Chapter 11

CARBON MONOXIDE

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INTRODUCTION

Carbon monoxide is a colorless, odorless, tasteless and nonirritating gas formed as a by-product in the incomplete combustion of carbonaceous materials. Frequently, but not reliably, the presence of carbon monoxide is accompanied by the odor of unburned organic matter or fuel.[1] Because of its high inherent toxicity and extensive exposure potential, carbon monoxide has historically been considered not only the most widespread poison known but also the most significant toxic gas in the workplace.[2] Human exposure to carbon monoxide has been estimated to account for approximately 2,300 suicides and 1,500 accidental deaths annually (ie, more than one-half the yearly poisoning deaths in the United States). In addition, an estimated 10,000 patients per year seek medical attention because of exposure to this chemical.[3]

Many of the effects of what we now recognize as carbon monoxide poisoning were discussed in ancient literature. During the Middle Ages, these effects were sometimes considered to be the work of demons and witches. Some of the worst workplace exposures occurred during the 19th and early 20th centuries, when industrial miners were frequently overcome by "white damp," a term applied to the "inodorous nature" of carbon monoxide and associated products of partial combustion.[2] Miners were often exposed, with frequent severe or fatal sequelae, after mine fires, explosions, and blasting operations.

Serious exposures have been reported in much less dramatic contemporary situations when individuals have used contaminated sources of compressed air for diving or positive-pressure respirators for industrial

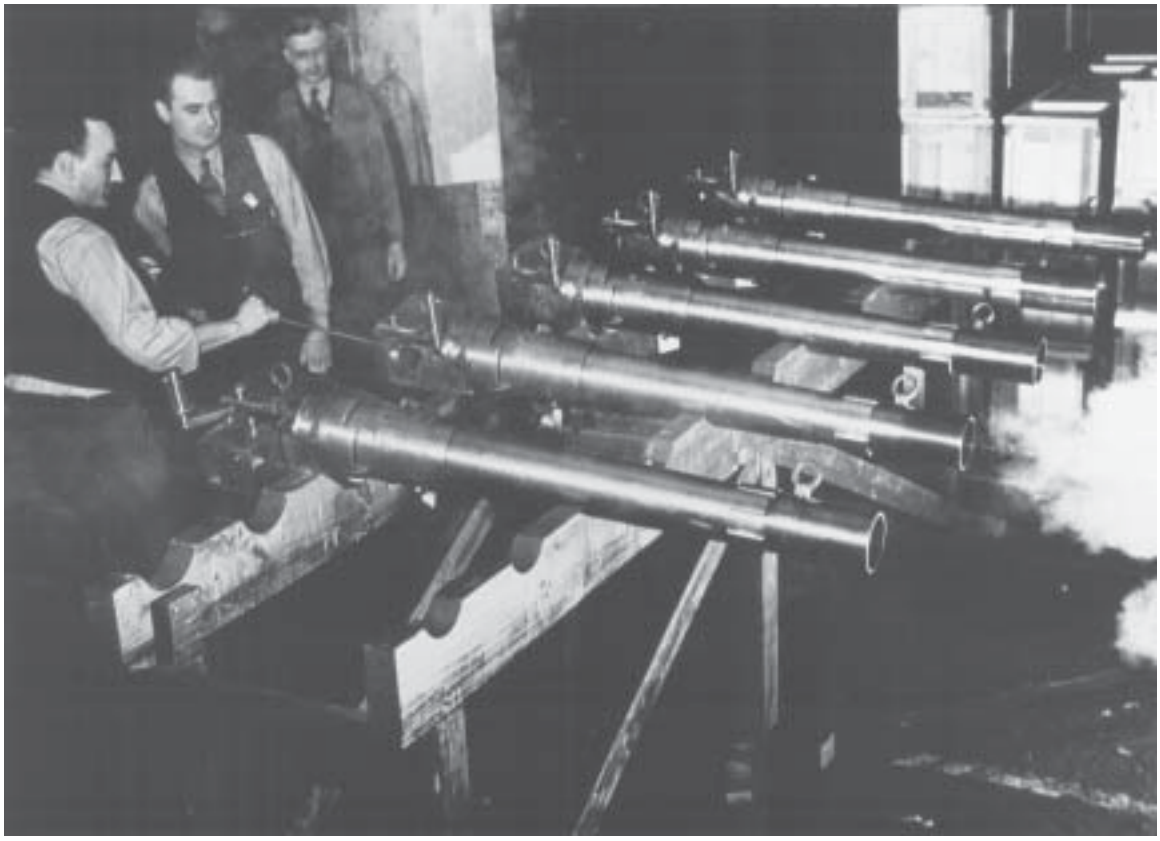

Fig. 11-1. These workers are testing new 75-mm howitzer tubes for the U.S. Army at the General Electric Plant, Erie, Pennsylvania, in June 1941. Such indoor testing, without adequate ventilation, quite likely exposed these workers to hazardous levels of carbon monoxide. Under today's standards, a powerful, frequently monitored indoor ventilation system would be required. Photograph: Courtesy of the US Army.

operations.[1] Exposures in the home or workplace may occur in poorly ventilated areas when using improperly adjusted or inadequately vented heaters, kitchen stoves, water heaters, or charcoal braziers.

Army field exposures commonly occur in tanks, troop compartments of armored vehicles, enclosed communications vans, enclosed areas where portable, gasoline-powered generators are operating, and indoor firing ranges. Military industrial exposures are possible during peace and war and can occur during maintenance and repair of internal combustion engines, indoor operations with motorized equipment such as fork lifts, and indoor proof-testing or firing of weapons (Figure 11-1).[1]

TYPICAL SOURCES OF EXPOSURE

Natural sources of carbon monoxide include volcanic eruptions, lightning strikes, and beds of growing kelp. But atmospheric carbon monoxide primarily results from the incomplete combustion of carbonaceous materials. In nonindustrial, urban environments, the major man-made source of carbon monoxide is the incomplete combustion of motor-vehicle fuels, with exhaust gases from internal combustion engines accounting for approximately 60% of emissions.[4] Because fuels manufactured during the early 20th century (eg, water gas, coal gas, and producer gas) usually contained high concentrations of carbon monoxide, they caused innumerable instances of poisoning. In contrast, natural gas—obtained from wells in coal-bearing areas—contained only trace amounts of carbon monoxide prior to incomplete combustion.[1,2]

Because carbon monoxide is a combustion by-product, toxic exposures are especially likely in conflagrations of buildings, kilns, and grates; explosions or fires in mines; the detonation of explosives; and even tobacco smoke.[1,5] Fires associated with timbering in mines, reinforcement of deep dugouts, and interiors of burning buildings are recognized as sources of significant exposures to carbon monoxide.[6] During the early years of the 20th century, toxic exposures to people who attempted to remain warm using open coke braziers were not uncommon, especially among occupants of dugouts or other small, ill-ventilated structures. The most common cause of death in fires is smoke inhalation and therefore carbon monoxide is a major cause of death in individuals who succumb to smoke inhalation.[4]

Effects of toxic gas exposures associated with the workplace were described by Tanguerel des Planches in 1839 and Dr. Hermann Eulenberg in 1865. Claude Bernard first discovered the complex identified as carboxyhemoglobin in 1858.[7] In the 1880s, Professor K. B. Lehmann and his students expanded the scientific database related to toxic gas exposures based on animal experimentation, industrial observations, and human control experiments. One of the first instances of the involvement of academic medicine in occupational health occurred during 1906, when the Medical Department of the University of Pennsylvania emphasized the importance of carbon monoxide exposures in the felt hat industry.[8]

Early 20th-century scientific and medical literature documents not only the magnitude of the interest, frequency, and types of poisoning potentials, but also the medical importance of carbon monoxide poisonings that occurred in both domestic and industrial environments.[2] Before equipment to quantify carbon monoxide was readily available, it was considered to be a prudent safety measure to regard all flames from carbonaceous sources that impinged against metal as potential carbon monoxide exposure hazards: the metal would cool the fire and the resultant incomplete combustion would produce carbon monoxide.[2] Several excellent historical reviews of carbon monoxide exposure, such as J.S. Haldane's, which was based on his 1915 Silliman Lectures at Yale University, contributed to the developing database.[2,7,9]

Steel Manufacturing

Blast-furnace gas was a product of the steel industry. The gas was produced during the smelting of iron ore, as a result of partial combustion when coke and limestone mixes were injected into the blast furnace. In a collection process from the upper stack, particulate and gaseous contaminants were removed using filtration and water scrubbing. The resultant blast-furnace gas was carried by overhead pipes to be reintroduced into the furnace as a combustible source of heat for blast stoves, steam production, and gas-engine power. Although the composition of blast-furnace gas was variable, major components were, on average, nitrogen (57%), carbon monoxide (26%), carbon dioxide (11%), and hydrogen (3%–4%).[2,10] Because the steel industry in the United States, with its numerous facilities and industrial employees, was a prime source of carbon monoxide poisoning, the industry provided the impetus for developing effective engineering and administrative controls.

Combustion Engine Exhaust

Shortly after gasoline engines were introduced as a source of motive power, operators of gasoline launches and drivers in taxicab garages frequently experienced signs and symptoms of carbon monoxide exposure.[2] Production of carbon monoxide was demonstrated to be greater before the engine had warmed to normal operating temperatures. Other conditions that generated increased amounts of the gas included engines that were poorly tuned or operated at idling speed without a load. Exhaust from the gas engine contained 9.3% carbon monoxide, and an average concentration of carbon monoxide of 0.042% was measured in ambient air in five motor garages.[10] Current United States emissions standards are met with automobile exhausts that contain as much as 8% carbon monoxide,[11] although current automobile exhaust technology usually results in substantially lower emissions.

Methylene Chloride

The industrial use of methylene chloride is an unusual example of an industrial carbon monoxide hazard because there is no actual exposure to carbon monoxide itself. Workplace exposures to methylene chloride have been followed by increases in carboxyhemoglobin levels as a result of humans' metabolism of the methylene chloride to carbon monoxide.[12] Methylene chloride is a readily volatile chemical that is widely used in industry as a paint stripper, aerosol propellant, and degreaser. As a consequence of the volatility and lipid solubility, with uncontrolled use of methylene chloride, exposure potentials are high and the material is readily absorbed. Ineffective industrial ventilation of operations such as degreaser tanks or improper use of personal protective equipment may cause carboxyhemoglobin levels to rise.[2]

Smoking

Inhaling tobacco smoke (whether as an active or passive smoker) is another source of workplace exposure to carbon monoxide. The presence of carbon monoxide in tobacco smoke and the associated elevation of carboxyhemoglobin levels were recognized and reported in the 1920s.[2] Carboxyhemoglobin levels above 3% were seen in 85% of smoking workers and 47% of nonsmoking workers in New York.[4] Most smok-ers were found to have carboxyhemoglobin levels higher than 2% compared to 1% or less for nonsmokers. Carboxyhemoglobin levels were found to increase by 1% to 9% with smoking. Heavy smokers were reported to have levels of 15% to 17%. Taxi drivers who smoke were reported to have carboxyhemoglobin levels as high as 13% (the mean concentration was 6.9%).

MILITARY EXPOSURES

Although exposures to carbon monoxide have been recognized as long as work has been done in association with partially burned carbonaceous fuels, military personnel may also experience significant exposures in ways quite different from those in the civilian sector. Some documented historical circumstances and weapon systems have resulted in substantial exposures and sometimes the deaths of exposed service members.

The use of mining in military operations dates from remote antiquity. Inadequate ventilation was recognized as an early cause of the difficulty of maintaining burning torches, especially when the galleries (mine tunnels) were long. It was widely reported that men were frequently overcome by what we now recognize as both oxygen deficiency and carbon monoxide accumulation within the mines. The effectiveness of asphyxiating gases in mine warfare was well known, with the earliest recorded use at the siege of Ambracia in 189 BC. The Aetolians filled jars with feathers, which were then set on fire; the smoke was blown into the faces of the oncoming Roman soldiers.[6]

World War I: Combat Mining Operations

Only mining operations that were used in a defensive tactical posture were employed during the early part of World War I. Mining operations were simple, with a single mine gallery constructed to guard important trenches or sectors of the line. By the fall of 1915 and increasingly later, mining was used in a more offensive posture. Offensive operations required more extensive tunnels, tunnel galleries, and larger quantities of high-explosive munitions. And as mining operations increased in frequency and intensity, more soldiers became poisoned by the gases associated with the detonations. Although carbon dioxide, hydrogen, methane, and oxides of nitrogen were also generated by the detonation, carbon monoxide was by far the most important poisonous gas associated with military mining (Figure 11-2).[6,13]

Mining was also used to promote forward movement of the troops at the front lines. An explosive in a forward-directed mine gallery would be detonated, which would create a crater 60 to 90 ft in diameter.

