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**Fundamental and Applied Toxicology, Vol. 9, No. 2,  
p.236-250, August 1987.**

#2, August

FUNDAMENTAL AND APPLIED TOXICOLOGY 9, 236-250 (1987)

## Effects of Exposure to Single or Multiple Combinations of the Predominant Toxic Gases and Low Oxygen Atmospheres Produced in Fires<sup>1,2</sup>

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Effects of Exposure to Single or Multiple Combinations of the Predominant Toxic Gases and Low Oxygen Atmospheres Produced in Fires. LEVIN, B. C., PAABO, M., GURMAN, J. L., AND HARRIS, S. E. (1987). *Fundam. Appl. Toxicol.* 9, 236-250. The toxicity of single and multiple fire gases is studied to determine whether the toxic effects of the combustion products from materials can be explained by the toxicological interactions (as indicated by lethality) of the primary fire gases or if minor, more obscure gases need to be considered. LC50 values for Fischer-344 rats have been calculated for the individual gases, carbon monoxide (CO), hydrogen cyanide (HCN), or decreased oxygen (O<sub>2</sub>), for 30-min exposures plus relevant postexposure periods using the NBS Toxicity Test Method. Combination experiments with CO and HCN indicate that they act in an additive manner. Synergistic effects have been found when the animals are exposed to certain combinations of CO and carbon dioxide (CO<sub>2</sub>). Five percent CO<sub>2</sub> raised the threshold for deaths due to hypoxia and decreased the LC50 of HCN. Decreasing the O<sub>2</sub> concentration in the presence of various mixtures of the other major fire gases increased the toxicity even further. A comparison of the concentrations of the major combustion products generated from a number of polymeric materials at their LC50 (30-min exposure plus 14-day postexposure) values with the combined pure gas results indicates that, in most cases, the observed toxicity may be explained by the toxicological interactions of the examined primary toxic fire gases. These results provide necessary information for the computer model currently being developed at the Center for Fire Research to predict the toxic hazard that people will experience under various fire scenarios. © 1987 Society of Toxicology.

The atmosphere produced by a fire is a dynamic, rapidly changing combination of toxic gases, particulates, reduced oxygen, and

high temperatures. Each component of this combination is capable of producing conditions which are incompatible with life or will act to prevent safe egress from a burning building. Since the majority of fire fatalities result from smoke inhalation and not from burns (Birky *et al.*, 1979), there have been extensive efforts to identify the large numbers of thermal degradation products produced from materials under different fire conditions. For example, over 400 combustion products were identified in a summary of a series of literature reviews on the identification and toxicity of the thermal decomposition products from seven plastics (Levin, 1986). The problem addressed here is to determine whether the toxicity (as indicated by lethality) of complex fire mixtures depends upon the combined toxicities of large numbers of products or whether

<sup>1</sup> This paper is a contribution of the National Bureau of Standards. The U.S. Government's right to retain a nonexclusive royalty-free license in and to the copyright covering this paper, for governmental purposes, is acknowledged.

<sup>2</sup> This material was presented in part at the annual meetings of the Society of Toxicology, San Diego, CA, March 1985, the American Chemical Society, Miami Beach, FL, April 1985, and the 16th Annual Meeting of Toxicology, Harry G. Armstrong Aerospace Medical Research Laboratory and U.S. Naval Medical Research Institute, Dayton, OH, October 30, 1986.

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it can be explained by the toxicities of a few primary gases, either singly or in combination.

While many toxicological studies have been performed with reduced O<sub>2</sub> atmospheres and on single fire gases such as CO, CO<sub>2</sub>, and HCN, only a few investigations have examined the toxicological effects of various combinations of these gases and decreased O<sub>2</sub> (see review by Kimmerle, 1974; plus more recent papers by Anderson *et al.*, 1979, 1981a,b, 1983; Cagliostro and Islas, 1982; Crane, 1985; Edginton and Lynch, 1975; Hartzell *et al.*, 1985c; Kishitani and Nakamura, 1979; Levin *et al.*, 1987; Lynch, 1975; Nelson *et al.*, 1978; Pitt *et al.*, 1979; Rodkey and Collison, 1979; Smith *et al.*, 1976; Yamamoto and Kuwahara, 1981). The results of some of these studies have been contradictory. For example, Kimmerle (1974) and Moss *et al.* (1951) claimed the toxicological interaction between CO and HCN was synergistic, while Kishitani and Nakamura (1979), Pitt *et al.* (1979), Hartzell *et al.* (1985c), Lynch (1975), and Smith *et al.* (1976) found CO and HCN act in an additive manner; on the other hand, Anderson *et al.* (1979, 1981a,b, 1983), Higgins *et al.* (1972), and Yamamoto (1976) found no measurable interaction. Rodkey and Collison (1979) and Nelson *et al.* (1978) found that the presence of CO<sub>2</sub> increased the toxicity of CO; whereas Crane (1985) and Edginton and Lynch (1975) observed no effect and Pryor *et al.* (1974) and Gaume *et al.* (1971) noted a possible antagonistic effect.

In this paper, the terms "additive," "synergistic," and "antagonistic" are used as defined in Klaassen and Doull (1980); that is, if two compounds are introduced simultaneously, the response may be equal to the sum of the effects of each chemical by itself (an additive effect) or the combined effect may be greater (i.e., synergistic) or less (i.e., antagonistic) than that predicted by simple additivity.

This investigation was undertaken to examine the toxicological interaction of various combinations of the primary fire gases, CO,

CO<sub>2</sub>, and HCN, with and without reduced oxygen, and to determine the extent to which their individual or combined actions could explain the lethality produced by the thermal degradation products of some common natural and synthetic polymeric materials.

## METHODS

*Materials.* The gases (CO, CO<sub>2</sub>, HCN, and N<sub>2</sub>) utilized in this study were commercially supplied in various concentrations in air or nitrogen. Since certain distributors add SO<sub>2</sub> to their HCN tanks as stabilizers, the HCN gas cylinder was analyzed by both infrared analysis and BaSO<sub>4</sub> precipitation. The results of these tests, which were confirmed by our distributor, indicated that less than 1 ppm SO<sub>2</sub> was present in our HCN cylinders.

The polymeric materials evaluated in this study were an acrylonitrile-butadiene-styrene (ABS), Douglas fir, flexible polyurethane foams with and without a fire retardant, a modacrylic, a polyphenylsulfone, a polystyrene, a 92% homopolymer of polyvinyl chloride (PVC), the same PVC with 5% zinc ferrocyanide, red oak, a rigid polyurethane, and a wool. These are the same materials as those studied previously in this laboratory (Levin *et al.*, 1983a,b).

*Animals.* Fischer-344 male rats, weighing 200–300 g, were obtained from the Harlan Sprague-Dawley Co.<sup>6</sup> (Walkersville, MD) or from Taconic Farms (German town, NY). They were allowed to acclimate to our laboratory conditions for at least 10 days prior to experimentation. Animal care and maintenance were performed in accordance with the procedures outlined in the National Institutes of Health's *Guide for the Care and Use of Laboratory Animals*. Each rat was housed individually in suspended stainless-steel cages and provided with food (Ralston Purina Rat Chow 5012) and water *ad libitum*. Twelve hours of fluorescent lighting per day was provided using an automatic timer.

*Animal exposure system.* All exposures were conducted using the combustion system (for evaluation of the polymeric materials only), the chemical analysis system, and the animal exposure system that was designed for the NBS Toxicity Test Method (Levin *et al.*, 1982) (Fig. 1). The animal exposure system is a closed design in which all the gases and smoke are kept in the 200-liter rectangular chamber for the duration of the experiment.

