Meetings

Carbon Monoxide

The effects of carbon monoxide on man's health are a most important and nearly neglected public health problem. This was the view of participants in the Carbon Monoxide Conference, Riverside, California, 11 April 1967. The 35 scientists present agreed that carbon monoxide, in most areas, is the most important constituent to be controlled in exhaust from motor vehicles. It was agreed that the success of the efforts to control it may influence the pattern of personal and public transportation in the future. Further, it may be the carbon monoxide content of cigarette smoke which is the agent responsible for the excesses in mortality from cardiovascular disease and possibly even from emphysema and lung cancer.

There are many gaps in our knowledge of this substance. Methods are needed for measuring small amounts of carbon monoxide in humans and in experimental animals, for estimating its distribution after emission from motor vehicles and other sources, and for understanding what happens to the carbon monoxide once it is emitted into the atmosphere.

Carbon monoxide is produced physiologically in the body by the breakdown of the heme molecule; already this information has led to the recognition that, in apparatus for administering anesthetic agents by rebreathing, carbon monoxide may build up to fairly substantial levels from the amount excreted by the patient himself. The role of carbon monoxide in motor vehicle accidents is being investigated both epidemiologically and experimentally. The epidemiological investigations gain in importance because of the findings reported that persons involved in motor vehicle accidents in Paris have higher carboxyhemoglobin levels than workmen and traffic policemen who had well-defined exposures. Experimentally, many of the studies which have used simple psychomotor or reaction-time tests have appeared to indicate that the substance had little or no effect; yet it is likely that some of the psychomotor effects of carbon monoxide exposure can be overcome by the attention of experimental subjects to the test conditions. What is more important is the effect of carbon monoxide under realistic conditions where attention may be distracted.

The meeting was opened by Hammond (American Cancer Society, New York) who pointed out that coal miners exposed largely to carbon monoxide were observed by Sayers many years ago to have an increased hematocrit. Experimentally, cigarette smokers were found to have an increase in hematocrit within minutes and also a long-term change—the former probably being due to changes in plasma volume and the latter due to the stimulus of the erythropoiesis or to delay in destruction of red cells. The short-term change is easily reversible but the long-term change only partially reversible. It has been shown that heavy smokers who have an increased hematocrit can reduce it when they stop smoking. The possibility that carbon monoxide may be involved in the mechanism is attractive. There is reason to suppose that with increased hematocrit there is an increased likelihood of clot growth; this could be a mechanism associated with the high cardiovascular mortality in cigarette smokers.

While both motor vehicle exhaust and cigarette-smoking exposures contribute substantial amounts of the substance, they have separate and distinctly different temporal patterns. Studies in cigarette-smoking beagles [*J. Am. Med. Assoc.* **199**, 241 (1967)] tend to show the same effects as the studies in human smokers. Interestingly enough, the animals appear to have a hematocrit increase for the first several hundred days of experimental smoking but subsequently the hematocrit drops at about the same time that emphysema develops. It is suggested that the loss of pulmonary surface area may therefore protect against high exposures of carbon monoxide in smoking. That the same mechanisms occur in man is suggested by the increasing mortality ratio with increasing age in smokers compared with nonsmokers from lung cancer and emphysema; the ratio of smoker to nonsmoker with coronary heart disease decreases with increasing age. The major defect in present experimental studies is the difficulty of determining carboxyhemoglobin from a single drop of blood.

Paul Chovin (Director of Laboratories, Prefecture of Police, Paris) described four sets of studies in Paris. The first had to do with the definition of the level of air pollution from motor vehicles; the second, with determining the extent to which policemen exposed in heavy traffic were affected by carbon monoxide; the third, the role of carbon monoxide exposures in motor vehicle drivers who were involved in accidents; and the fourth, the control of carbon monoxide in underground garages. The definition of air pollution levels was obtained by dividing the city of Paris by a rectangular grid and obtaining 317 sampling points, one in each rectangle, in or near heavy traffic. Carbon monoxide at these points was sampled in quadruplicate at the rate of 20 locations a day by using 2-liter samples taken in plastic bags for infrared analysis. Sampling locations and times were chosen to obtain evidence concerning the maximal exposure risk. These data, when averaged, produced a map of the relative intensity of air pollution in different parts of of the city; the pattern is very similar for the years from 1959 to 1966. Approximately 2 percent of the values exceed 100 parts per million. The effect of increased wind speed is to reduce the average value; the effect of increased motor vehicle traffic is to increase it. Similar sampling patterns are used in road tunnels. There is a significant correlation between the length of the tunnel and the mean value of carbon monoxide obtained. There does not seem to be any increasing trend for carbon monoxide in the city as a whole during the last 6 years.