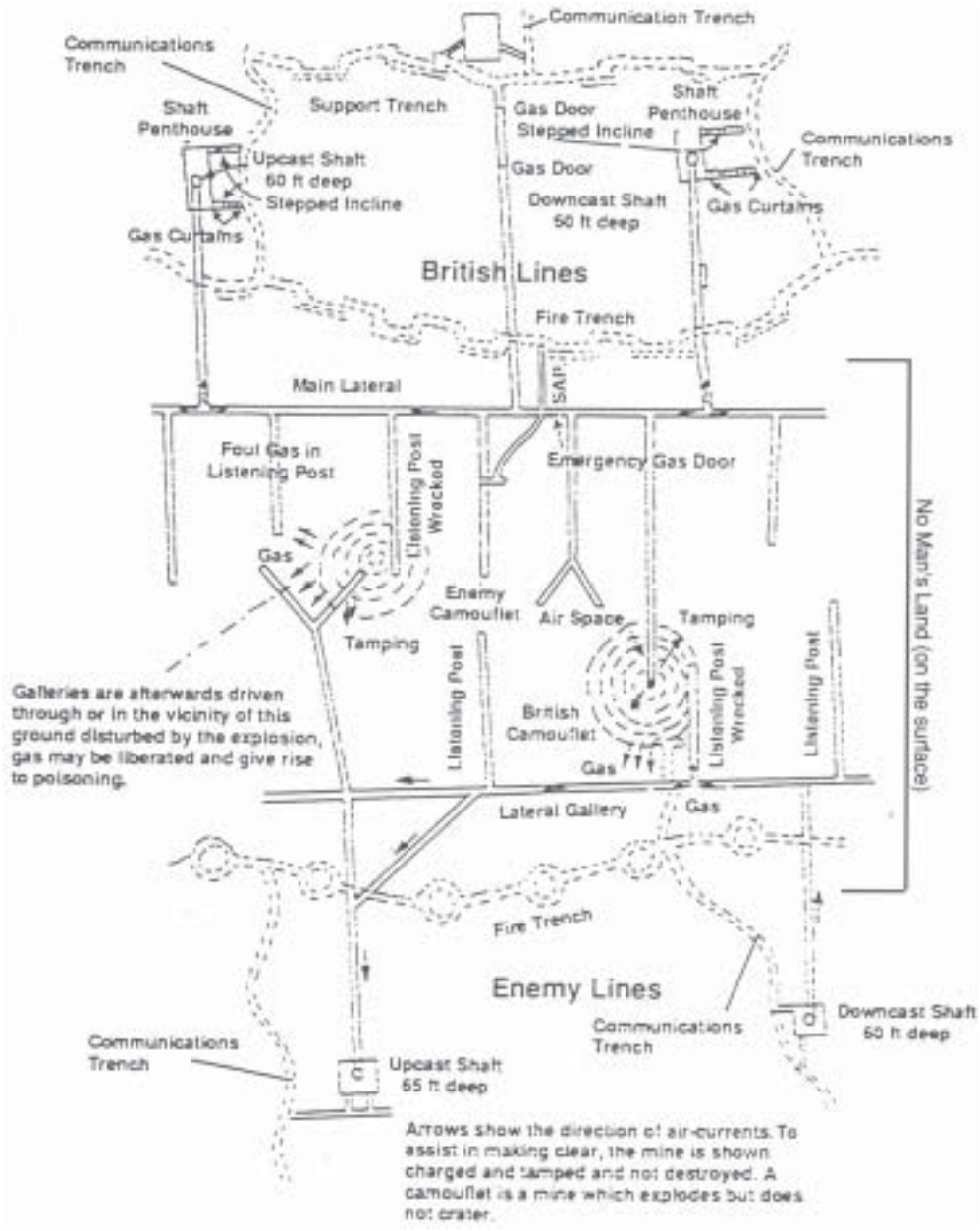

Fig. 11-2. Extensive military mine and trench operations were used during World War I. The above-ground area on the drawing between the British and the enemy lines is No Man's Land, but active warfare was being waged below. Offensive mining involved developing an extensive underground network of downshafts, tunnels directed toward the front line, main laterals (perpendicular to and crossing the forward-directed tunnels), and numerous forward-directed mine *galleries* (shafts). The galleries were used to listen for enemy operations, as conduits for additional mining operations, and as sites for placing offensive or defensive munitions. Tremendous quantities of tightly packed explosives were carefully placed in a procedure called *tamping*. This diagram shows the locations of two explosions, each of which wrecked a listening post. After the explosions, shafts might have been driven through the disturbed ground, potentially liberating carbon monoxide. The arrows show the direction of air currents. Reprinted from Macpherson WG, Herringham WP, Elliot TR, Balfour A. *History of the Great War Based on Official Documents: Medical Services Diseases of the War*. Vol 2. London: His Majesty's Stationery Office; 1923.

Within a few minutes, the infantry would move forward, occupy the crater, establish bombing posts, and consolidate their position. Although the loosened soil usually permitted rapid dissipation of the carbon monoxide, soldiers were frequently overcome as a result of gas entrapment, incomplete detonation with its subsequent gas collection, and absence of wind or "dull, heavy atmosphere."[6] Burning gas, which followed an incomplete detonation, could often be seen as a blue flame that could persist for 12 hours.[6]

Compressor engines were used to ventilate the mines and mine galleries. Carbon monoxide poisoning was often associated with the interruption of the engine power (in order to listen), the use of substitute lubricants containing mineral oil (such as castor oil) for the cylinder of the engine, and unexpected breakdowns from belt trouble. Small petrol engines, usually installed in dugouts, were often used as sources of energy for electric lights and power requirements within the mines. Carbon monoxide poisonings associated with petrol engines in mines were common, especially when the engines were new and care was not taken to ensure that the exhaust was discharged into the open air.[6]

Because carbon monoxide poisoning was a well recognized hazard, soldiers working in the mines often used mice or canaries as biological detectors. (Mice were sometimes preferred because they could be trained to be carried in a soldier's pocket.) However, the use of canaries was occasionally counterproductive, as the following anecdote illustrates:

> One of the canaries kept in a mine rescue station escaped from its cage and flew into the middle of "No Man's Land," where, alighting on a bush, it began to sing. Consternation was caused in the British lines, for the discovery of this bird by the enemy would indicate the presence of mining operations and would mean that the work of weeks would go for naught. The infantry in the trenches were immediately ordered to open fire on the canary, but it continued singing, heedless of the bullets which whistled round it. It was not until the trench mortars were called on to assist that a well-placed shell wiped out completely the bird, the bush, and the song.[6]

Although some medical historians of World War I identified carbon monoxide (along with dichloroethyl-sulphide, sulfuretted hydrogen, and nitrous fumes) as possible sources of poisonous substances of military significance, a medical treatise published in France in 1918 emphasized the risk of carbon monoxide.[13] This treatise, entitled (translated from the French) *The Clinical and Therapeutic Aspects of Gas Poisoning*, was directed toward diagnosing gas-intoxicated soldiers and providing appropriate therapy. Data for the treatise were gleaned from human exposures and laboratory animal experimentation with an extensive series of toxic gases.

The French writers identified several hazards associated with exposures in enclosed spaces:

- gun fire from closed shelters with inadequate ventilation,
- mine or camouflet [a mine that explodes but does not crater] explosions with subsequent contamination of communicating galleries,
- tunnel-construction operations in contaminated areas, and
- explosions of incoming enemy projectiles that secondarily contaminated dugouts, shelters, or produced entrapped pockets of the gas.[13]

The dangers of carbon monoxide exposures were enhanced by the absence of odor, color, and irritation. The gas was so insidious that an exposed individual could fail to grasp the exposure danger until he noticed that the use of his extremities was impaired. However, despite its advantages and possibly because of its limitations, carbon monoxide itself was never used as an offensive chemical warfare agent.[6]

World War II: Tank Warfare

The World War II experience with carbon monoxide was dominated by problems associated with large numbers of soldiers fighting in armored fighting vehicles (AFVs). The need for an accurate methodology applicable to quantitative detection of carbon monoxide led scientists at the Armored Medical Research Laboratory at Fort Knox, Kentucky, to develop an infrared gas analyzer that was not only reliable but was sufficiently transportable to be used for measurement within AFVs. Peak levels of carbon monoxide were detected shortly after firing bursts in the M3A4 tank.[14] After firing five rounds from the 75-mm gun, the level of carbon monoxide was found to increase rapidly to 0.718% within 1 minute. If no additional rounds were fired, ambient carbon monoxide decreased rapidly to baseline levels within 4 minutes. Carbon monoxide levels recorded with 37-mm firing were substantially lower than those found with the 75-mm gun (Figure 11-3).

The same problem had, of course, been recognized during World War I. In the early days of tank warfare, crews who spent prolonged times inside their tanks complained of headache and faintness. These problems became more severe as later tank models were introduced. Signs and symptoms of exposure were