<sup>6</sup> Certain commercial equipment, instruments, materials or companies are identified in this paper in order to adequately specify the experimental procedure. In no case does such identification imply recommendation or endorsement by the National Bureau of Standards, nor does it imply that the equipment or material identified is necessarily the best available for the purpose.

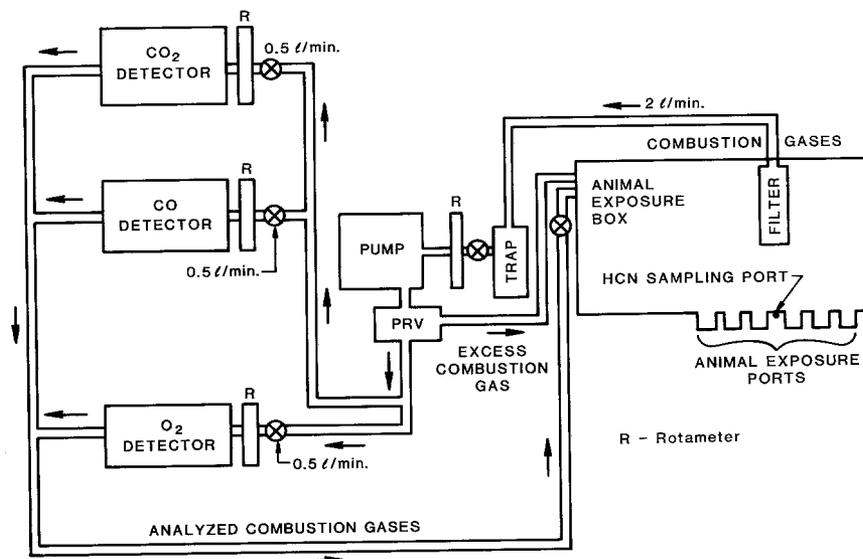


FIG. 1. Schematic of the National Bureau of Standards Toxicity Test Method. PRV = pressure relief valve.

In the gas experiments, the animals received either square-wave or gradual exposures. In the square-wave exposures, the various gases were added to the chamber until the given concentrations (monitored as described below) were reached. A fan in the chamber was used to ensure adequate mixing of the gases prior to exposure of the animals. In the gradual exposures, the animals were exposed to the initial buildup of gases (approximately 5 min out of the total 30 min of exposure time).

The polymeric materials were decomposed in a cup furnace located directly below the animal exposure chamber such that all the combustion products from the test materials evolved directly into the chamber. The materials were examined under separate nonflaming and flaming conditions which were achieved by setting the furnace 25°C below and above each material's predetermined autoignition temperature. In most cases, the CO concentration (an indicator of the completeness of combustion) reached a steady state in 5–10 min (Levin *et al.*, 1982). Douglas fir and red oak continued to produce CO throughout the 30-min exposures.

**Gas analysis.** Carbon monoxide and CO<sub>2</sub> were measured continuously by nondispersive infrared analyzers. Oxygen concentrations were measured continuously with either a galvanic cell or a paramagnetic analyzer. The CO, CO<sub>2</sub>, and O<sub>2</sub> data were recorded by an on-line computer every 15 sec. All combustion products and gases (except HCN) that were removed for chemical analysis were returned to the chamber. Syringe samples (100 μl) of the chamber atmosphere were analyzed for HCN approximately every 3 min with a gas chromatograph equipped with a thermionic detector (Paabo *et al.*, 1979). All given gas concentrations are the average expo-

sure values which were calculated by integrating the area under the instrument response curve and dividing by the exposure time.

**Blood analyses.** Animals designated for blood analysis were cannulated. This procedure involved anesthetizing the animals with pentobarbital sodium (0.09 g/kg) and surgically inserting a cannula into the animal's femoral artery. Sixteen to twenty-four hours later, blood samples (0.5 ml) were taken during and following the exposures from unanesthetized cannulated rats with syringes flushed with heparin. Carboxyhemoglobin (COHb) and oxyhemoglobin (O<sub>2</sub>Hb) were measured by a Co-Oximeter 282 (Instrumentation Laboratory Inc., Lexington, MA).

**Test procedure.** Six rats were exposed in each experiment. Animals were placed in restrainers which were then inserted into the six portholes located along the front of the exposure chamber such that only the heads of the animals were exposed. To achieve square-wave exposures, these portholes were fitted with rubber stoppers, during the time that the gas concentrations were reaching equilibrium. Insertion of the restrained animals caused the rubber stoppers to fall into the chamber and simultaneously exposed the animals to the chamber atmosphere. In the gradual gas and polymeric material experiments, the animals were inserted in the portholes first so that they were exposed to the initial generation (usually 5 min) of the test atmosphere as well as the later steady-state conditions.

Exposures were for 30 min, during which time blood was taken from the cannulated animals at zero time, approximately halfway through the exposure, and just before the end of the exposure (one or two animals were

cannulated in each experiment). The toxicological endpoint was death. The percentage of animals dying at each gas or fire effluent concentration was plotted to produce a concentration-response curve from which LC50 values were calculated for the 30-min exposures, for the 30-min exposures plus 24 hr (if most of the animals died in 24 hr as in the case of HCN), or for 30-min exposures plus 14-day postexposure observation period (as in the cases of the polymeric materials' combustion products). The LC50 in these cases is defined as the concentration of test gas in the chamber (ppm or %, where 1% = 10,000 ppm) or the amount of material placed in the furnace divided by the exposure chamber volume (mg/liter) which caused 50% of the animals to die during the exposure only or during the exposure plus the postexposure observation period. The LC50 values and their 95% confidence limits were calculated by the statistical method of Litchfield and Wilcoxon (1949). All animals (including the controls) were weighed daily from the day of arrival until the end of the 14-day postexposure observation period except for the cannulated ones which were sacrificed following exposure.

*Experimental design for individual and combined gas studies.* The 30-min LC50 values and their 95% confidence limits were determined, where possible, for the individual gases—CO, CO<sub>2</sub>, HCN, and reduced O<sub>2</sub> (Fig. 2). A matrix was designed depicting the LC50s of the individual gases. When two gases were studied, the concentrations were chosen from the area of the matrix in which no deaths would be expected from exposures to the individual gases. In some cases, the concentration of one gas was kept constant while the concentration of the other gas was varied to determine the effect on the LC50. When three gases were examined, the CO<sub>2</sub> was kept constant at approximately 5% and the concentrations of the other two gases were chosen from the area of the matrix where no deaths had occurred from the two-gas combinations.

*Kinetic blood uptake studies.* Some experiments were designed to determine the effect that the presence of other gases had on the rate of formation and final equilibrium level of COHb. In these experiments, all six rats were cannulated and exposed to preset concentrations of the gases. Blood (0.5 ml) was sampled at approximately 1-min intervals sequentially from different rats such that an excessive amount of blood was not taken from any one rat.

## RESULTS

### *Individual Gases*

The 30-min LC50 value determined in rats receiving square-wave exposures to CO in air was 4600 ppm with 95% confidence limits of

4400 to 4800 ppm (Fig. 2). Rats receiving gradual exposures to CO in air had 30-min LC50 values of 5000 ppm with 95% confidence limits of 4400 to 5600 ppm. The COHb levels in the cannulated animals just prior to the end of exposures equivalent to the LC50 were approximately 83%, and no animals with lower than this level died from exposures to CO alone. All deaths from the 30-min exposures to CO occurred during the exposures and not during the 14-day postexposure observation period.

Hydrogen cyanide produced deaths during both the 30-min square-wave exposures and the postexposure observation period. The 30-min LC50 was 160 ppm with 95% confidence limits of 140 to 180 ppm (Fig. 2). Most of the postexposure deaths occurred within 24 hr; the few deaths noted beyond that time did not significantly affect the LC50 values. If the 24-hr postexposure deaths were included in the calculation, the LC50 value was reduced to 110 ppm with 95% confidence limits of 97 to 127 ppm.