It is estimated that the average risk of people living adjacent to the streets is approximately one-third of the maximum risk obtained. The data fit a log-normal distribution with a geometric mean for 1966 of 16.6 parts per mil-

lion and an arithmetic mean of about 24.6 parts per million. There is a close correlation between long-term average carbon monoxide values and atmospheric lead levels. Carbon monoxide does not correlate with benzo(a)pyrene, however. This is interpreted to mean that lead and carbon monoxide pollution both have a common source, namely, motor vehicles, while benzo(a)pyrene is derived mostly from other sources.

A total of 331 policemen were studied while on duty for approximately 5 hours where their exposure was between 10 and 12 parts per million. Blood samples were taken before and after the duty hours. The average increase in carbon monoxide in the blood (in milliliters of carbon monoxide per 100 milliliters of blood) was 0.024 times the average carbon monoxide exposure (in parts per million by volume) minus 0.07. The average carbon monoxide content for nonsmoking policemen was 0.28 milliliter per 100 milliliters of blood and the increase was an average of 0.11. Since the study was done during spring weather, the maximal exposure was not likely to occur during this period.

From 1959 to 1963 the municipal laboratory examined the blood of drivers who were responsible for, or involved in, accidents, usually within an hour after the accident occurred. The resulting data were compared with data obtained from town inhabitants who thought they might have carbon monoxide intoxication and with samples obtained from workmen who had some risk of exposure to carbon monoxide. The drivers as a group had substantially higher levels than either of these two populations. All three groups include smokers and nonsmokers, hence the source of the increased carboxyhemoglobin was probably the motor vehicle exhaust. Studies in Cincinnati by Brice and Roesler have shown that in 10 percent of motor vehicles there are more than 30 parts per million of carbon monoxide when the cars are in heavy traffic.

When underground garages were constructed in Paris it was found that the values of carbon monoxide sometimes exceeded 200 parts per million averaged over 20 minutes and 80 to 100 parts per million averaged over an hour. By simple adjustments of the carburetor in cars used by Paris police, a substantial decrease in emissions was produced. Before adjustment, 56.5 percent of the vehicles had exhaust with more than 4 percent carbon monoxide, but after adjustment only 8.5 percent exceeded this value. Engine adjustment is thus one way to control carbon monoxide exposures in garages. The other way, of course, is ventilation.

Following the recommendation of Frederick from Detroit, ventilation of parking garages has been required to keep carbon monoxide to less than 50 parts per million averaged over 8 hours and 100 parts per million for instantaneous measurements. The most important topics for international agreement were, according to Chovin, standardization of methods for measurement and sampling of carbon monoxide, air quality standards for motor vehicular garages, and finally, since there is much commerce in motor vehicles, efforts should be made not to encourage the marketing in Europe of cars which produce pollution meeting a lower standard than is acceptable in the United States.

Goldsmith (California State Department of Public Health, Berkeley) reviewed the carbon monoxide effects which are of importance to public health. They include the interference with oxygen transport to the tissues; the possibility of increased morbidity or mortality in sensitive groups, because of interference with oxygen transport; the impairment of sensory and psychomotor functions; the possible long-term effects due to altered hematocrit or changes in the lung; and the interference with heme catabolism or production of red blood cells. He also predicted that specific enzyme and biochemical lesions would ultimately be found to be affected by carbon monoxide. The interference with oxygen transport occurs because of two reasons. One reason is the inactivation of a certain fraction of the circulating hemoglobin because of its combination with carbon monoxide. The other reason is because of the shift in the oxyhemoglobin dissociation curve in the presence of carbon monoxide. At a given level of oxyhemoglobin, oxygen is less readily given up than when carbon monoxide is lower. In recent years measurements of carbon monoxide levels in certain parts of California have been sufficiently high to suggest the possibility of increased morbidity or mortality from acute vascular episodes in sensitive segments of the population. The possibility is being investigated. Perkins (California State Department of Public Health, Berkeley) presented a study of the representativeness of the sampling station in Los Angeles which has given the most consistently high values. This was obtained by a polar coordinate grid which identified locations at the different distances and angles from the sampling point. A field team then collected grab samples systematically over the points of this grid. While there was no systematic pattern by direction or distance from the sampling point, the average of the field sample values was somewhat lower than the monitoring station, suggesting that the monitoring station was not entirely representative of the community exposure in the area.