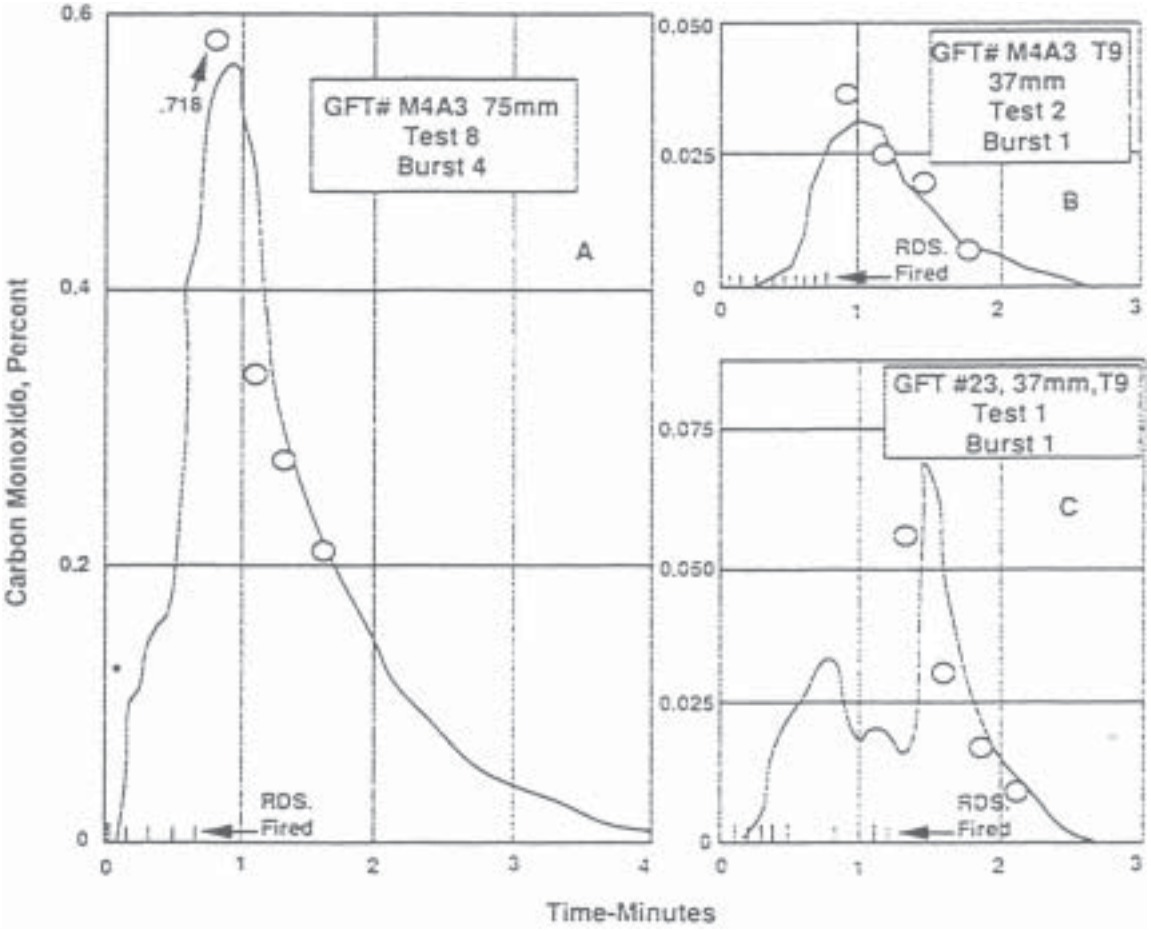

Fig. 11-3. Carbon monoxide concentrations are measured by means of a continuous recorder (——) and grab samples (o) after firing five rounds from the 75-mm gun, **A**, or ten rounds from the 37-mm gun, **B**, of the M3A4 tank. (Note that these graphs, which were originally published in 1945, contain an apparent misprint: the tank is identified as an M4A3. Because the data refer to both 37-mm and 75-mm guns, however, we know that the correct designation would be M3A4. The GFT seen in the test-identification boxes may have stood for ***g***as ***f***iring ***t***est.) In both these graphs, the recorder did not show the true peak as measured by the grab samples. This is due to the relatively slow response time inherent in real-time monitors, which results in an "averaging" effect, and is to be expected. Source: Adapted from Nelson N. *NDRC Infra-Red Gas Analyzer for Carbon Monoxide*. Fort Knox, Ky: Armored Medical Research Laboratory; 1945. Provided by Alexandria, Va: Defense Technical Information Center. Report AD 655578.

clearly related to exposure to the toxic exhaust gases and ambient heat burden.[15] Although the soldiers sometimes became unconscious while in the tanks, they more frequently collapsed after reaching fresh air.[6] Their symptoms were aggravated when they fired the Hotchkiss[6,16] and 6-pounder guns.[6]

The interior design of the early tanks permitted heat accumulation and exposure to toxic combustion gases because the exhaust lines ran along the inside of the tank for some distance before they perforated the plating to the outside. As a consequence, carbon monoxide exposures from both internal leakage and backdraft from other tanks were common. The restricted crew space within the tank allowed significant accumulation of moisture, which further complicated the heat-exposure potential. In one incident, reported in 1918, the first and second tank drivers became unconscious. When the tank commander took control as the driver, he also succumbed and the tank was unable to get into action because of the condition of the crew. Clearly, improved tank ventilation was required. A supply of fresh, outside air was provided via infiltration around gun ports and other openings.[6]

Carbon monoxide exposures were measured in tanks towed behind each of two medium tanks (M4A1 and M3A4) and two recovery vehicles (M32B1 and M32B3).[17] Operational test variables included two courses (a flat surface and a 4% grade) and the use of

either a towing bar or towing cable. Carbon monoxide levels were measured in four crew positions within the towed vehicle: driver, assistant driver, loader, and commander.

Hazardous levels of carbon monoxide were not found in the towed vehicle when it was towed behind the M3A4 medium tank or the M32B3 recovery vehicle. In sharp contrast, however, the earlier M4A1 model tank and M32B1 model towing vehicle were designed with their engine exhausts directed rearward.[17] When either of these earlier models was the towing vehicle, riders in the towed tank were exposed to levels of carbon monoxide in excess of 0.2%. Exposures were affected by changes in wind direction, surface grade, monitoring position, and whether the towing cable or towing bar was used.

For the M4A1 tank and the M32B1 recovery vehicle, an exhaust deflector shield was developed and employed as a short-term remediation.[17] The deflector baffle design permitted retrofitting at the first-echelon maintenance unit. When it was attached to the towing M4A1 tank, the deflector directed the exhaust toward the ground and effectively limited the exposure of the soldiers who were required to ride in the towed vehicle (Figure 11-4).

The Modern Era: Armored Fighting Vehicles

The risks associated with carbon monoxide exposure and military equipment have been recognized for a long time. Why then does this remain an important, unresolved issue? During World War II, only about 3% of soldiers in the U.S. Army were deployed in AFVs. However, if a war were fought today the U.S. Army would deploy at least 30% of its soldiers in AFVs.[18] Not only are more soldiers likely to be exposed but the levels of exposure may also be significantly higher if control measures should fail. For example, as ammunition has become increasingly larger, the amount of propellant charge required to fire the larger round is even greater (round size is measured as a squared variable, charge volume as a cubic variable). Even the development and use of more effective ventilation systems and cleaner burning propellants have not completely eliminated the risk associated with carbon monoxide in today's AFVs.

M1E1 Tank

In 1984, an unusual exposure to carbon monoxide was reported during the operational test (OT II) of the M1E1 tank. The official memorandum filed after the event said, in part:

> At 1330 on 20 February, tank #120-5 began a silent watch and firing exercise as part of the [OT] II program. The exercise was run in accordance with conditions specified in the current Detailed Test Plan which called for it to be run with hatches closed, the primary NBC [nuclear, biological, and chemical] system off, and the backup system (M13A1) on. The silent watch portion of the exercise was run with the engine off and the breech open (no round chambered). The engine was started periodically to recharge the batteries, but the NBC system (which starts automatically when the engine is started) was selected "off" immediately upon actuation. The crew was dressed in MOPP IV [mission-oriented protective posture]. Breathing air was supplied to the protective masks through the M13A1 gas particulate filter unit. The driver stated that he used his mask only for the last 90 minutes of the exercise. The tank operated in silent watch mode until 2015, when it moved to the firing range. The firing portion of the exercise included firing thirteen main gun and approximately 100 coaxial machine gun rounds.
>
> Six main gun rounds and the coax rounds were fired between 2015 and 2040. The remaining seven main gun rounds were fired in the next seven minutes. At the end of the exercise, the loader slumped forward in his seat and appeared to be in physical distress. A short time later, the tank commander observed this condition, aroused the gunner, and assisted him out of the turret. After performing this action, the tank commander also experienced dizziness and [lay] down on the tank. The medics arrived at 2051 and the loader and tank commander were taken to —— Army Community Hospital, arriving a[t] 2121 hours. The hospital records show admission at 2145. . . .[19]

During the medical evaluation of the tank's crew members after this exposure, and shortly after their admission, carboxyhemoglobin levels were obtained. The loader had a level of 33% carboxyhemoglobin and the tank commander had a level of 27.8%. As a consequence of the two admissions and the results of the blood analyses, the remaining crew members, the gunner and driver, were brought and admitted to the hospital several hours later. Their admission carboxyhemoglobin levels were 16.5% (the gunner) and 12.7% (the driver). After treatment, all crew members were discharged without apparent sequelae of exposure.[19]

In March 1984, recommendations were offered for improving the M1E1 tank:

- Reroute the air intake for the M13A1 gas particulate filter unit from the turret area to the outside air (for intake).

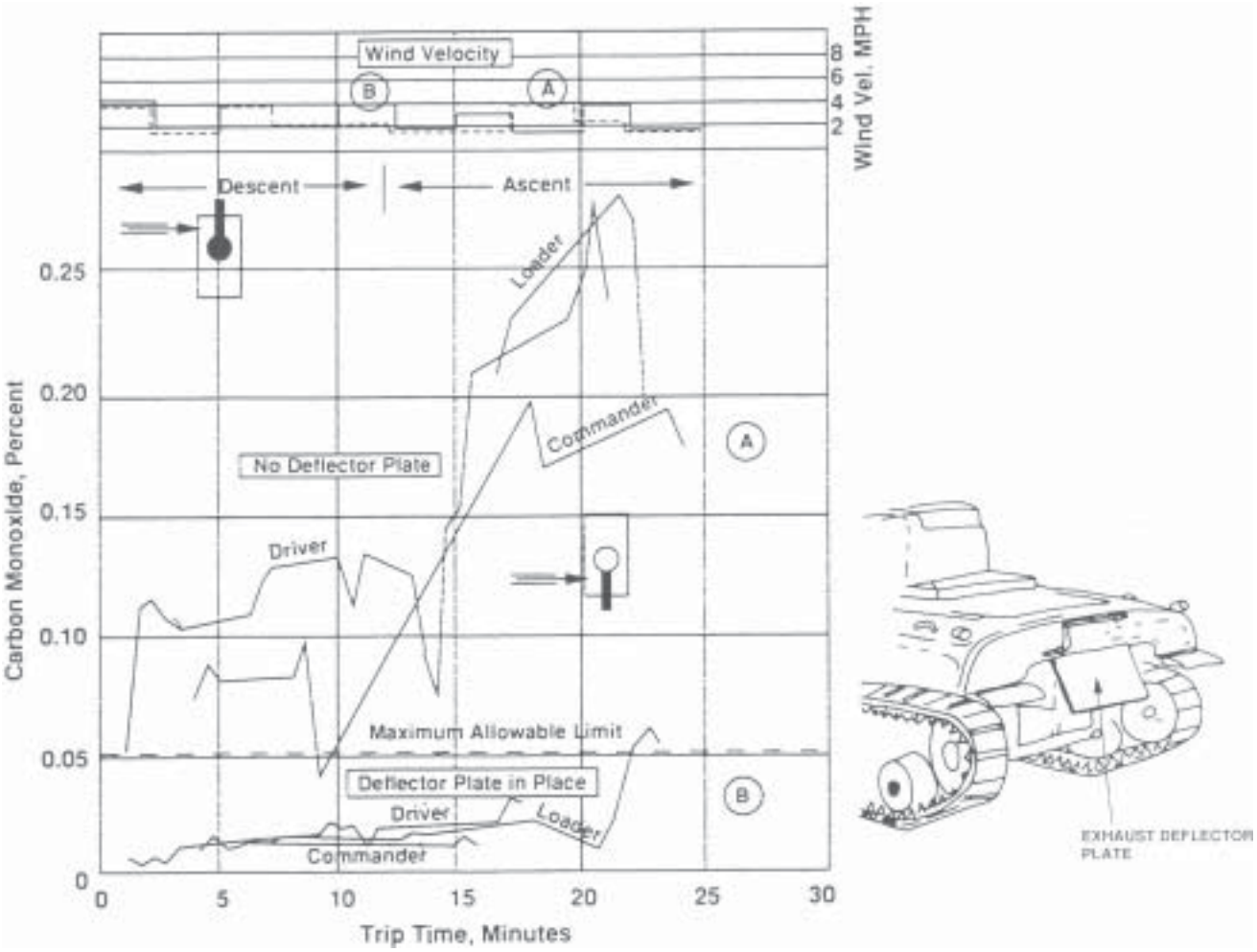

Fig. 11-4. Carbon monoxide was measured at three crew locations when a tank was towed by an M32B1 recovery vehicle with and without an exhaust deflector, and using a towing bar on a 4% grade. Placing an exhaust deflector (small drawing), as a product improvement on the towing vehicle, reduced the concentration of carbon monoxide within the tank. This graph conveys some of the complexity of making field determinations of carbon monoxide exposures. Many variables, if not controlled, must at least be accounted for (eg, wind direction and speed, engine speed, degree of surface grade, duration of the experiment, the location of the monitoring instruments within the tank, the reliability of the instruments). The increased concentration of carbon monoxide seen during observation **A** may be due to a combination of engine speed, the 4% grade, and the elapsed time. The missing tracing at the loader position in observation **A** may be due to equipment malfunction. What this graph clearly demonstrates, however, is that attaching an exhaust deflector plate to the rear of the towing vehicle—a seemingly minor modification made for observation **B**—significantly lowers the concentration of carbon monoxide at the crew positions. Source: adapted from Nelson N. *NDRC Infra-Red Gas Analyzer for Carbon Monoxide*. Fort Knox, Ky: Armored Medical Research Laboratory; 1945. Provided by Alexandria, Va: Defense Technical Information Center Report AD 655578.