Exposures to low atmospheric concentrations of O<sub>2</sub> also produced deaths primarily during the exposures (only 1 out of 42 exposed rats died postexposure and this death occurred on Day 4). The 30-min LC50 value was 7.5% with 95% confidence limits of 7.3 to 7.7% (Figs. 2 and 3A). In a series of experiments in which the atmospheric O<sub>2</sub> ranged from 7.3 to 7.9%, the 15-min oxyhemoglobin (O<sub>2</sub>Hb) levels decreased from control values of  $94.1 \pm 1.8\%$  ( $n = 180$ ) to values ranging from 4.0 to 22.6% (Fig. 3B). Oxyhemoglobin values from blood taken 15 mins into the 30-min exposures usually were 6 to 20% lower than those sampled just prior to the end of the exposures.

Carbon dioxide by itself produced no deaths during either exposure or postexposure at any of the tested concentrations (up to 14.6%).

As explained under Methods, Fig. 2 depicts a matrix which shows the 30-min LC50 values and the 95% confidence limits for CO, HCN, and O<sub>2</sub>. Based on these individual gas LC50s, the concentrations below the 95%

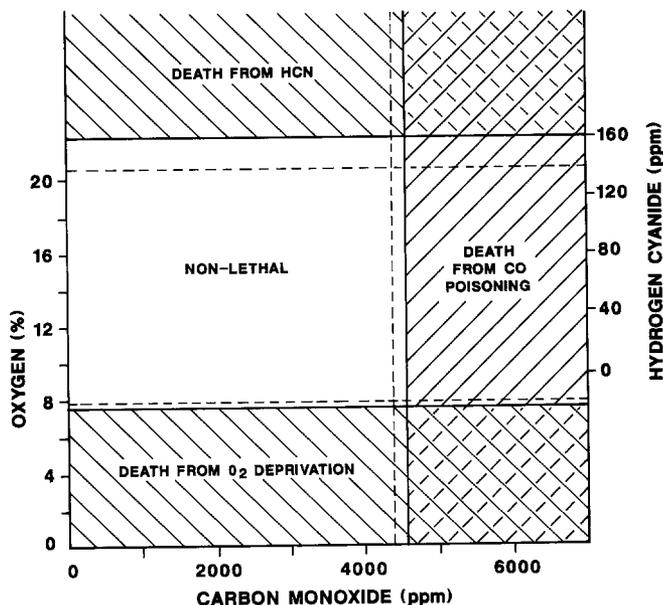


FIG. 2. Matrix depicting lethal concentrations of HCN, CO, and O<sub>2</sub> based on their LC50 values and 95% confidence limits (dashed lines) in rats exposed for 30 min.

confidence limits for CO and HCN and above that of O<sub>2</sub> could be considered "nonlethal."

#### Combined Gases

*Carbon monoxide and hydrogen cyanide.* Thirty-minute experiments on the lethal effects of combinations of CO and HCN in air indicated that these two gases act in an additive manner such that if

$$\frac{[\text{CO}]}{\text{LC50 CO}_{(30\text{min})}} + \frac{[\text{HCN}]}{\text{LC50 HCN}_{(30\text{min})}} \geq 1, \quad (1)$$

then some or all of the exposed animals will die (the values in brackets are the test concentrations of the gases). If the left-hand side of the above equation is less than 1, the animals will live. Ideally, when this equation is equal to 1, 50% of the test animals should die. In actuality, the data supporting this equation show that the sum of the normalized concentrations producing some deaths are between approximately 0.98 and 1.10 (Table 1).

Above and below these values (see Experiments 4 and 8, Table 1), all or no deaths were observed. As the concentration-response curves of CO, HCN, or O<sub>2</sub> as individual gases are very steep (Fig. 3A is an example), the deaths of 1 to 5 animals during these 30-min experiments are indicative that the concentrations of the combined gases are close to the LC50 values. Within the range of approximately 0.98 and 1.10, the number of deaths could vary as observed in Experiments 5 and 7 in Table 1.

Table 1 also shows that as [CO] decreases and [HCN] increases, the animals die at lower concentrations of CO and, consequently, COHb levels lower than if the CO were given alone. A standard curve developed in our laboratory of equilibrium levels of COHb generated at various atmospheric CO concentrations showed that the COHb values obtained in the combined CO and HCN experiments are systematically lower than those expected at equilibrium from comparable CO exposures (Fig. 4A). The degree of reduction of COHb depends on the HCN concentration. The polymeric materi-

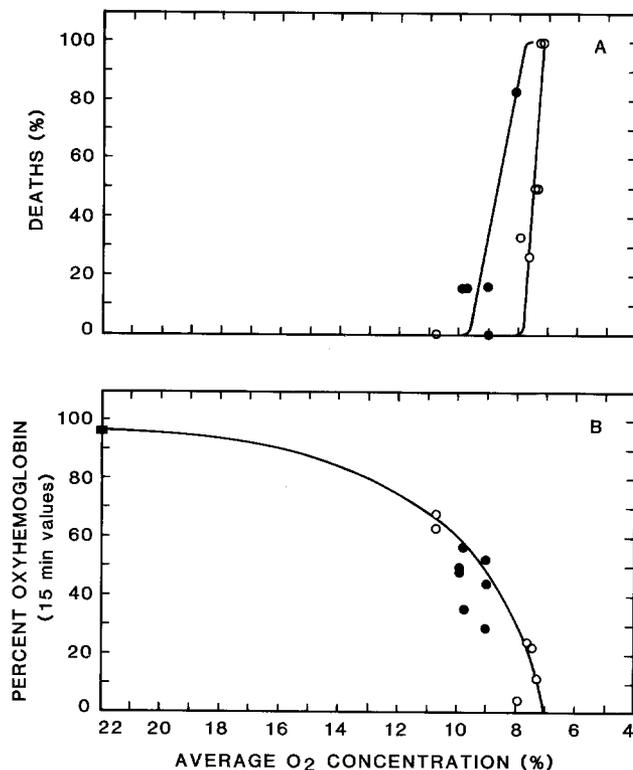


FIG. 3. (A) Concentration-response curves depicting deaths of rats exposed for 30 min to reduced O<sub>2</sub> atmospheres with (●) or without 5% CO<sub>2</sub> (○). (B) Oxyhemoglobin levels in rats exposed to reduced O<sub>2</sub> atmospheres with (●) and without 5% CO<sub>2</sub> (○). ■ = mean of 180 control values. Standard deviation of controls was 1.8%.

als showed similar results in that animals exposed to the thermal decomposition products from polymeric materials which produce relatively high HCN concentrations have lower levels of COHb than that predicted by the atmospheric concentrations of CO (Fig. 4B). On the other hand, 40 mg/liter of flexible polyurethane foam (FPU) only produced 22 ppm of HCN which apparently was not sufficient to produce this effect.

This lower than expected level of COHb in the presence of both HCN and CO was examined to determine if the HCN was affecting the initial rate of uptake and formation of COHb and/or the final equilibrium levels. Figure 5 shows that at the concentrations tested (1470 ppm of CO alone or 1450 ppm CO plus 100 ppm HCN), the initial rate of formation of COHb was the same in the pres-

ence and absence of HCN. The final COHb equilibrium, however, was lower when the animals were exposed to both gases.