Impairment of visual discrimination has been documented by MacFarland, and of temporal discrimination by Beard and Wertheim. Schulte has reported on the effect of carbon monoxide on complex task performance, effects being noted with a carboxyhemoglobin concentration of above 2 percent; in general, however, laboratory studies of psychomotor responses of persons exposed to carbon monoxide often fail to reveal expected changes in response. This probably is due to the ability of the experimental subject to overcome, by increased attention, the effect which is present with exposure to the pollutant.

Since Sjöstrand had shown that the breakdown of the heme molecule will yield sufficient carbon monoxide to be readily detected in persons who have no exogenous exposure, there has been relatively little investigation of this problem until Coburn and Forster presented systematic studies of the phenomenon. It is quite possible that carbon monoxide from motor vehicle exhaust or cigarette smoking inhibits certain parts of the catabolic system and the experiments reported by Coburn and his colleagues [*J. Clin. Invest.* **46**, 346 (1967)] suggest that this is occurring. It is possible, according to Goldsmith, that the role of carbon monoxide in regulating the volume of the body's circulating red cells has not been fully considered.

The problem of hemoglobin and related tetrapyrrole compound metabolism has been studied with tracer techniques by Landaw (University of California, Berkeley). In his experiments, the catalytic oxidizing substance "hopcalite" is highly efficient in oxidizing carbon monoxide. It possibly would be helpful in filters to remove the carbon

monoxide from cigarette smoke. At room temperature hopcalite does not oxidize many other substances.

The desirability of large-scale, cooperative epidemiologic studies was brought up by Hammond and echoed by others. It is likely that several hundred thousand people who live and work in the same area will need to be studied in order to see what the effects of both environmental pollution and cigarette smoking might be. Among other new problems for which research is needed are the study of closed systems such as anesthesia-rebreathing systems, and even the small enclosed oxygen cribs in which newborn infants are cared for. Some of the infants with hemolytic disease may excrete fairly large amounts of carbon monoxide and thus produce important levels of carboxyhemoglobin.

For example, if the nuclear submarine *Nautilus* were submerged for 5 days and cigarette smoking or other forms of combustion were prohibited, the endogenous carbon monoxide produced by its crew members would be sufficient to exceed 25 parts per million in the vessel's atmosphere.

Schueneman (U.S. Public Health Service, Cincinnati) felt that the persons whose reactions were critical were those who spend a large portion of their lives in motor vehicles and who are cigarette smokers; exhaust control systems must be designed to protect them. However, it was pointed out that a small fraction of the population also have unusual types of hemoglobin and those individuals might very well be unusually susceptible. Ayres (St. Vincent's Hospital, New York) pointed out that small amounts of carbon monoxide may increase the significance and severity of angina pectoris and other vascular diseases. This has been observed occasionally under controlled conditions. Myocardial oxygen consumption is substantially decreased when significant amounts of carbon monoxide are present, since the myocardium tends to extract a larger fraction of the available oxygen from the circulating blood than do other organs.

Neiberger (Meteorology Department, University of California, Los Angeles) discussed the mechanisms by which carbon monoxide is removed from the atmosphere. While these are not entirely clear, the evidence is suggestive that the substance is oxidized to carbon dioxide by either hydroxy radicals, by other oxygenated substances, or by molecular oxygen in the upper atmosphere. Xintaras (U.S. Public Health Service, Cincinnati) emphasized the need for studying the effect of carbon monoxide on sleep cycles. Many of the participants emphasized the importance of the additional pollutants to which most people exposed to carbon monoxide are also exposed.

Ayres and Goldsmith both called attention to the ability to estimate carbon monoxide exposures in populations through the study of carboxyhemoglobin since the respiratory and circulatory system of the human is a type of integrating sampler. Estimation of carboxyhemoglobin by the measurement of expired carbon monoxide after breathholding equilibration is a very rapid, simple, and valid technique for such studies. The possibility that further research on carbon monoxide effects could well be done in athletes was stressed by Peeples (University of California, Davis). Hammond raised the question as to whether carbon monoxide was an important factor in the genesis of cancer.

The meeting was chaired by O. C. Taylor (acting director, Statewide Air Pollution Research Center, Riverside).

It was concluded that carbon monoxide may be the most underestimated pollutant of this era and the participants agreed to cooperate in further research on this subject.