- Advise individuals at all test sites that a hazard is associated with firing the main gun and/or coaxial machine gun with the hatches closed and NBC system off.
- Instruct test personnel at all test sites that the M13A1 gas particulate filter provides no carbon monoxide protection as configured.
- Revise the operator manuals to (*a*) include warnings of the carbon monoxide hazard associated with weapons fire and the inability of the M13A1 system to protect against carbon monoxide exposure and (*b*) describe the types of ventilation required for silent watch.[19]

Infantry Fighting Vehicle

Toxic fumes testing was conducted at the U.S. Army Environmental Hygiene Agency (USAEHA) in

the infantry fighting vehicle (IFV) in 1980.[20] Real-time monitoring was done inside the IFV during a worst-case firing scenario to determine peak and total carbon monoxide exposure concentrations. The real-time samples were collected using direct reading instruments connected to appropriate recorders. Area samples were obtained from "the approximate breathing zones" of the crew compartment, driver's compartment, and the crew members. In one event, 200 rounds of 25-mm and 75 rounds of 7.62-mm ammunition were fired over approximately 6 minutes. In the turret, a peak exposure concentration of 1,920 ppm, average exposure concentration of 825 ppm, and total exposure concentration of 4,950 ppm-minutes were measured. (The term "ppm-minutes" used with the total exposure concentration is based on the concept that the cumulative personnel exposure dosage is a product of the average measured airborne concentration and total exposure time.)

It was decided that the initial exposure measurement period for the IFV firing event "should have been fired over a 20-minute period rather than the 6-minute firing."[20] Carbon monoxide measurements were obtained when the firing scenario was repeated over both 20- and 60-minute periods of weapons fire. Several peak exposures in the turret were above 600 ppm, with an average exposure concentration of 190 ppm and a total exposure concentration of approximately 11,400 ppm-minutes. The firing-exposure scenario was repeated; this time, peaks that were measured in the turret exceeded 800 ppm and total exposure concentrations measured approximately 24,730 ppm-minutes. In the driver's compartment, peaks in excess of 400 ppm and total exposure concentrations of about 10,600 were measured. In the crew compartment, peak exposures above 400 ppm and total exposure concentrations of approximately 8,200 ppm-minutes were measured.

In summary, total concentration exposures in the IFV were found to exceed the acceptable limit of 6,000 ppm-minutes established in Military Standard 800.[21] With respect to the measured peak levels, some peak exposures were above 800 ppm, which exceeds excursion values "considered acceptable by any standards-setting body."[20] For the IFV, under the conditions of the firing scenarios, the study concluded that exposures could result in carboxyhemoglobin levels of about 15% in 15 minutes. The potential exposures were considered to represent a health risk that could cause significant symptoms and signs consistent with impairment of combat effectiveness.[20]

In a study of the Bradley Fighting Vehicle (BFV) performed in 1984, carbon monoxide measurements were obtained using a dual channel, nondispersive, infrared, carbon monoxide analyzer for real-time carbon monoxide measurements.[22] Even though the detection methodology represented acceptable industrial hygiene practice, it was noted that the equipment was incapable of detecting rapid transient concentrations of carbon monoxide. Conditions in the BFV that were associated with firing and shown to affect carbon monoxide concentrations included the type of weapon fired, the position of the hatches (open or closed), the crew position, and the position of the turret with respect to the hull.

Firing conditions were limited by selecting wind-speed conditions. Closed-hatch firing was not permitted at wind speeds greater than 10 mph, and open-hatch firing was not permitted at wind speeds greater than 5 mph. Hull fans were turned off, gun bags were zippered, gas particulate filter units (GPFUs) were turned on, and both 7.62-mm and 25-mm rounds were fired.[22]

The results and conclusions of the 1984 study differed from those in a 1982 medical report, which indicated that no medical hazard was identified with firing the weapons in the infantry fighting vehicle.[23] With the single exception of one measurement (4.8% carboxyhemoglobin) in the 1984 study, all firing conditions were expected to generate carboxyhemoglobin levels above 5%, and in three of the conditions, carboxyhemoglobin levels ranged between 11.0% and 13.4%. The maximum peak concentration, 1,462 ppm, was measured at the driver position; levels of 1,087 and 1,200 ppm were identified in the troop compartment. Operation of the M13 GPFU, which has no capacity to remove carbon monoxide, resulted in uptake of carbon monoxide within the driver's compartment with subsequent distribution to each crew member and troop occupant.[22]

M109 Howitzer

The health hazard assessment on the M109 Howitzer Improvement Program (HIP) identified carbon monoxide exposure as an area of medical concern in the development of the howitzer. The HIP, designated as the M109A3E2, is an armored, full-tracked howitzer carrying a minimum of 34 complete, conventional-geometry rounds and two oversized projectiles on board.[24] The main armament is a modified, 155-mm, M185 cannon assembly (the M284), and M178 gun mount. The modified muzzle break deflects propellant gases back along the gun tube, rather than perpendicularly as the unmodified predecessor models did. The M109 howitzer is generally operated by a crew of four and is operationally supported by ammunition resupply vehicles.

Numerous environmental, sampling, and configuration variables influenced the concentrations of propellant combustion testing with the M109 howitzer evaluations.[24] Tube-firing elevation, wind speed, wind direction, hatch configuration, ventilator mode, propellant type, propellant quantity, system component failure, fire rate, and industrial hygiene sampling practices all appeared to influence the study results. The bore evacuator is a pressure-responsive, tube-evacuation system that is designed to promote the movement of postfire combustion gases from the breech toward the muzzle. Both compromised bore evacuator function and wind direction (ie, a head wind blows combustion gases out the breach despite a functional bore evacuator) are critical variables associated with exposure concentrations after firing.

Although the authors of the health hazard assessment, which was performed at USAEHA in 1988, conclude that the lack of data replication limits the general applicability of the findings, they consider several observations to be reliable. In general, they state that the worst-case firing scenario occurred when the vehicle's hatches were closed. In that operational mode, the crew compartment was maintained under a slight negative pressure, which drew combustion gases from the breech into the crew compartment when the cannon breech was opened. They concluded that a head wind significantly increased the exposure to combustion gases. Finally, they concluded that reconfiguring the muzzle break could actually increase the crew's exposure to the combustion gases.[24]

Projected exposure data for the M109 were developed for carbon monoxide based on the Operational Mode Summary/Mission Profile (OMS/MP). Carbon monoxide data have been used in a concurrent calculation of the maximum allowable consecutive episodes (MACE) to limit the M109-associated carboxyhemoglobin to 10%. The OMS/MP stipulates 5 rounds per mission, 51 missions per day, and a total of 254 rounds per day. Average carbon monoxide exposure levels during the HIP firings were identified in a broad range, from 0 to 2,300 ppm at the crew positions. The health hazard assessment team at USAEHA arbitrarily chose an average level of 120 ppm and calculated the 24-hour exposure risk of the development of a 2.09% carboxyhemoglobin level. Their estimate that a 5.3-minute exposure may be repeated 17 times (ie, the MACE) without exceeding a 10% carboxyhemoglobin level remains unconfirmed, but has been recommended for M109 training and testing missions. Similarly, their position that the risk of firing-associated health impairment is negligible is speculative and remains unconfirmed. As a consequence, medical monitoring for carbon monoxide exposure effects is currently required during operational testing of the M109 howitzer developmental series.[24]

Military Aviation

Unacceptable carbon monoxide exposures have been demonstrated in military aviation, where uncontrolled exposures in early piston-driven aircraft were responsible for the deaths of many pilots. One early investigator reported on a death that occurred in 1930:

> The source of carbon monoxide poisoning which forms the basis of this article is the exhaust gas of the gasoline motor of the airplane and airship and was brought to attention by the death of Capt. Arthur H. Page, United States Marine Corps, at the national air races, Chicago, September 1, 1930, and the subsequent report of the finding of carbon monoxide in his blood shortly after the crash.[5]

In a 1944 report, an aircraft pilot experienced carbon monoxide exposure as a result of a defective engine exhaust; his behavioral responses were recorded by his fellow aviators. They reported that the pilot's behavior appeared to be related to the simultaneous interaction of carbon monoxide and altitude (in other words, the decreased partial pressure of oxygen). At low altitude, the pilot's flight responses were normal. However, after ascending to 10,000 feet with his aviation section, he made only the first flight entry correctly. His subsequent flight patterns and behavioral responsiveness progressively deteriorated. As a result of the actions of another aircraft pilot, the availability of in-flight oxygen, and the decrease in altitude, the pilot improved enough to properly land his craft. The pilot recalled that he was aware that there were difficulties with his flight (his hand shook violently and he had difficulty grasping the throttle). He also remembered that he could not always see his section leader, the horizon, or the clouds, but had a feeling of "What's the difference?" Unfortunately, the pilot's carboxyhemoglobin levels were not determined.[25]

Although carbon monoxide exposures have been eliminated from the exhaust system of aircraft, high, transient exposures to the toxic fumes have been associated with gunfire when weapons are used aboard aircraft. In 1988, an evaluation was performed of the carbon monoxide emissions from the M134 minigun, mounted in the UH-60A Black Hawk helicopter. In the tests, a range of 1,400 to 2,700 rounds were fired in five replicates of five separate firing conditions. The highest average ambient carbon monoxide–exposure concentration was 79.4 ppm for a duration of 4 minutes. The calculated maximum predicted carboxyhemoglobin response was 4.90%, and no firing restrictions

were recommended.[26] Peak levels of carbon monoxide were not reported.

Household Heating

Exposure to carbon monoxide in the military is not limited to weapons systems: inadequate home ventilation is a common source of exposure. Large numbers of U.S. Army forces have been stationed in Germany, where coal has been used as a source of heat in family housing. Case reports of carbon monoxide poisonings involving family members living in military housing facilities have been reported.[27]

Charcoal block heating, the custom of heating homes with coal or charcoal fires inside or under the structures that is common in Korea, is a significant source of carbon monoxide during the winter months.[28] In one recent incident, a U.S. Army field commander and his family awakened in the middle of the night with severe headaches. Evaluation at the nearest medical facility confirmed carbon monoxide exposure and etiology.

PATHOPHYSIOLOGY OF EXPOSURE

The need to develop an effective treatment for carbon monoxide poisoning had a disproportionately large impact on medicine. Not only did it enable us to treat the poisoned patient, it also provided an insight into respiratory physiology. Carbon monoxide complexes with hemoglobin to form carboxyhemoglobin, which perverts hemoglobin's normal function: oxygen transport.