*Carbon monoxide and carbon dioxide.* In 30-min. experiments, sublethal concentrations of CO<sub>2</sub> (1 to 17.3%<sup>7</sup>) in combination with sublethal levels of CO (2500 to 4000 ppm) caused deaths of some of the rats both during exposures and during the following 24 hr (Fig. 6) (Levin *et al.*, 1987). The solid line in Fig. 6 was drawn to separate the experiments in which some animals died from those with no deaths. Based on this line, the most toxic combination of these two gases appears to be approximately 5% CO<sub>2</sub> and 2500

<sup>7</sup> Even though 17.3% CO<sub>2</sub> was not tested by itself, it is considered nonlethal because 17.7% CO<sub>2</sub> in the presence of 3200 ppm of CO did not produce any deaths (Fig. 6).

TABLE 1  
CARBON MONOXIDE AND HYDROGEN CYANIDE  
30-MIN EXPOSURES

Expt	Fraction of LC50			No. died/6 animals	COHb (%)
	CO	HCN	CO + HCN		
1	1.00	0	1.00	3	84 <sup>a</sup>
2	1.00	0	1.00	5	83
3	0.75	0.27	1.02	4	79 <sup>a</sup>
4	0.75	0.38	1.13	6	67 <sup>a</sup>
5	0.52	0.58	1.10	3	—
6	0.50	0.53	1.03	5	67 <sup>a</sup>
7	0.49	0.49	0.98	5	71 <sup>a</sup>
8	0.38	0.48	0.86	0	—
9	0.28	0.78	1.06	3	45 <sup>a</sup>
10	0.27	0.79	1.06	3	43 <sup>a</sup>
11	0	0.98	0.98	2	—
12	0	1.00	1.00	1	—
13	0	1.08	1.08	4	—

Note. LC50 of CO = 4600 ppm; LC50 of HCN = 160 ppm. These LC50 values were based on deaths within the 30-min exposures only.

<sup>a</sup> Animal died during exposure.

ppm CO. Above and below 5% CO<sub>2</sub> (1 to 17.3%), more CO (but still concentrations below the 95% confidence limits of the CO LC50 value) was necessary to produce the deaths. The effect of the combined gases, CO and 5% CO<sub>2</sub>, on the matrix shown in Fig. 2 is illustrated in Fig. 7. An empirical mathematical relationship derived to predict deaths of some of the animals from exposures to CO plus CO<sub>2</sub> is

$$\frac{m[\text{CO}]}{[\text{CO}_2] - b} \approx 1, \quad (2)$$

where [CO] and [CO<sub>2</sub>] are the atmospheric concentrations of CO and CO<sub>2</sub> in ppm, respectively;  $m$  and  $b$  are the slope and  $y$  intercept, respectively, of the solid line in Fig. 6 and equal -28 and 117,000 ppm, respectively, if the atmospheric concentration of CO<sub>2</sub> is  $\leq 5\%$  and equal 150 and -313,000 ppm, respectively, if CO<sub>2</sub> is  $> 5\%$ . If the left-hand side of Eq. (2) is less than approximately 1, then the animals will live.

*Low oxygen and 5% carbon dioxide.* According to the concentration-response curve

obtained for O<sub>2</sub> alone, no deaths would be expected at O<sub>2</sub> levels above 8% (Fig. 3A). However, in the presence of 5% CO<sub>2</sub> (chosen because this concentration appeared to be the most toxic when combined with CO), animals died at O<sub>2</sub> concentrations higher than 8%. The LC50 increased to 8.8% with 95% confidence limits of 8.4 to 9.2% and deaths were observed as high as 9.9% O<sub>2</sub> (Fig. 3A). The decrease in arterial O<sub>2</sub>Hb produced from exposures to low O<sub>2</sub> concentrations plus 5% CO<sub>2</sub> was similar to that seen with low O<sub>2</sub> alone (Fig. 3B). If anything, the curve may shift slightly such that at the same concentration of O<sub>2</sub>, the O<sub>2</sub>Hb would be slightly lower in the presence of CO<sub>2</sub>. Figure 7 shows the further encroachment on the zone labeled "nonlethal" when 5% CO<sub>2</sub> is added to the low O<sub>2</sub> exposures.

*Hydrogen cyanide and 5% carbon dioxide.*

When the animals were exposed to both HCN and 5% CO<sub>2</sub>, deaths occurred during the 30-min exposures and the following 24 hr. Comparison of the LC50 values (including the postexposure deaths) for HCN alone or with CO<sub>2</sub> indicated that the LC50 was lower (75 ppm with 95% confidence limits of 62 to 91 ppm) for the combined gases than for the HCN alone (110 ppm with 95% confidence limits of 97 to 127 ppm).

*Carbon monoxide, low oxygen, and 5% carbon dioxide.* A number of experiments were undertaken to delineate further the area in Fig. 7 designated as nonlethal. In all experiments, the concentration of CO<sub>2</sub> was approximately 5% [mean concentration was 50,800  $\pm$  a standard deviation of 1020 ppm ( $n = 9$ )]. The CO concentrations ranged from 410 to 2300 ppm and the O<sub>2</sub> concentrations were between 9.9 and 15.8%. With the exception of one animal which died 3 days postexposure, all deaths occurred either during the 30-min exposures or during the following 3 hr. Examination of the matrix in Fig. 7 will indicate the concentrations of the three gases which together cause deaths in the previously designated nonlethal area. The zone considered nonlethal becomes even smaller when

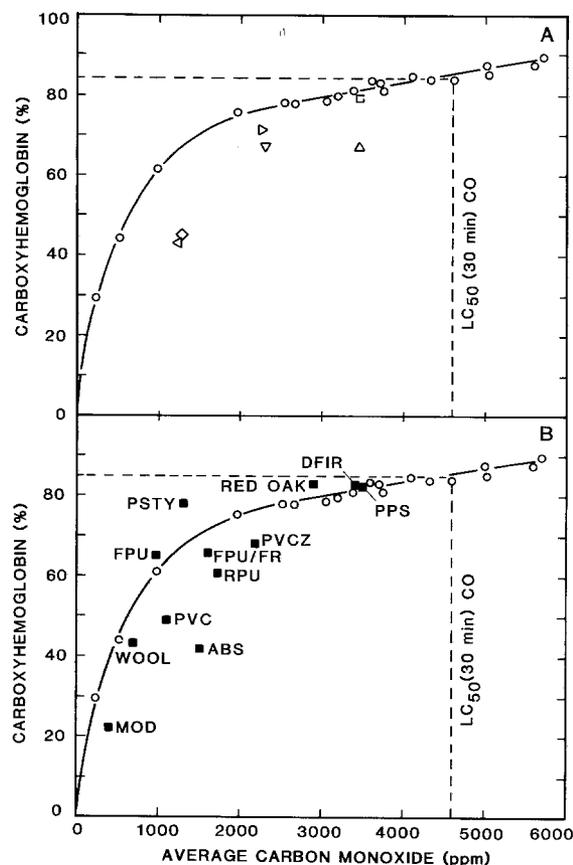


FIG. 4. (A) Comparison of carboxyhemoglobin equilibrium levels in rats after exposure to CO (○) or CO plus various concentrations of HCN: 43 ppm (□); 61 ppm (△); 78 ppm (▽); 85 ppm (◇); 125 ppm (◁); 126 ppm (▷). (B) Comparison of carboxyhemoglobin levels in rats after exposure to CO as a separate gas (○) or from the CO from materials (flaming mode) at their LC<sub>50</sub> values (■). For abbreviations and concentrations of CO and HCN from the material decomposition, see Table 2.

the additive effects of CO and HCN are overlaid (Fig. 7).

$$\frac{m[\text{CO}]}{[\text{CO}_2] - b} + \frac{[\text{HCN}]}{d} \approx 1 \quad (3)$$

