCENTRATIONS IN 1-DAY-OLD RATS PRENATALLY EXPOSED TO CARBON MONOXIDE (150 ppm.) OR TO AIR

Treatment	*Body weight (g.)*	*Wet brain weight (mg.)*	*Wet brain weight/ body weight*	*Brain protein (mg./g.)*
Air	5.94±0.17	233.0±6.40	39.98±0.68	81.77±2.46
CO	5.53±24	243.9±6.83	43.76±0.80	63.36±4.08*

Values given are mean ± S.E.M.
*Significantly different from comparable control group at P < 0.01
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in weight was due to a significantly greater amount of water. Protein, DNA, and RNA, while not significantly different from control, were uniformly lower among CO-exposed offspring.

Additional reports on the effect of prenatal carbon monoxide exposure on behavioral performance in offspring are given in the work of Abottello

and Mohrman.[15] These authors exposed pregnant Swiss Webster mice to carbon monoxide and found that it did not influence the amount of time needed by the offspring to learn to penetrate a maze. Independent of carbon monoxide exposure, a highly significant difference between male and female offspring with regard to time required to learn the maze was seen. When exposed-versus-control groups were compared, the number of errors made by the males was significantly greater than made by the females.

CONCLUSIONS

Clearly, carbon monoxide is a common indoor air pollutant whose major toxic action from a public health and indoor air pollution standpoint appears to be associated with very subtle changes in neonatal growth, learning, and activity when low to moderate concentrations are tested. Such concentrations might occur after cigarette smoking or from living in poorly ventilated homes that use gas stoves for heating. It is clear that tobacco smoking is a form of self abuse to be discouraged. In any case, utilization of unvented internal and external combustion systems at home should be discouraged. In times of decreased public funding and decreased availability of public assistance, the increased utilization of gas stoves to heat homes and apartments is likely. The potential adverse health effects of combustion products to children from such exposure may be quite substantial.

SUMMARY

Carbon monoxide, found in indoor as well as outdoor environments, is produced indoors by combustion of natural gas, as well as by tobacco smoking. Concentrations in human blood range from less than 1% in nonsmokers to 5-10% in smokers. In fetuses of smoking mothers, as much as 7.6% of CO-HB was reported. Such voluntary intoxication as well as involuntary exposure associated with indoor air pollution are considered with respect to the effects of carbon monoxide on behavior and performance of the offspring.

Questions and Answers

MR. HARVEY SACHS (Princeton University): It is almost incidental, but are there any sources of combustion gases on nuclear submarines except cigarette smoke?

DR. JAEGER: The answer is no.

DR. FERRAND: Carbon monoxide is produced when fuels don't burn too well. When they do burn well, we begin to produce nitrogen oxides.

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