Carbon Monoxide's Hemoglobin-Binding Affinity

The complicated physiology of oxygen transport and carbon monoxide's deleterious effects on it are best understood when placed in their historical context. Controversy and difference of scientific opinion enveloped toxicity studies for carbon monoxide exposures during the early 20th century and were reflected in the early literature. Haldane believed that the effects of carbon monoxide exposure were caused by the preferential binding of carbon monoxide to hemoglobin, with resultant tissue hypoxia. Henderson, Karasek, and Apfelbach supported Haldane's view. In contrast, Poelchen had reported in 1888 that carbon monoxide toxicity resulted from a direct toxic effect on the tissues. The direct-effect theory was based on the rapid onset of narcosis, early muscular weakness in the lower limbs, occurrence of gangrene as a complication, and damage of the lenticular nucleus of the brain. Hill, Semerak, and Lanossier supported Poelchen's view. They noted that animal deaths occurred more rapidly, and were associated with different signs, when placed in an atmosphere containing carbon monoxide compared to simple asphyxiation with nitrogen.[2]

Studies that investigated carboxyhemoglobin stability and the recovery of hemoglobin's oxygen-binding capacities were performed in the early 1900s. Although some scientists reported finding carbon monoxide in blood 24 hours after the exposure to carbon monoxide had been terminated, one prominent researcher could identify no residual carbon monoxide 6 hours after exposure (using a spectrophotometric technique; the lower limit of sensitivity was 0.25%).[2] One researcher concluded, in 1920, that carboxyhemoglobin was actually metabolized in the liver, with metabolic components secreted into the bowel through the biliary tract.[29] The postulated method of animal and human excretion of carbon monoxide was thought to involve hepatic metabolism, with the carbon monoxide molecule probably remaining with the globulin end of the hemoglobin metabolite. This view held that the globulin moiety was presumed to be disposed of as a urea product and that carbon monoxide was "treated as foreign material and excreted."[29]

As a result of his interest in coal mining–related carbon monoxide poisonings, Haldane initiated studies in the mouse, which were first reported in 1905. He demonstrated that the mouse, when exposed to a partial pressure of 2 atm of oxygen and 1 atm of carbon monoxide, survived without difficulty. The mouse's only apparent limitation was a diminished exercise tolerance. Therefore, Haldane (*a*) discounted others' scientific claims concerning the potential inherent toxicity of carbon monoxide and (*b*) demonstrated that the adverse effect of carbon monoxide was related to its powerful, competitive, hemoglobin-binding affinity.[7]

Haldane and Douglas published their classic findings related to carboxyhemoglobin-dissociation curves in human blood in oxygen-deficient atmospheres in the early 1900s. They reported an apparent paradox: an individual with a normal hemoglobin level, of which 50% is carboxyhemoglobin, has more severe symptoms than does an individual with a 50% decrement in hemoglobin, none of which is carboxyhemoglobin. It appears that carbon monoxide has some effect on symptomatology that is unrelated to the amount of hemoglobin available for oxygen transport. Haldane and Douglas explained that the paradox arose

from the relative binding affinities of the differing oxygen-binding sites on the hemoglobin molecule. Hemoglobin molecules with one-half the available binding sites occupied by carbon monoxide released oxygen with great difficulty from the remaining two binding sites on each hemoglobin molecule.[7]

In Haldane and Douglas's early reports, comparisons of the relative oxygen- and carbon monoxide–binding affinities with the hemoglobin molecule had been performed using samples of their own blood. Interestingly, the relative carbon monoxide–oxygen binding affinity of Douglas's hemoglobin was reported as 246; Haldane's hemoglobin binding affinity was 299.[7]

In 1927, Haldane demonstrated that mechanisms in addition to the effective production of carboxyhemoglobin might account for the health effects from carbon monoxide exposure. Animals that he exposed to high concentrations of carbon monoxide under hyperbaric conditions developed a tissue toxicity despite adequate oxygenation. In these experiments, Haldane exposed animals to 3.1 atm of oxygen, then added an additional atmosphere of carbon monoxide. The animals' carboxyhemoglobin levels rose to 98%, but as long as oxygen was dissolved in the plasma, the rats suffered no ill effects. However, when a second atmosphere of carbon monoxide was added, the rats promptly died. This indicated to Haldane that carbon monoxide had a direct effect on tissues, probably at the cellular level. This explanation was supported in 1950 when a researcher demonstrated that microsomes in cells were inhibited by carbon monoxide, and that this inhibition involved enzymes associated with electron transport, specifically the cytochrome P-450 system.[12] The cytochrome P-450 system is now recognized as one of the most important metabolic biotransformation path-ways in the human body. Carbon monoxide apparently affects oxidative and reductive reactions in these pathways.

Carboxyhemoglobin and Oxyhemoglobin Dissociation

The most commonly recognized primary action of carbon monoxide is its preferential binding with hemoglobin. This deprives hemoglobin of its normal oxygen-combining function and results in a condition that can be thought of as "anemic" hypoxia.[30] The chemical reaction is a reversible mass-action equilibrium and proceeds based on the mass or partial pressure (tension) of the gases in pulmonary air, an action that allows effective treatment.[9] In addition, carbon monoxide chemically binds to a number of heme-containing proteins including hemoglobin, myoglobin, cytochrome oxidase, cytochrome P-450, and hydroperoxidases. (However, these account for only 10%–15% of the extravascular carbon monoxide in a well individual.)[4]

The interaction between carbon monoxide and hemoglobin is graphically represented as the carboxyhemoglobin dissociation curve (Figure 11-5). At first glance the curve appears to be very similar in shape to the oxyhemoglobin dissociation curve (Figure 11-6). On closer inspection, however, it becomes apparent that the range used for the oxygen pressure scale ranges from 0 to 150 mm Hg while the range used for carbon monoxide is between 0 and 0.5 mm Hg. This difference represents the differential affinities of oxygen and carbon monoxide for hemoglobin; the difference is approximately 230-fold.[31] When oxyhemoglobin and carboxyhemoglobin dissociation curves are plotted along the same abscissa, the line representing saturation with carbon monoxide curves steeply upward to the left of the curve representing oxyhemoglobin. If the graph for oxyhemoglobin dissociation were to be superimposed on the graph of carboxyhemoglobin dissociation, complete saturation of the hemoglobin with carbon monoxide would occur prior to (to the left of) the steep upward slope of the oxyhemoglobin concentration. These differing curves demonstrate the difference between hemoglobin's oxygen- and carbon monoxide–binding affinities.

The National Institute for Occupational Safety and Health (NIOSH) defines the term *affinity constant* as "the number of moles of oxygen which must be present with each mole of carbon monoxide in order to maintain an equal saturation of hemoglobin."[32] Reported differences in the binding affinities appear to reflect individual researcher's preferences; for example, some accept 210, others 230, and others 250. When carbon monoxide binds with hemoglobin, the binding affinity of the carboxyhemoglobin complex for oxygen is increased, compared to that of normal hemoglobin. Not only does the hemoglobin combine preferentially with carbon monoxide rather than oxygen, the oxyhemoglobin dissociation curve is also affected so that oxygen is released less readily within the tissues (Figure 11-7).[5]

The physiological and clinical effects of carbon monoxide are primarily those of anoxemia (oxygen want) from a decrease in tissue oxygen (a combined effect of the reduced oxygen-carrying capacity and impaired oxyhemoglobin dissociation). As a result, the tissue hypoxia that is produced following carbon monoxide exposure is greater than the amount caused by an equivalent reduction of ambient oxygen (eg, altitude) or equivalent reduction in hemoglobin (eg, anemia).[4] After dissociating from carbon monoxide, the regenerated hemoglobin shows no impairment or

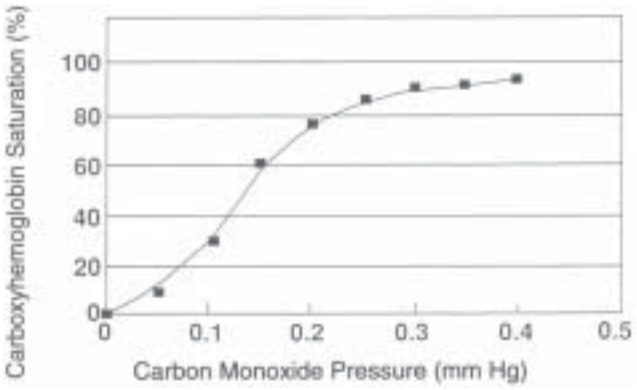

Fig. 11-5. The carboxyhemoglobin dissociation curve.

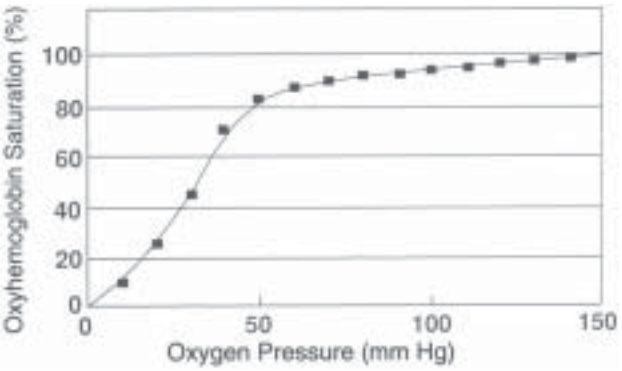

Fig. 11-6. In an oxyhemoglobin dissociation curve, decreased affinity of hemoglobin for oxygen shifts the dissociation curve to the right, whereas increased affinity for oxygen shifts the curve toward the left.

Figure 11-7 is not shown because the copyright permission granted to the Borden Institute, TMM, does not allow the Borden Institute to grant permission to other users and/or does not include usage in electronic media. The current user must apply to the publisher named in the figure legend for permission to use this illustration in any type of publication media.

Fig. 11-7. The progressive left shift of the oxyhemoglobin dissociation curve is caused by increasing saturation of hemoglobin with carbon monoxide (I = 0%, II = 10%, III = 25%, IV = 50%, and V = 75%). This is Haldane's great contribution to our understanding of the pathophysiology of carbon monoxide exposure. Reprinted with permission from Haldane JS. *Respiration*. New Haven, Conn: Yale University Press; 1922. © 1922 Yale University Press.

residual decrement of oxygen-carrying capacity. The hemoglobin molecule resumes its normal configuration and functions. The residual clinical effects following carbon monoxide poisoning appear to be secondary to tissue damage caused by oxygen deprivation at the level of the affected organ.[9]

However, because 10% to 15% of the body's total carbon monoxide is bound in the extravascular space,[33,34] it may be that some of carbon monoxide's toxicity is not directly related to defective oxygen transport. Cytochrome a_3 oxidase has been suggested as the (or perhaps *a*) major site of toxic action of carbon monoxide.[12,33] In addition to cytochrome oxidase, other extravascular proteins that bind with carbon monoxide include other heme proteins such as myoglobin, and cytochrome P-450. The interaction of carbon monoxide with the hyperperoxidases might cause oxygen radicals to be generated, which would result in cellular damage.[33]

More subtle modes of injury or dysfunction may also be possible. Humans normally produce small quantities of carbon monoxide through the action of the enzyme heme oxygenase. The fact that heme oxygenase is present in high concentration in several areas of the brain, together with carbon monoxide's known ability to activate intracellular enzymes that are important in the regulation of cellular function, suggests that carbon monoxide might serve as a neurotransmitter in the central nervous system (CNS).[35] It is easy to imagine that small amounts of exogenous carbon monoxide might cause undesirable effects that are not associated with carbon monoxide's effect on oxygen transport, not only in the CNS but perhaps elsewhere as well.

HEALTH EFFECTS

In experiments using himself as the study subject in 1895, Haldane reported that he noted the first apparent effects of carbon monoxide exposure at a concentration of approximately 20% carboxyhemoglobin.[7] At that level, he noted (in association with running up stairs) dizziness, palpitation, and hyperpnea. Haldane reported increased pulse rate and deeper breathing at 30% carboxyhemoglobin saturation; however, because he feared he would faint, he did not report on exertion at 40% saturation. His hearing, vision, and intellect seemed impaired at levels of 50%, with impaired motor function, diminished writing ability, and impaired perception. Associated signs included extreme exercise intolerance and collapse at 50% carboxyhemoglobin content.

Early reports indicated that death resulted at a level of approximately 80% carboxyhemoglobin. Most unconscious individuals did not immediately regain consciousness with treatment, and individuals who remained unconscious for periods longer than 24 hours after their removal from exposure were considered to have significant potential CNS or cardiac sequelae.[6]

Haldane initially postulated that a concentration of 0.05% carbon monoxide in ambient air would be required to produce an in vivo concentration of 30% carboxyhemoglobin in humans. The observations and conclusions derived from subsequent experiments resulted in the revision of the exposure level to 0.02% (200 ppm) of ambient carbon monoxide to produce 30% saturation.[7]

The relation between carbon monoxide's toxicity and its concentration in ambient air had been emphasized by the French authors of the 1918 medical treatise (discussed earlier in this chapter), who concluded that

- 1 part carbon monoxide per 10,000 parts ambient air may produce casualties;
- 2 parts per 10,000 may be fatal; and
- 3 parts per 10,000 is fatal within 20 minutes for a man at rest and much sooner during physical exertion.[13]

Symptomatology and collapse from exposures had been correlated with exposures early in the 20th century: a rough estimate of time to lethality for man was associated with breathing 0.2% carbon monoxide for 4 to 5 hours, or 0.4% for 1 hour. For air containing 2% to 5% carbon monoxide, such as is found in mine explosions, a few breaths were considered lethal, with death occurring as "quickly as in drowning" or "rapidly as if struck by lightning."[2] In cases of rapid collapse, no apprehension or other apparent prodromal warnings were reported. Poisonings associated with lower concentrations of carbon monoxide were reported to cause headache, tinnitus, epigastric distress, weakness, hallucinations, blurred vision, and convulsions.