#### *Thermal Decomposition of Polymeric Materials*

The gas concentrations (CO, CO<sub>2</sub>, HCN) and the COHb levels produced at the LC<sub>50</sub> values (30-min exposures and 14-day postexposure periods) from 12 different polymeric materials thermally decomposed under both flaming and nonflaming conditions are shown in Table 2. Equations (1) and (2) were combined to predict deaths from the material decomposition products as follows:

where [CO], [CO<sub>2</sub>],  $m$ , and  $b$  are the same as in Eq. (2) and [HCN] and  $d$  are the atmospheric test and the lethal concentrations of HCN, respectively. The value of  $d$  will vary depending on whether it is the within-exposure deaths (160 ppm) or the within exposure plus postexposure deaths (110 ppm) that are of concern. Table 2 indicates that in 14 out of 21 cases where deaths occurred, the value of the left-hand side of Eq. (3) was 0.95 or higher. In the three cases (nonflaming fire-retarded flexible polyurethane foam, nonflaming polystyrene, and nonflaming rigid poly-

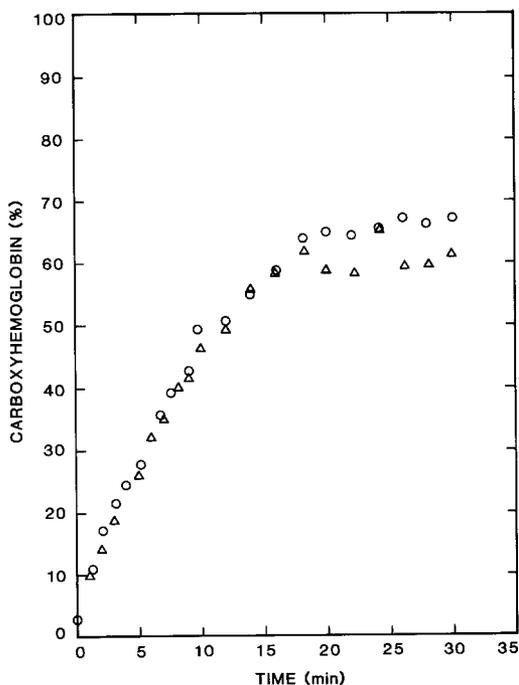


FIG. 5. Generation and equilibrium levels of carboxyhemoglobin in rats exposed to 1470 ppm of CO alone (○) or 1450 ppm of CO plus 100 ppm HCN (△).

urethane foam) where no deaths occurred, the value was less than 0.84. Therefore, in 17 out of 24 cases, the deaths, or lack thereof, were predictable based on the interaction of the combined gases as delineated by Eq. (3). There were, however, 7 cases in which Eq. (3) ranged from 0.15 to 0.67 and deaths occurred.

#### DISCUSSION

Although smoke is a composite of many gases and particulates, it is still common practice for emergency personnel to assume deaths are primarily due to CO and to treat the survivors of such accidents as though CO were the only fire gas of any major toxic consequence (Strohl *et al.*, 1980). In direct contradiction to this assumption, the epidemiological studies in the United States and Great Britain show that many people dying in fires have less than 50% COHb in their blood.

These studies indicate that other factors in addition to CO are contributing to these deaths (Birky *et al.*, 1979; Anderson *et al.*, 1981b). Our studies compared the concentrations of CO generated from 12 polymeric materials decomposed under separate flaming and nonflaming conditions at their LC50 values to the lethal concentrations of CO by itself and found that the deaths could be attributed to the concentration of CO alone in only one case (specifically, polyphenylsulfone in the nonflaming mode).

The approach taken in this series of experiments has been to determine the extent to which a limited number of primary fire gases, CO, CO<sub>2</sub>, HCN, and low O<sub>2</sub>, either singly or in combination can explain the toxicity produced by the flaming and nonflaming combustion products from polymeric materials or if minor and/or more obscure products need to be examined. There are at least three documented cases in which such minor products do play a role (Kalman *et al.*, 1985; Petajan *et al.*, 1975; Williams and Clarke, 1983). These cases include a fire-retarded rigid polyurethane foam and a synthetic lubricant oil (both of which produced a bicyclic phosphite neurotoxic agent) and polytetrafluoroethylene (where the identity of the toxic agent is still a matter of controversy).

Combined exposures to CO and HCN showed that the toxicity of these two gases were additive if calculated as ratios of their 30-min LC50s and that as the CO concentrations decrease and the HCN concentrations increase, the COHb levels decrease (Table 1). This decrease is actually lower than the COHb equilibrium level expected from the comparable CO concentration. Our investigation of the kinetic uptake of CO and the formation of COHb in the presence and absence of HCN showed that the initial rate of formation of COHb is the same; however, the final COHb equilibrium level is reduced when HCN is present (Fig. 5). These results do not support the hypothesis of Kimmerle (1974) and Moss *et al.* (1951) that HCN increases the respiration rate, thereby producing a more rapid uptake of CO. Our results indicate that the animals are not receiving

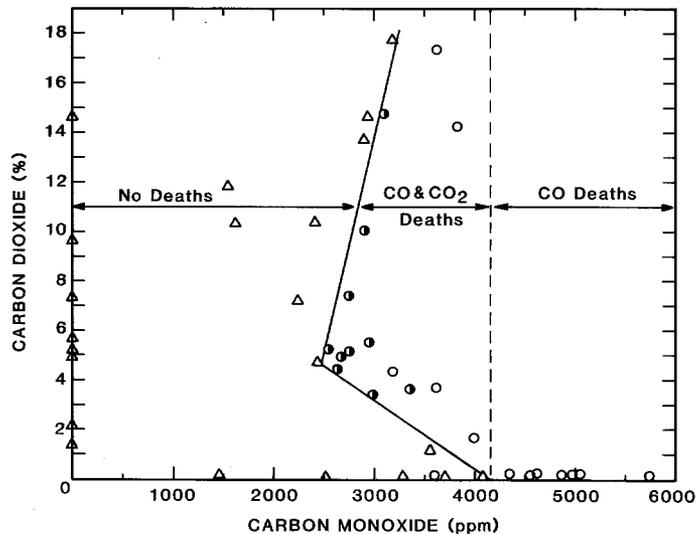


FIG. 6. Deaths resulting from CO or CO<sub>2</sub> alone and from combined exposures to CO plus CO<sub>2</sub>. No deaths (Δ); within-exposure deaths (○); within and post exposure deaths (●). The solid line separates the experiments in which no deaths occurred from those in which one or more animals died.

more CO in the presence of HCN, but less (Fig. 4A). This depressive effect of HCN on CO uptake may help explain why some people dying in fires have low COHb levels (<50%) (Birky *et al.*, 1979; Anderson *et al.*, 1979, 1981a,b, 1983).

Higgins *et al.* (1972), however, did not observe any significant changes in the 5-min

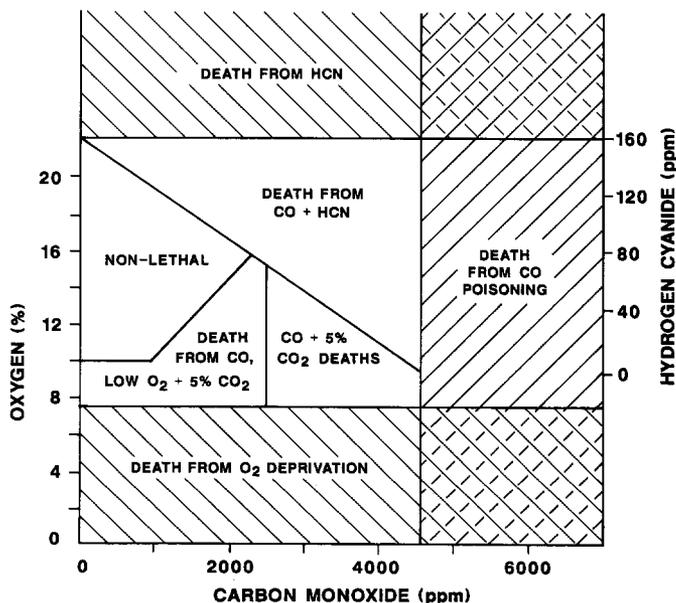


FIG. 7. Lethal concentrations of individual gases, CO, O<sub>2</sub>, and HCN, and various combinations of these gases with and without 5% CO<sub>2</sub>.