JOHN R. GOLDSMITH
Environmental Hazards Evaluation Unit, California State Department of Public Health, Berkeley

Calendar of Events—August

National Meetings

27–31. American Soc. for **Pharmacology and Experimental Therapeutics**, fall mtg., Washington, D.C. (Executive Officer, 9650 Wisconsin Ave., Bethesda, Md.)

27–1. American Congr. of **Physical Medicine and Rehabilitation**, 45th annual session, Miami Beach, Fla. (Executive Director, 30 N. Michigan Ave., Chicago, Ill.)

27–1. American Inst. of **Biological Sciences**, 18th annual mtg., College Station, Tex. (AIBS, 3900 Wisconsin Ave., NW, Washington, D.C.)

The following societies will meet in conjunction with the AIBS. Additional information is available from AIBS or from the program chairmen listed below.

American **Bryological** Soc. (Secretary-Treasurer, Box 36, S.W. Missouri State College, Springfield)

American Soc. for **Horticultural Science**. (Executive Director, 615 Elm St., St. Joseph, Mich. 49085)

American Soc. of **Human Genetics**. (c/o Division of Medical Genetics, Dept. of Medicine, Johns Hopkins Hospital, Baltimore, Md.)

American Soc. of **Naturalists**. (Executive Director, 3900 Wisconsin Ave., NW, Washington, D.C. 20016)

American Soc. of **Plant Physiologists**. (Secretary, c/o Dept. of Biology, Yale Univ., New Haven, Conn.)

American Soc. of **Plant Taxonomists**. (Secretary, c/o Botany Dept., Univ. of California, Berkeley)

Botanical Soc. of America. (Secretary, c/o Botany Dept., Indiana Univ., Bloomington)

Ecological Soc. of America. (Secretary, c/o Ecology Section, Health Physics Div., Oak Ridge National Lab., Oak Ridge, Tenn.)

Genetics Soc. of America. (Executive Director, 3900 Wisconsin Ave., NW, Washington, D.C. 20016)

Mycological Soc. of America. (Secretary-Treasurer, c/o Pioneering Res. Div., Natick Labs., Natick, Mass.)

28–30. Gatlinburg Conf. on Special Topics in **Nuclear Education and Research**, Gatlinburg, Tenn. (J. E. Mott, Oak Ridge Associated Universities, Box 117, Oak Ridge, Tenn. 37830)

28–30. Preparation and Properties of **Electronic Materials**, 9th annual conf., New York, N.Y. (L. R. Weisberg, RCA Labs., David Sarnoff Research Center, Princeton, N.J. 08540)

28–30. **Space** Program Issues of the 70's, conf., Seattle, Wash. (AIAA, Meetings Manager, 1290 Sixth Ave., New York 10019)

28–31. **Clay Minerals** Soc., 16th natl. conf., Golden, Colo. (L. G. Schultz, U.S. Geological Survey, Bldg. 25, Federal Center, Denver, Colo. 80225)

28–1. **Electron Microscope** Soc. of America, 25th annual mtg., Chicago, Ill. (Executive Director, c/o School of Chemical Engineering, Olin Hall, Cornell Univ., Ithaca, N.Y. 14850)

28–2. **Alaska Science** Conf., 18th, College. (P. Morrison, Inst. of Arctic Biology, Univ. of Alaska, College 99735)

29–31. Association for **Computing Machinery**, 22nd natl. conf., Washington, D.C. (T. Willette, Box 6, Annandale, Va. 22003)

29–1. **Electron Microscopy** Soc. of America, annual mtg., Chicago, Ill. (A. V. Loud, Pathology Dept., College of Physicians and Surgeons, Columbia Univ., 630 W. 168 St., New York 10032)

31–2. American **Physical Soc.**, Seattle, Wash. (Executive Secretary, 538 W. 120 St., New York 10027)

31–6. American **Psychological** Assoc., annual mtg., Washington, D.C. (APA, 1200 17th St., NW, Washington 20036)

International and Foreign Meetings

27–1. Laurentian **Hormone** Conf., Mont Tremblant, P.Q., Canada. (The Conference, 222 Maple Ave., Shrewsbury, Mass. 01545)

27–2. **Ionization Phenomena in Gases**, 8th intern. conf., Vienna, Austria. (F. Viehbock, Osterreichische Studiengesellschaft fur Atomenergie, Lenaugasse 10, A-1082 Vienna VIII)