Autopsy Findings

Early reports of death attributed to carbon monoxide poisoning indicated that anatomic autopsy findings were helpful in diagnosis of the cause of death. The skin color of the poisoned person differs from the skin color of persons dying of other causes.[9] The face may be bright red and rose-red spots may be present on the face, neck, breast, and limbs. The color of the

skin between the red areas is also likely to be abnormal and may be cyanotic. Blood color in poisoned individuals can range from bright red to very dark red to black. There is no change in blood coagulation. Ecchymoses, effusions, or hemorrhages occur with reddening of the digestive tract. There are no marked characteristic changes in the respiratory tract, although a thick, frothy mucus or digestive contents have been found in the upper respiratory passages. Hyperemia of the brain, with edema and blood-tinged intraventricular fluids are characteristic findings at autopsy. Local hemorrhagic lesions may range from microscopic to "the size of an apple."[9]

Other pathological abnormalities including spectroscopic evidence of carboxyhemoglobin, bronchopneumonia, fatty degeneration of blood vessels and heart, extensive tissue hemorrhage, necrosis of the lenticular nucleus, thrombosis, and encephalitis were commonly reported sequelae.[2]

Signs and Symptoms of Carbon Monoxide Poisoning

The progression of signs and symptoms of carbon monoxide poisoning and increasing levels of carboxyhemoglobin were described in 1923 and have been reproduced, with minimal modifications, in medical textbooks for more than half a century (Table 11-1).[9] Although more recent researchers have recognized that the carboxyhemoglobin level may not always correlate with the degree of clinical impairment associated with intoxication, the tabular information remains useful as a general guideline.[12]

The critical target organs of carbon monoxide exposure (*a*) are metabolically active and (*b*) require continuous supplies of oxygen-rich blood. The most critical organ systems appear to be the heart and the CNS.[4,11,32,36,37]

A carbon monoxide–exposed individual may appear to be grossly normal and the typical findings of carbon monoxide poisoning may not be identified during a routine exam. The findings are more apparent if the examination is directed toward abnormalities of function of the basal ganglia. Insults of basal ganglia function are characteristic of carbon monoxide intoxication and include tremor, slowed reaction time, impaired manual dexterity, impaired hand–eye coordination, and difficulty sequencing complex movements.[11]

With high-concentration exposures, carbon monoxide is readily absorbed and the carboxyhemoglobin content increases rapidly. In this circumstance, only transient weakness or dizziness may be noted before the individual becomes unconscious. When exposures are more prolonged and the carboxyhemoglobin content increases slowly, affected individuals may remain conscious but unable to escape because of weakness or impaired judgment.[1,2]

Based on lay accounts and clinical observations, the military circumstance in which exposure conditions

TABLE 11-1
SIGNS AND SYMPTOMS OF CARBON MONOXIDE POISONING

Carboxyhemoglobin Saturation (%)	Signs and Symptoms
0–10	None
0–20	Tightness across forehead, possibly slight headache, dilation of cutaneous blood vessels
20–30	Headache, throbbing in temples
30–40	Severe headache, weakness, dizziness, dimness of vision, nausea and vomiting, collapse
40–50	Same symptoms as at 30%–40%, but with greater possibility of collapse and syncope, and increased rates of respiration and pulse
50–60	Syncope, increased rates of respiration and pulse, coma with intermittent convulsions, Cheyne-Stokes's respiration
60–70	Coma with intermittent convulsions, depressed heart action and respiration, possibly leading to death
70–80	Weak pulse, slowed respiration, respiratory failure, and death

Source: Adapted from Sayers RR, Yant WP. Dangers of and treatment for carbon monoxide poisoning. *Reports of Investigations.* US Department of the Interior, Bureau of Mines; May 1923. RI 2476. Available from UPDATA Publications, Inc, Los Angeles, Calif.

were superimposed on combat conditions complicated the individual's awareness of the symptoms of carbon monoxide poisoning. With the moderate exposures experienced during World War I, the onset of symptoms of intoxication associated with uncomplicated anoxemia was often first noticed as a loss of power in the limbs. Giddiness, confusion, breathlessness, and palpitations were reported to follow increasing ambient carbon monoxide concentrations. Mental confusion caused individuals to appear drunk: shouting incoherently, laughing, swearing, or praying. The mental confusion appeared to suppress the desire or ability to seek escape despite apparent danger. As limiting factors in egress and avoidance, the mental impairments associated with carbon monoxide exposure appeared to be compounded by the loss of strength in the limbs. With progressive apathy and helplessness, many individuals passed gradually into coma and death.[6]

In contrast to the rapidly progressive signs of acute exposures to high ambient carbon monoxide concentrations, many cases of mild poisoning developed more slowly and were associated with the nonspecific clinical warning signs of headache and nausea, similar to those experienced with mountain sickness.[6] The degree of clinical response depends on the

- rate of absorption,
- final carboxyhemoglobin concentration in the blood,
- duration of hypoxia,
- preexisting health status, and
- concurrent whole-body oxygen requirement.[1]

The earliest and most constant ocular signs of carbon monoxide exposure are congestion of the retinal vessels and hyperemia of the optic disc. W. H. Wilmer noted in 1921 that findings of amblyopia and complete blindness were sequelae "not infrequently" observed.[10]

Staging of Signs and Symptoms

Since 1909, the signs and symptoms associated with exposures have been divided into two stages, depending on the responses of the nervous system.[9] Stage I, from normal to the onset of syncope, is often associated with neurological stimulation. Stage I signs and symptoms may include tightness across the forehead, cutaneous vasodilatation, frontal or basal headache, throbbing of the temporal regions, weakness, dizziness, nausea, vomiting, loss of strength or muscular control, increased pulse or respiration, and collapse. Signs and symptoms are more severe when exposure is associated with exercise:

> Men at rest have often been exposed to carbon monoxide all day without noticing any marked ill-effects, but on walking home or exercising have experienced severe symptoms, even to unconsciousness.[9]

In cases of high-dose exposures, the onset of syncope may be rapid and not associated with other signs or symptoms.[9]

Stage II, from syncope to coma and death, is characterized by nervous-system depression. These signs and symptoms include an increase in pulse and respiration, fall in blood pressure, loss of muscular control, loss of sphincter tone, loss of reflexes, convulsions, Cheyne-Stokes respiration, slowed pulse, decreased respiratory activity, apnea, and death.[9]

Exposure and Muscular Exertion

The character and degree of symptoms associated with carbon monoxide exposure depend on the duration and concentration of exposure and the amount of muscular activity. The symptoms and after-effects of exposure are more severe after prolonged than after short-term, high-level exposure. Muscular activity increases oxygen demand and accentuates exposure effects; resting individuals may experience no symptoms prior to the onset of unconsciousness.[9,38]

The relationship between carbon monoxide absorption and exercise is directly proportional to the amount of air breathed. At moderate exercise, a person breathes approximately twice as fast as at the resting rate; therefore, carbon monoxide absorption is approximately doubled. Heavy work increases the respiratory rate by approximately 3- to 4-fold, with a proportional increase in carbon monoxide absorption.[9] Firefighters are at extreme risk of carbon monoxide exposure while working at a heavy degree of exertion. For example, researchers have estimated that a firefighter has a 2.5% increase in carboxyhemoglobin after 2 minutes of exposure to a concentration of 1,000 ppm (0.1%). With heavy exercise, a 60% increase in carboxyhemoglobin content is predicted after a 2-minute exposure to 2% carbon monoxide and a 75% increase is predicted after a 1-minute exposure to 5% (50,000 ppm).[16] Other factors such as low oxygen pressures, high temperature, and high humidity also cause a relative increase in carbon monoxide absorption.[9]

Central Nervous System Effects

The plethora of signs and symptoms of carbon monoxide poisoning are characteristic of those seen with progressive hypoxia, but they also can mimic virtually any neurological or psychiatric illness. Signs

consistent with multiple sclerosis, parkinsonism, bipolar disorder, schizophrenia, and hysterical conversion reaction have been reported in association with acute carbon monoxide intoxication.[11] Numerous CNS sequelae following carbon monoxide poisoning have been reported. They may include headache, muscular pain, loss of strength, loss of memory, paralysis, temporary blindness, and mental derangement. In most cases, the sequelae clear within a few days, but may be seen for months or years following the acute event.[9] CNS sequelae have been reported to include choreiform movements and convulsions,[5,28] cortical blindness, peripheral neuropathy, and delayed neurological sequelae.[28] Neuropsychiatric sequelae may be more common than is generally appreciated, with findings of permanent sequelae such as personality deterioration or memory loss in 0.3% to 10% of patients.[39]

Acute neurobehavioral effects of carbon monoxide exposure such as compromised dark adaptation and impaired visual tracking have been postulated to impair performance in aircraft handling and target acquisition. Military medical concerns about the presumed impact of the neurobiological effects on performance resulted in the promulgation of carboxyhemoglobin levels for carbon monoxide exposure levels and equipment-design specifications.[40] Visual acuity appeared to be impaired by carboxyhemoglobin levels in the range of 3% to 5%.[36]

Scientific studies performed and published within the last several years have failed to replicate the findings of earlier neurobehavioral studies. For example, individuals who were exposed to carbon monoxide sufficient to produce carboxyhemoglobin levels of 16% to 23% failed to exhibit significant differences related to clinical symptoms, electroencephalographic recordings, and compensatory visual tracking from the control group.[41–44]

Circulatory Effects

The heart depends almost exclusively on aerobic metabolism and is a highly sensitive organ to the decrease of oxygen secondary to carbon monoxide exposures. Under normal conditions, the heart muscle extracts both pyruvate and lactate for use in metabolic oxidation. However, at carboxyhemoglobin levels above 8.7%, neither is extracted and both are produced by the myocardium.[12]

Individuals with compromised cardiac vascularity may have increased sensitivity to carbon monoxide exposures and could experience angina at low carboxyhemoglobin concentrations. A preliminary series of studies suggested an earlier onset of angina in individuals with carboxyhemoglobin concentrations as low as 2% to 3%. Although those studies failed to endure peer review, it has been postulated that angina could occur in working individuals following carbon monoxide exposure.[4] Other studies indicate that myocardial irritability may result in abnormalities of the electrocardiograph or arrhythmias with carboxyhemoglobin levels above approximately 9%.[36]

Chest pain and tachycardia, in response to tissue hypoxia, may be present with carbon monoxide poisoning. Carbon monoxide lowers the threshold for ventricular tachycardia and therefore death secondary to arrhythmia is commonly associated with poisoning.[11] Individuals with preexisting cardiac disease, coronary artery disease, anemia, and lung disease are more susceptible to the effects of carbon monoxide–induced tissue hypoxia.[11,31]

A study titled *Non Invasive Ambulatory Assessment of Cardiac Function and Myocardial Ischemia in Healthy Subjects Exposed to Carbon Monoxide (CO)* is in progress at the U.S. Army Biomedical Research and Development Laboratory (USABRDL), Fort Detrick, Frederick, Maryland. The proposed research attempts to explore the potential interaction between progressive levels of carbon monoxide exposures and myocardial responses in human subjects. It is hypothetically plausible that increasing levels of exposure may induce signs or symptoms or both of myocardial ischemia among crews of armored vehicles. In these vehicles, the crew is routinely exposed to the same levels of carbon monoxide that have been associated with ischemic responses in experimental animals and human subjects.[45,46] It is possible that a soldier with early cardiovascular disease could suffer an adverse myocardial event if he or she is exposed to the concentrations of carbon monoxide that can be generated when armored vehicles are operated.

Specific objectives of this study are to identify the potential adverse relationships between cardiopulmonary response and progressively increasing levels of carboxyhemoglobin. Dosage ranges for carbon monoxide exposures will be manipulated by monitoring control of carboxyhemoglobin levels in a range of 5% to 20%. In addition, the simultaneous performance of simulated work loads approximating moderate effort at the tank loader position will be superimposed.