TABLE 2  
CONCENTRATIONS OF CARBON MONOXIDE, CARBOXYHEMOGLOBIN, CARBON DIOXIDE,  
AND HYDROGEN CYANIDE FROM MATERIALS EXAMINED AT THEIR LC50 VALUES

Material	Mode <sup>a</sup>	LC50 <sup>b</sup> (mg/liter)	CO <sup>c</sup> (ppm)	COHb <sup>d</sup> (%)	CO <sub>2</sub> <sup>c</sup> (%)	HCN <sup>c</sup> (ppm)	Value of Eq. (3) <sup>e</sup>	Observed deaths <sup>f</sup>	Predicted results <sup>e</sup>
ABS	F	19.3	1500	42	1.07	130	1.21	W	Yes
	NF	30.9	670	27	0.53	160	1.62	P	Yes
Douglas fir (DFIR)	F	39.8	3400	83	3.71	—	1.19	W	Yes
	NF	22.8	2700	81	0.69	—	0.67	W, P	No
Flexible polyurethane (FPU)	F	>40	960 <sup>g</sup>	65 <sup>g</sup>	4.79 <sup>g</sup>	22 <sup>g</sup>	0.53	W	No
	NF	26.6	820	54	0.32	10	0.29	P	No
Flexible polyurethane, fire-retarded (FPU/FR)	F	27.8	1600	66	2.28	76	0.95, 1.17	W, P	Yes
	NF	>40	400 <sup>g</sup>	—	0.31 <sup>g</sup>	<1	0.10	*	Yes
Modacrylic (MOD)	F	4.4	400	22	0.39	180	1.22, 1.73	W, P	Yes
	NF	5.3	430	16	0.53	250	1.67	W	Yes
Polyphenylsulfone (PPS)	F	19.8	3500	82	2.27	—	1.22, 1.73	W, P	Yes
	NF	9.5	4400	84	0.51	—	1.67	W	Yes
Polystyrene (PSTY)	F	38.9	1300	78	1.95	—	0.37	W	No
	NF	>40	72 <sup>g</sup>	6 <sup>g</sup>	0.21	—	0.02	*	Yes
Polyvinyl chloride (PVC)	F	17.3	1100	49	0.55	—	0.28	P	No
	NF	20.0	590	27	0.46	—	0.15	P	No
PVC + zinc ferrocyanide (PVCZ)	F	15.0	2200	68	0.97	110	1.26, 1.57	W, P	Yes
	NF	11.3	1200	36	0.53	150	1.66	P	Yes
Red oak	F	56.8	2800	83	4.06	—	1.03	W	Yes
	NF	30.3	2400	80	0.72	—	0.61	P	No
Rigid polyurethane (RPU)	F	13.3	1700	61	1.20	130	1.27	W	Yes
	NF	>40	1700 <sup>g</sup>	47 <sup>g</sup>	0.94 <sup>g</sup>	44 <sup>g</sup>	0.72, 0.84	*	Yes
Wool	F	28.2	700	43	ND	130	1.03, 1.40	W, P	Yes
	NF	25.1	920	41	0.71	240	1.73, 2.42	W, P	Yes

<sup>a</sup> F, flaming material decomposition; NF, nonflaming material decomposition.

<sup>b</sup> Based on deaths during 30-min exposures plus 14-day postexposure periods.

<sup>c</sup> Average 30-min concentration.

<sup>d</sup> Value obtained prior to end of 30-min exposure.

<sup>e</sup> Results predicted from Eq. (3) (see text). If two numbers are given, left is for within-exposure deaths only and right includes postexposure deaths.

<sup>f</sup> W, within-exposure deaths; P, postexposure deaths; \*, no deaths in range studied.

<sup>g</sup> Value obtained when 40 mg/liter of material was tested.

LC50 value of HCN when the animals were also exposed to enough CO to generate 25% COHb. In this case, the amount of HCN needed to produce death from a 5-min exposure may be sufficiently high that the effect of 25% COHb was not apparent. Anderson and his co-workers (1979, 1981a,b, 1983) in their studies of fire deaths in the Glasgow area and the United Kingdom found that 78% of the fire deaths had blood cyanide levels greater than normal. Although they considered HCN a contributory factor, they did not find any evidence of the additivity of the toxicities of CO and HCN. Their conclusions are based

on the assumption that 50% COHb is the lethal concentration and since high levels of blood cyanide were usually found in conjunction with high levels of CO, they concluded that these deaths (>50% COHb) were due to CO. If, however, as found in our animal studies, 50% COHb is not sufficient to cause death, then reevaluation of their data may show the additive effects of CO and HCN.

There is a range of CO concentrations (2500 to 4100 ppm) which when presented alone to the animals has a very low probability of causing death, but in the presence of certain levels of CO<sub>2</sub> (>1.5%) will act with a

much higher probability to cause the death of the animals. The mechanism for this synergistic interaction appears to be due to an increased rate of formation of COHb, a very severe degree of acidosis (both metabolic acidosis resulting from exposure to CO alone and a respiratory acidosis resulting from CO<sub>2</sub>), and a decreased rate of recovery from this acidosis following the exposures (Levin *et al.*, 1987). The end result is that the animals die both during the combined exposures to sublethal levels of CO and CO<sub>2</sub> and during the following 24 hr.

Five percent CO<sub>2</sub> was chosen to determine its effect on other gases (i.e., low O<sub>2</sub>, HCN, or the combination of CO and low O<sub>2</sub>) since this concentration of CO<sub>2</sub> appeared to cause the greatest increase in the toxicity of CO. This concentration of CO<sub>2</sub> is well below the concentration (40%) determined necessary to kill mice in 4 hr (Pryor *et al.*, 1974). The addition of 5% CO<sub>2</sub> caused deaths of the animals at O<sub>2</sub> concentrations which in the absence of CO<sub>2</sub> would not be lethal. As only one concentration of CO<sub>2</sub> was examined, more work similar to that done in the case of the combined toxicities of CO and CO<sub>2</sub> is needed to delineate whether this effect of CO<sub>2</sub> on low O<sub>2</sub> toxicity is additive or synergistic. Pryor *et al.* (1974) in 4 hr experiments on mice also found deaths at 7.5% O<sub>2</sub>, but none at the next higher tested concentration of 11%. In their combination experiments, deaths were now observed at both 11 and 13.5% O<sub>2</sub> when 30% CO<sub>2</sub> was present.

The presence of 5% CO<sub>2</sub> also increased the toxicity of HCN. Since only one concentration of CO<sub>2</sub> was examined, albeit the concentration which appears to produce the worst case conditions, it is not possible to determine whether the combined effect is linearly additive or synergistic.

The presence of all three gases, CO, low O<sub>2</sub>, and 5% CO<sub>2</sub>, further exacerbates the conditions that would have been considered nonlethal based on the evaluation of the separate gases or even the various combinations of two. Pryor *et al.* (1974) examined many combinations of CO, CO<sub>2</sub>, and low O<sub>2</sub> in their 4-

hr experiments on mice. Examination of the single variables showed that 7.5% O<sub>2</sub> or 1250 ppm CO or 40% CO<sub>2</sub> was necessary for deaths to occur. With the combinations of the three gases, it was found that deaths occurred at 13.5% O<sub>2</sub>, 500 ppm CO, and 5% CO<sub>2</sub>. If the hypothesis of linear additivity can be assumed for these three gases, then death would have been predicted by the sum of the ratios of the atmospheric concentrations of each gas to its lethal concentrations as follows:

$$\frac{500}{1250} + \frac{5}{40} + \frac{(21 - 13.5)}{(21 - 7.5)} \approx 1.$$

This equation adds up to 1.08 which is not significantly different and could be interpreted to indicate linear additivity under these conditions.

Another purpose of this series of experiments was to determine whether the results on the primary toxic fire gases, CO, CO<sub>2</sub>, and HCN, could be used to predict the deaths of the animals exposed to the thermal decomposition products from polymeric materials. Examination of 12 different polymers thermally decomposed under separate flaming and nonflaming conditions showed that Eq. (3) based on our pure-gas results would correctly predict the deaths in 17 out of 24 cases. In cases where the equation did not correctly predict the outcome, toxic species other than those studied must be contributing to the overall toxicity and need further investigation.

One interesting observation was that in some cases, the value of Eq. (3) at the LC50 value of the material was notably greater than one. These cases were those in which the HCN concentration is close to or greater than its LC50 value of 160 ppm (within-exposure deaths) or 110 ppm (within-exposure plus 24-hr deaths). The situation in which the HCN concentration is greater than its LC50 value would indicate that either the animals are not inhaling the amount of HCN expected from the atmospheric concentrations or other gases or combustion products are interfering with the action of the toxicant (acting as an antagonist).

Another case unexplained by Eq. (3) was that of PVC. Since it is well known that upon thermal decomposition, approximately 58% of the mass of pure PVC will be HCl, we calculated whether sufficient HCl could be produced to account for the deaths. When evaluated according to the NBS Toxicity Test Method, the LC50 values of the tested PVC (a 92% homopolymer) were found to be 17.3 and 20 mg/liter in the flaming and nonflaming modes, respectively. Assuming a conservative yield of 50% of the PVC mass is HCl, these LC50 values would equate to 5800 ppm (flaming) and 6700 ppm (nonflaming) of HCl. The possibility that some of the HCl in our exposure system was lost in the lines leading to the analytical instruments was also considered. Since 2 liters/min of the combustion atmosphere are removed from the 200-liter animal exposure chamber, flow through a cold trap, and then through the analytical instruments before being returned to the exposure chamber, in the worst case (where all the HCl in the sample removed for analysis was lost), the HCl concentration in the exposure chamber would be reduced by 14%, leaving approximately 5000 and 5800 ppm of HCl in the flaming and nonflaming modes, respectively. Since experiments with rats at Southwest Research Institute showed that the HCl LC50 value for 30-min exposures plus 14-day postexposure periods was 3700 ppm with 95% confidence limits of 2500 to 5400 ppm (Hartzell *et al.*, 1985a), these values of HCl alone are sufficient to account for the deaths of the animals following exposure to the thermal decomposition products of PVC. Therefore, it appears that there is no need to examine the added contributions of other gases, although some experiments on combinations of HCl with CO over a limited range have been reported (Hartzell *et al.*, 1985b; Higgins *et al.*, 1972). The experiments by Hartzell *et al.* (1985b) are not useful in explaining the observed postexposure deaths since only the time to incapacitation and death during the exposures were examined. In the experiments by Higgins *et al.* (1972), LC50 values (based on mortalities in mice

and rats from 5-min exposures to HCl plus 7-day postexposure periods) were determined with and without sufficient CO to produce a 25% COHb blood level. No statistically significant differences in LC50 values were observed, indicating that this low level of CO did not affect the 5-min LC50 of HCl.

#### *A Bioanalytical Approach to Toxicity Testing of Fire Effluents*

One of the consequences of the research described in this paper is the development of a bioanalytical approach for assessing the toxicity of combustion products (Babrauskas *et al.*, 1986). This bioanalytical procedure consists of two steps. First, the LC50 values of combustible materials is predicted based on the concentrations of the primary toxic gases produced during thermal decomposition and knowledge of their combined toxicities as delineated in this study. Second, the validity of these predicted values is checked with approximately two animal tests. If the predicted values agree with the results of the animal tests based on deaths of >0 and <100% of the animals (an approximate LC50 value since the concentration-response curves of the thermal decomposition products of most materials are extremely steep), then further testing would be deemed unnecessary. If, however, all the exposed animals died, the material is probably producing toxic products other than those examined and further testing is needed to determine the more exact LC50 or the responsible toxic product(s). The advantages of this bioanalytical approach include (1) minimizing the use of animals in the experiments; (2) significantly decreasing the cost and time necessary to test materials; and (3) detecting the presence, but not necessarily the identity, of extremely or unusually toxic thermal decomposition products. These results and their obvious extension will be directly applicable to the implementation of a fire hazard computer model currently being developed at the National Bureau of Standards to predict the hazards generated in fires

and the occupant response to combustion atmospheres (Jones, 1984).

*Note added in proof.* The values of  $m$  and  $b$  in Eq. (2) are empirically determined under well-defined conditions. Changes in these conditions may necessitate re-evaluation of these parameters.