The initial study will evaluate cardiac performance profiles in 20 apparently healthy research volunteers. Five experimental conditions will be imposed, with the subjects

1. at rest,
2. on a treadmill,
3. performing upper-body exercise,
4. on a treadmill and exposed to increasing

levels of carbon monoxide exposures (5%, 10%, 15%, and 20% carboxyhemoglobin), and
5. performing upper-body exercise and exposed to comparable increases in carbon monoxide.

In one report, the capacity of individuals with carboxyhemoglobin levels of 15% to 20% to perform short-duration, submaximal physical work was not compromised. Individuals with 10% to 13% carboxyhemoglobin levels who performed work at 35% of the maximal work rate demonstrated only minimal increases in heart rate after working periods of 3.5 hours. The maximum work capacity (as defined by the maximum amount of oxygen that can be transported by the cardiopulmonary systems, which is described as VO_2 *max*) is decreased following carbon monoxide exposures that generate carboxyhemoglobin levels less than 5%. The capacity to perform physical work is dramatically compromised at carboxyhemoglobin levels in excess of 40% to 45%.[4] Time to fatigue and time to angina are both shortened after carbon monoxide exposure.[37]

Chronic Effects

Effects of chronic exposures to carbon monoxide were reported in the early 1920s.[2] Two groups of workers were identified: those who become acclimated and those who do not. E. R. Hayhurst believed that the acclimation difference was probably associated with cardiac condition at the time of exposures. Those individuals who were able to become acclimatized developed compensating increases in their erythrocyte counts and hemoglobin content. Although Hayhurst's conclusion remains controversial, other investigators have concluded that long-term exposures to carbon monoxide may be associated with arteriosclerotic heart disease.[33,37]

After being removed from carbon monoxide exposures, patients usually progressively improve without sequelae to complete recovery. However, some patients may have a transient period of apparent normal physiological recovery for days to weeks after poisoning, then develop evidence of CNS or cardiovascular-system impairment.[1,11] In early reports, the prognosis of recovery following carbon monoxide exposure was considered to be associated with the degree of asphyxia related to the exposure. In many cases, men who were exposed to carbon monoxide in mines were thought to develop a permanent weakness of the heart muscle as a consequence.[2] Other severe exposures were reported to cause loss of vision, speech, or other CNS defects. However, more recent reports suggest that carboxyhemoglobin levels correlate with neither the severity of the acute poisoning nor the potential for delayed effects.[11]

The sequelae of nonlethal acute exposure to carbon monoxide reported in the literature of the early 1900s included pneumonia, psychoses, paralysis, bullous skin lesions, and gangrene.[2] The spectrum of medical opinion concerning potential sequelae of exposure reported in the literature was broad and controversial. For example, the chief surgeon of an Illinois steel company, who had extensive experience in caring for carbon monoxide–poisoned workers, reported that he had never seen a case of psychosis directly attributed to the carbon monoxide exposure. In contrast, a contemporary practitioner listed 105 neuropsychiatric conditions that were associated with carbon monoxide exposure sequelae. The most common acute-onset neurological sequelae are aggressiveness, moodiness, irritability, impulsiveness, and memory loss. Transient CNS disorders may include neurological deficits, memory loss, cognitive difficulty, and personality change.[3,11]

Bilateral, low-density lesions in the area of the globus pallidus are characteristic findings associated with carbon monoxide poisoning and may be identified using computed tomography or magnetic resonance imaging. The lesions are usually seen in about 50% of individuals with severe poisoning; however, neuro-radiological studies may not be positive for 2 to 3 days following acute poisoning. Lesions in the gray matter of the basal ganglia may regress, but lesions in the white matter are likely to become permanent and a delayed neuropathy will ensue.[11]

The delayed neuropsychiatric syndrome may occur as long as 6 weeks after the patient has recovered from acute toxic exposure to carbon monoxide. The syndrome occurs as a complication in 2% to 30% of carbon monoxide–poisoned patients.[3] The first case was reported in 1926. A 58-year-old woman had attempted suicide with carbon monoxide inhalation. After acute recovery, the woman became mute and suffered progressive disorientation and parkinsonism, followed by death. The autopsy revealed bilateral necrosis of the globus pallidus and widespread demyelinization of the subcortical white matter.[11]

Delayed sequelae appear to be frequent in the young and old, but more commonly occur in elderly patients who have suffered coma. All individuals who suffer coma do not experience delayed neurological sequelae,[11] but coma has been identified as a risk factor in other reports.[28] Clinical signs of delayed sequelae may include urinary or fecal incontinence, weakness, gait disturbances, tremor, mutism, speech abnormalities, and mental deterioration. Complete recovery occurs in about 75% of individuals within a year.[3]

DIAGNOSIS AND TREATMENT

It cannot be emphasized too strongly that the signs and symptoms of carbon monoxide poisoning are pleomorphic: headaches of varying degrees of severity, dizziness, nausea and vomiting, blurred vision, impaired thinking, and numbness and seizures.[47,48] Therefore, physicians must maintain a high degree of suspicion when confronted with a patient who manifests some or all of these signs and symptoms. A diagnosis of carbon monoxide poisoning will *never* be made unless the physician thinks to order confirming laboratory tests.

Clinical Diagnosis

Laboratory evaluations for carbon monoxide–poisoned patients are usually deceptively normal, with the exceptions of the blood carboxyhemoglobin content[11] and elevated carbon monoxide concentrations in exhaled breath.[12] The arterial oxygen contents appear normal and fail to confirm the initial diagnostic impression of anoxemia. This is because conventional laboratory analysis depends on two determinations: (1) measurement of the partial pressure of oxygen dissolved in the plasma, which is used to estimate the oxygen saturation of hemoglobin from a standard oxyhemoglobin dissociation curve (see Figure 11-6). This value, in conjunction with the measured concentration of hemoglobin, is used (2) to estimate the arterial oxygen content. Unfortunately, neither the partial pressure of oxygen dissolved in plasma nor the concentration of hemoglobin is affected by the presence of carbon monoxide in the blood. Because the laboratory determination of arterial oxygen saturation depends on two parameters that are not directly affected by carbon monoxide, it is not surprising that significant hemoglobin desaturation may be missed.

Analyzing exhaled air has been advocated recently as a method of measurement of blood levels of carboxyhemoglobin following carbon monoxide exposure. Measuring the carbon monoxide concentration in end-alveolar breath samples after the subject has held his or her breath for 20 seconds has two advantages: the equipment is field transportable and takes minimal training for proper use. Some authorities indicate that the method is an acceptable technique for documenting workplace exposure controls.[16]

Commonly available laboratory modalities are rarely diagnostic but may be confirmatory. Metabolic acidosis may be reflected by an increased level of lactic acid. Blood glucose level and nonspecific enzyme levels indicative of tissue injury (eg, creatine kinase, lactate dehydrogenase, alanine transferase, and aspartate transferase) may be elevated.[11]

Electrocardiographic findings are not specific for carbon monoxide intoxication, but demonstrate changes consistent with hypoxemia. Individuals with coronary artery disease may complain of angina with carboxyhemoglobin levels as low as 10%.[11] At a minimum, an electrocardiograph should be obtained for all individuals with chest pain who have been exposed to carbon monoxide. At carboxyhemoglobin levels above 25%, ST segment depression may be seen in leads II, V_5, and V_6. Depression of the ST segment has been used as a criterion for instituting hyperbaric oxygen therapy.[12]

Treatment

The essential first step in treating an individual suspected of being poisoned by carbon monoxide is to remove the patient from the potentially contaminated environment. This action is necessary not only to prevent further poisoning of the patient but also—and of equal importance—to prevent poisoning the healthcare provider. The following measures should be instituted once the patient is in a safe environment:

- Insert an endotracheal airway if the patency of the patient's upper airway is compromised.
- Ventilate mechanically if the patient's respiratory gas exchange is inadequate.
- Infuse intravenous fluids and vasoactive drugs if circulatory shock is present.

The patient should receive supplemental oxygen at a concentration of 100% as soon as possible. This requirement will necessitate the use of a tight-fitting face mask if intubation of the upper airway has not been performed.

The treatment of carbon monoxide poisoning is, in theory, extremely simple: increase the partial pressure of oxygen in the lungs so as to displace carbon monoxide from the carboxyhemoglobin. Although delivering 100% oxygen at 1 atm is an effective modality, this displacement can be accelerated by using higher ambient pressures. The technology for creating ambient environments of super-atmospheric pressures has long existed (its first known use was in 1664) but its use until recently was confined to treating deep-sea

divers stricken with decompression sickness. Because delivering pure oxygen at hyperbaric pressures is now used to treat a number of conditions, it is not surprising that hyperbaric oxygen has also been applied to carbon monoxide–poisoned patients.[49]

Carboxyhemoglobin response curves using room air, 100% oxygen, and hyperbaric oxygen treatment modalities can be compared, using the half-life of carboxyhemoglobin concentrations for room air (5 h and 20 min), 100% oxygen delivered by tightly fitting mask (1 h and 20 min), and hyperbaric oxygen at 3 atm (23 min) (Figure 11-8). Delivery of hyperbaric oxygen at 3 atm results in the physical dissolving of 6.4 volumes percent (eg, 6.4 mL oxygen in 100 mL plasma), which is sufficient to displace carbon monoxide from cytochrome a_3 oxidase in tissues.[12] When the patient breathes oxygen pressurized to 3 atm, adequate oxygen—sufficient to support metabolism even in the complete absence of functioning hemoglobin—is forced to dissolve in the plasma. Because the arteriovenous difference in cerebral blood flow is only 6.1 volume percent, the patient's ability to adequately oxygenate the brain and other tissues improves immediately.

The immediate therapeutic goals of hyperbaric oxygen therapy are to reduce cerebral and myocardial hypoxia, reduce cerebral edema, and enhance carbon monoxide elimination.[28] Actual and suggested benefits of hyperbaric oxygen therapy are that it

- rapidly provides sufficient dissolved plasma oxygen to meet the metabolic oxygen requirement;
- significantly enhances carboxyhemoglobin dissociation;
- causes increased carbon monoxide clearance[11,12]; and
- is beneficial in managing cerebral edema, a complication of carbon monoxide poisoning, reducing secondary intracranial pressure by 50% within 1 minute of its administration.[12]

It is important to note that some authorities believe that no conclusive evidence yet demonstrates a relationship between a shortened duration of symptoms and the frequency of delayed sequelae of poisoning.[11] However, one researcher uses hyperbaric oxygen at carboxyhemoglobin levels above 25% even if the patient is not particularly ill. It has been his experience that patients treated with hyperbaric oxygen are spared the prolonged headache and nausea and might experience fewer delayed aftereffects of poisoning.[12]

Although some researchers conclude that the use of hyperbaric oxygen is controversial,[11] another states that failure to administer hyperbaric oxygen for severely poisoned patients has resulted in successful malpractice litigation.[12] Others stress the therapeutic efficacy of hyperbaric oxygen administration.[28] Authorities generally agree that, for individuals with no other risk factors, hyperbaric oxygen is beneficial if carboxyhemoglobin levels are in excess of 25%.[3,11] The most important reason for administering hyperbaric oxygen appears to be the presence of neurological deficits such as disorientation or focal signs, loss of consciousness, and seizures.[50] Other indications include cardiac ischemia, metabolic acidosis, and pregnancy.[3]

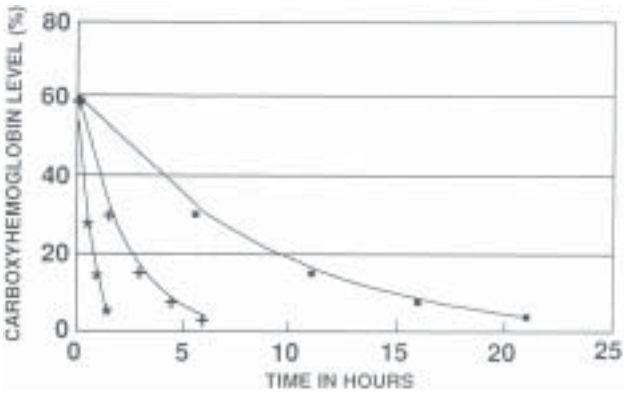

Fig. 11-8. Carboxyhemoglobin half-life. The comparative benefits of medical management for carbon monoxide–intoxicated patients using room air (■), 100% oxygen (+), and hyperbaric oxygen at 3 atm pressure (*). Reprinted with permission from Kindwall EP. Carbon monoxide poisoning. *Hyperbaric Oxygen Rev*. 1980:1(2):115–122.