## REFERENCES

- ANDERSON, R. A., THOMSON, I., AND HARLAND, W. A. (1979). The importance of cyanide and organic nitriles in fire fatalities. *Fire Mater.* **3**, 91-99.
- ANDERSON, R. A., WATSON, A. A., AND HARLAND, W. A. (1981a). Fire deaths in the Glasgow area. I. General considerations and pathology. *Med. Sci. Law* **21**, 175-183.
- ANDERSON, R. A., WATSON, A. A., AND HARLAND, W. A. (1981b). Fire deaths in the Glasgow area. II. The role of carbon monoxide. *Med. Sci. Law* **21**, 288-294.
- ANDERSON, R. A., WILLETTS, K. N., CHENG, K. N., AND HARLAND, W. A. (1983). Fire deaths in the United Kingdom 1976-82. *Fire Mater.* **7**, 67-72.
- BABRAUSKAS, V., LEVIN, B. C., AND GANN, R. G. (1986). A new approach to fire toxicity data for hazard evaluation. *ASTM Stand. News* **14**, 28-33.
- BIRKY, M. M., HALPIN, B. M., CAPLAN, Y. H., FISHER, R. S., MCALLISTER, J. M., AND DIXON, A. M. (1979). Fire fatality study. *Fire Mater.* **3**, 211-217.
- CAGLIOSTRO, D. E., AND ISLAS, A. (1982). The effects of reduced oxygen and of carbon monoxide on performance in a mouse pole-jump apparatus. *J. Combust. Toxicol.* **9**, 187-193.
- CRANE, C. R. (1985). Are the combined toxicities of CO and CO<sub>2</sub> synergistic? *J. Fire Sci.* **3**, 143-144.
- EDGINTON, J. A. G., AND LYNCH, R. D. (1975). *The Acute Inhalation Toxicity of CO from Burning Wood*. Fire Research Note No. 1040, Fire Research Station, Salisbury, Wiltshire, England.
- GAUME, J. G., BARTEK, P., AND ROSTAMI, H. J. (1971). Experimental results on time of useful function (TUF) after exposure to mixtures of serious contaminants. *Aerospace Med.*, pp. 987-990.
- HARTZELL, G. E., PACKHAM, S. C., GRAND, A. F., AND SWITZER, W. G. (1985a). Modeling of toxicological effects of fire gases. III. Quantification of post-exposure lethality of rats from exposures to HCl atmospheres. *J. Fire Sci.* **3**, 195-207.
- HARTZELL, G. E., STACY, H. W., SWITZER, W. G., PRIEST, D. N., AND PACKHAM, S. C. (1985b). Modeling of toxicological effects of fire gases. IV. Intoxication of rats by carbon monoxide in the presence of an irritant. *J. Fire Sci.* **3**, 263-279.
- HARTZELL, G. E., SWITZER, W. G., AND PRIEST, D. N. (1985c). Modeling of toxicological effects of fire gases. V. Mathematical modeling of intoxication of rats by combined carbon monoxide and hydrogen cyanide atmospheres. *J. Fire Sci.* **3**, 330-342.
- HIGGINS, E. A., FIORCA, V., THOMAS, A. A., AND DAVIS, H. V. (1972). Acute toxicity of brief exposures to HF, HCl, NO<sub>2</sub>, and HCN with and without CO. *Fire Technol.* **8**, 120-130.
- JONES, W. W. (1984). *A Model for the Transport of Fire, Smoke and Toxic Gases (FAST)*. NBSIR 84-2934, National Bureau of Standards, Gaithersburg, MD.
- KALMAN, D. A., VOORHEES, K. J., OSBORNE, D., AND EINHORN, I. N. (1985). Production of a bicyclic phosphite neurotoxic agent during pyrolysis of synthetic lubricant oil. *J. Fire Sci.* **3**, 322-329.
- KIMMERLE, M. G. (1974). Aspects and methodology for the evaluation of toxicological parameters during fire exposure. *J. Fire Flammability/Combust. Toxicol. Suppl.* **1**, 4-51.
- KISHITANI, K., AND NAKAMURA, K. (1979). Research on evaluation of toxicities of combustion gases generated during fires. In *Fire Research and Safety* (M. A. Sherald, Ed.), National Bureau of Standards Special Publication 540, Proceedings of the Third Joint Panel Conference of the U.S.-Japan Cooperative Program in Natural Resources held at the National Bureau of Standards, Gaithersburg, MD (March, 1978).
- KLAASSEN, C. D., AND DOULL, J. (1980). Evaluation of safety: Toxicological evaluation. In *Casarett and Doull's Toxicology* (J. Doull, C. D. Klaassen, and M. O. Amdur, Eds.), Chap. 2. Macmillan Co., New York.
- LEVIN, B. C. (1986). *A Summary of the NBS Literature Reviews on the Chemical Nature and Toxicity of the Pyrolysis and Combustion Products from Seven Plastics: Acrylonitrile-Butadiene-Styrenes (ABS), Nylons, Polyesters, Polyethylenes, Polystyrenes, Poly(vinyl chlorides) and Rigid Polyurethane Foams*. NBSIR 85-3267, National Bureau of Standards, Gaithersburg, MD.
- LEVIN, B. C., FOWELL, A. J., BIRKY, M. M., PAABO, M., STOLTE, A., AND MALEK, D. (1982). *Further Development of a Test Method for the Assessment of the Acute Inhalation Toxicity of Combustion Products*. NBSIR 82-2532, National Bureau of Standards, Gaithersburg, MD.
- LEVIN, B. C., PAABO, M., AND BIRKY, M. M. (1983a). *An Interlaboratory Evaluation of the 1980 Version of the National Bureau of Standards Test Method for Assessing the Acute Inhalation Toxicity of Combustion Products*. NBSIR 83-2678, National Bureau of Standards, Gaithersburg, MD.
- LEVIN, B. C., PAABO, M., FULTZ, M. L., BAILEY, C., YIN, W., AND HARRIS, S. E. (1983b). *An Acute Inhalation Toxicological Evaluation of Combustion Products from Fire Retarded and Non-fire Retarded Flexible Polyurethane Foam and Polyester*. NBSIR 83-2791, National Bureau of Standards, Gaithersburg, MD.
- LEVIN, B. C., PAABO, M., GURMAN, J. L., HARRIS, S. E., AND BRAUN, E. (1987). *Toxicological Interac-*

- tion between Carbon Monoxide and Carbon Dioxide: Proceedings of the 16th Annual Meeting of Toxicology, Harry G. Armstrong Aerospace Medical Research Laboratory and U.S. Naval Medical Research Institute, Dayton, OH, October 30, 1986. Air Force Aerospace Medical Research Laboratory, Wright-Patterson Air Force Base, OH.
- LITCHFIELD, J. T., AND WILCOXON, F. (1949). A simplified method of evaluating dose-effect experiments. *J. Pharmacol. Exp. Ther.* **96**, 99-113.
- LYNCH, R. D. (1975). *On the Non-existence of Synergism between Inhaled Hydrogen Cyanide and Carbon Monoxide*. Fire Research Note No. 1035, Fire Research Station, Borehamwood, Hertfordshire, England.
- MOSS, R. H., JACKSON, C. F., AND SEIBERLICH, J. (1951). Toxicity of carbon monoxide and hydrogen cyanide gas mixtures. *Arch. Ind. Hyg. Occup. Med.* **4**, 53-64.
- NELSON, G. L., HIXON, E. J., AND DENINE, E. P. (1978). Combustion product toxicity studies of engineering plastics. *J. Combust. Toxicol.* **5**, 222-238.
- PAABO, M., BIRKY, M. M., AND WOMBLE, S. E. (1979). Analysis of hydrogen cyanide in fire environments. *J. Combust. Toxicol.* **6**, 99-108.
- PETAJAN, J. H., VOORHEES, K. J., PACKHAM, S. C., BALDWIN, R. G., EINHORN, I. N., GRUNNET, M. L., DINGER, B. G., AND BIRKY, M. M. (1975). Extreme toxicity from combustion products of a fire-retarded polyurethane foam. *Science* **187**, 742-744.
- PITT, B. R., RADFORD, E. P., GURTNER, G. H., AND TRAYSTMAN, R. J. (1979). Interaction of carbon monoxide and cyanide on cerebral circulation and metabolism. *Arch. Environ. Health* **34**, 354-359.
- PRYOR, A. J., FEAR, F. A., AND WHEELER, R. J. (1974). Mass life fire hazard: Experimental study of the life hazard of combustion products in structural fires. *J. Fire Flammability/Combust. Toxicol. Suppl.* **1**, 191-235.
- RODKEY, F. L., AND COLLISON, H. A. (1979). Effects of oxygen and carbon dioxide on carbon monoxide toxicity. *J. Combust. Toxicol.* **6**, 208-212.
- SMITH, P. W., CRANE, C. R., SANDERS, D. C., ABBOTT, J. K., AND ENDECOTT, B. (1976). Effects of exposure to carbon monoxide and hydrogen cyanide. In *Proceedings of an International Symposium on the Physiological and Toxicological Aspects of Combustion Products, University of Utah, March 1974*, pp. 75-88. Natl. Acad. Sci., Washington, DC.
- STROHL, K. P., FELDMAN, N. T., SAUNDERS, N. A., AND O'CONNOR, N. (1980). Carbon monoxide poisoning in fire victims: A reappraisal of prognosis. *J. Trauma* **20**, 78-80.
- WILLIAMS, S. J., AND CLARKE, F. B. (1983). Combustion product toxicity: Dependence on the mode of product generation. *Fire Mater.* **7**, 96-97.
- YAMAMOTO, K. (1976). Acute combined effects of HCN and CO with the use of the combustion products from PAN (polyacrylonitrile)-gauze mixtures. *Z. Rechtsmed.* **78**, 303-311.
- YAMAMOTO, K., AND KUWAHARA, C. (1981). A study on the combined action of CO and HCN in terms of concentration-time products. *Z. Rechtsmed.* **86**, 287-294.