Hyperbaric oxygen therapy has also been recommended for individuals who are considered to be more susceptible to carbon monoxide effects or sequelae (infants and children, and adults who have preexisting cardiac ischemia or seizure disorders,[11] arterial vasospasm, past myocardial infarct, anemia, and pregnant females).[38] The fetus is much more susceptible to carbon monoxide than the mother. The oxyhemoglobin dissociation curve for fetal hemoglobin is to the left of that for adult hemoglobin (oxygen does not dissociate as easily from fetal as from adult hemoglobin). As it does in adult hemoglobin, carbon monoxide reacts to form fetal carboxyhemoglobin, which accentuates the left shift. Carboxyhemoglobin levels in the fetus lag behind those in the mother; however, the final fetal hemoglobin level may be 10% to 15% higher than the maternal level.[33] In addition,

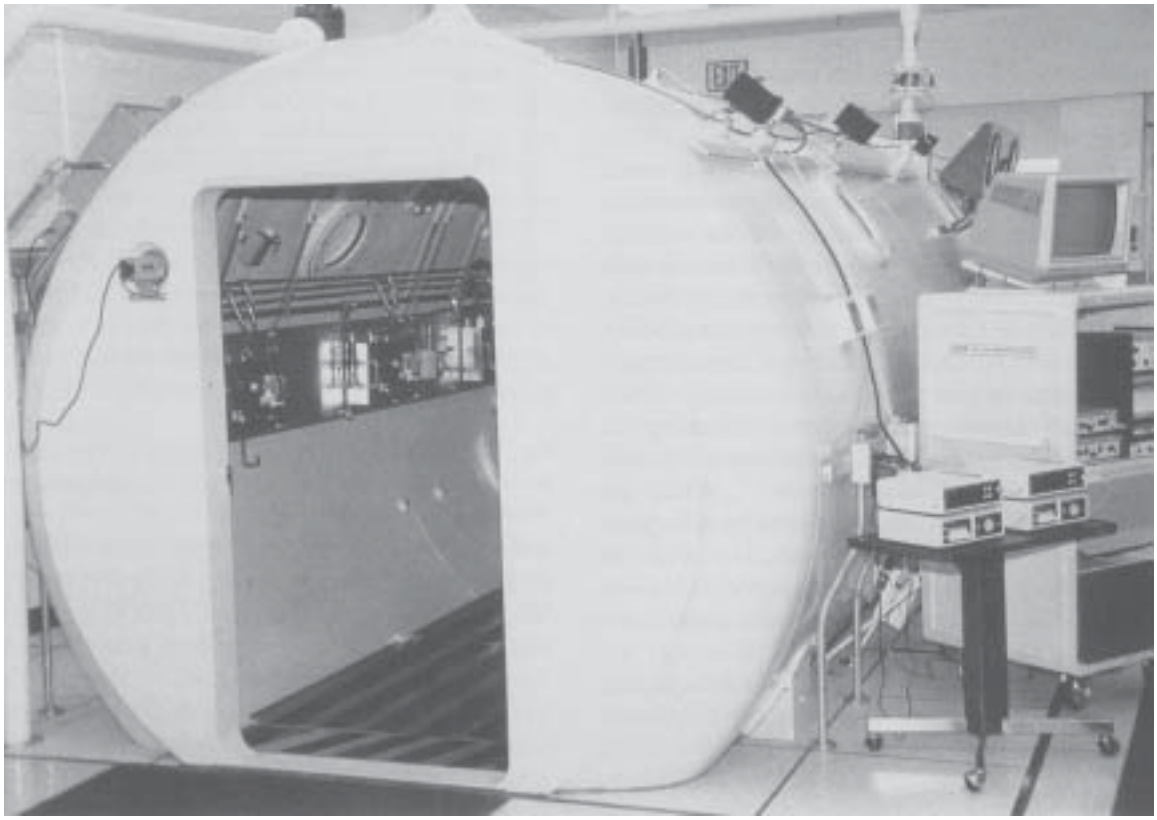

Fig. 11-9. Large walk-in clinical hyperbaric medicine facility, Travis Air Force Base, California. Photograph: Courtesy of the US Air Force.

the half-life of fetal carboxyhemoglobin is 15 hours; therefore, it takes 5-fold longer to regenerate oxyhemoglobin in the fetus than in the mother.[11]

Hyperbaric oxygen facilities are either a large walk-in chamber (Figure 11-9) or a small chamber that will accommodate only one person. The U.S. Air Force School of Aerospace Medicine at Brooks Air Force Base, Texas, maintains a 24-hour per day telephone system to help physicians locate the nearest hyperbaric oxygen treatment facility.[51] Although a specialist in hyperbaric medicine will probably manage the patient on arrival at the hyperbaric oxygen facility, it is important for occupational medicine physicians to understand these therapeutic procedures.

One clinician uses a walk-in hyperbaric chamber and routinely manages carbon monoxide–poisoned patients using 3 atm of oxygen pressure for 56 minutes (2 half-lives).[12] If the carboxyhemoglobin remains greater than 10% at that time, the pressure is decreased to 2 atm for the remainder of the treatment or until the carboxyhemoglobin is less than 10%. In very severe cases, the U.S. Navy Decompression Treatment Table 6 is used.[52] The table begins at 2.8 atm of oxygen for 4 hours, then decreases to 1 atm over 285 minutes, with 5- to 15-minute "air breaks" interspersed in the schedule. Occasionally, patients require therapy once or twice daily for several days. Patients may recover their memory after the second treatment, and patients treated with hyperbaric therapy do not appear to develop delayed cardiac or neurological sequelae of carbon monoxide poisoning.[12]

Hyperbaric oxygen administration has a number of therapeutic advantages, but is also associated with potential complications. Minor complications include tooth, ear, or sinus pain or discomfort. However, more serious complications—evidence of oxygen poisoning—can occur, including substernal pain, decreased vital capacity, or pulmonary microhemorrhage, although these conditions occur rarely. If individuals are treated for more than 6 hours with oxygen at 2 atm, pulmonary oxygen toxicity with microhemorrhage and fibrosis has been reported.[12] The only absolute contraindication against hyperbaric oxygen therapy is an untreated pneumothorax.[53]

HEALTH STANDARDS

Determining the exposure levels at which carbon monoxide causes health effects has been difficult; thus developing consistent, valid exposure standards has been problematic. This is due to both the large number of exposure variables that influence carbon monoxide poisoning and a high degree of fluctuation for many of the variables. For example, the respiratory rate, level of work effort, baseline carbon monoxide level, and individual tolerance for carbon monoxide must all be considered—in addition to carbon monoxide levels in air. Additionally, a *high rate of increase* in carboxyhemoglobin concentration may increase the probability that symptoms will develop. No direct, consistent relationship between estimates or measured carboxyhemoglobin levels and health effects has been demonstrated, at least for low-to-moderate levels of exposure.

The estimates of human toxicity were the subjects of early scientific controversy. Some scientists reported onset of symptoms at ambient carbon monoxide concentrations of 0.01%, while others reported onset of signs and symptoms at 0.05%. Another early investigator estimated the limit of toxicity as 0.2%. Such conflicts result from differing exposure scenarios and individual study differences.

Occupational Safety and Health Administration

The federal statutory exposure limits are promulgated by the Occupational Safety and Health Administration (OSHA). The current permissible exposure limit (PEL) for carbon monoxide is 35 ppm, with a ceiling concentration of 200 ppm. OSHA has defined *ceiling* as a concentration that should not be exceeded during any part of the workday. However, if instantaneous monitoring is not feasible, the ceiling must be assessed as a 15-minute time-weighted average (TWA).[54]

The PEL is intended to maintain the carboxyhemoglobin levels of exposed employees below 5%. The standard was developed to protect individuals with cardiovascular or pulmonary impairment and to protect healthy workers during conditions of heat stress, exertion, and strenuous conditions.[33] The immediately dangerous to life or health (IDLH) concentration promulgated by OSHA is 1,500 ppm. The IDLH for carbon monoxide is defined as the concentration that an unprotected worker could escape from within 30 minutes without experiencing irreversible health effects.[54] It has been estimated that for light activity (minute ventilation of 9–10 L/min), a carbon monoxide exposure concentration of 1% (10,000 ppm) could result in death in less than 10 minutes.[36]

American Conference of Governmental Industrial Hygienists

The term Threshold Limit Value (TLV) is published as an exposure recommendation for specific hazards by the American Conference of Governmental Industrial Hygienists (ACGIH). The TLV is defined as an 8-hour TWA concentration of a specific chemical to which nearly all workers may be exposed for 40 hours per week, day after day, without adverse effect.[33] The present recommended TLV for carbon monoxide is 50 ppm, with the indication that the ACGIH intends to reduce the recommended TLV to 25 ppm in 1993.

While the current TLV is intended to maintain carboxyhemoglobin concentrations below 10% in exposed workers, the intended 25 ppm level is expected to maintain carboxyhemoglobin levels below 3.5%. The decreased limit is intended to reduce exposure risks for susceptible workers such as pregnant women who must perform psychomotor tasks, or employees who have chronic cardiac or respiratory disease. Although the ACGIH currently recommends a 15-minute short-term exposure limit (STEL) of 400 ppm, the organization has expressed the intent to omit the STEL from future carbon monoxide exposure recommendations.[33]

Committee on Toxicology

The Committee on Toxicology of the National Research Council has developed and recommended emergency exposure guidance levels (EEGLs) for carbon monoxide (a ceiling limit for unpredicted exposure for a single, isolated, exposure time—usually less than 60 min, but never longer than 24 h) (Table 11-2). The EEGL has replaced an older term, the emergency exposure limit (EEL).[4]

In response to specific sponsor requests, the Committee on Toxicology will develop and provide recommendations for continuous exposure guidance levels (CEGLs). An older term, the continuous exposure level (CEL) was developed in response to a U.S. Navy request for guidance tailored to submarine environments. The CEGL is defined as a recommended exposure limit with the potential for continuous exposure for a duration up to 90 days. It is intended as a ceiling limit, and is designed to avoid both the degradation of

TABLE 11-2

CURRENT (1985) AND PREVIOUS (1965) EXPOSURE LEVELS FOR CARBON MONOXIDE

Exposure	1985 EEGL	1965 EEL	1985 CEGL	1965 CEL
10 min	1,500 ppm	1,500 ppm	—	—
30 min	750 ppm	800 ppm	—	—
60 min	400 ppm	400 ppm	—	—
24 h	50 ppm	200 ppm	—	—
90 d	—	—	20 ppm	25 ppm

EEGL: emergency exposure guidance level
EEL: emergency exposure limit
CEGL: continuous exposure guidance level
CEL: continuous exposure level
Source: Committee on Toxicology. *Emergency and Continuous Exposure Guidance Levels for Selected Airborne Contaminants*. Vol 4. Board on Toxicology and Environmental Health Hazards, Commission on Life Sciences, National Research Council. Washington, DC: National Academy Press; 1985.

military-mission performance and immediate or delayed adverse health effects among exposed military members. The current CEGL for carbon monoxide is 20 ppm, a decrease from the 1965 CEL of 25 ppm.[4]

In the past, both EELs and CELs have been used as design criteria for military equipment with enclosed environments such as submarines and spacecraft. The conditions and terms of applicability of the levels were related to narrowly defined occupational exposure groups and were not intended for general population exposure. They include no consideration of hyper-susceptible individuals.[4] In 1985, the Committee on Toxicology provided the revised exposure levels (ie, EEGLs and CEGLs).

The Committee on Toxicology predicted that the recommended exposure levels should never result in carboxyhemoglobin levels above 10% as a result of exposure. The committee also predicted that an individual exposed to the 24-hour limit of 50 ppm should not demonstrate carboxyhemoglobin levels greater than 7.5%, or if exposed to 20 ppm for the 90-day limit, should not produce carboxyhemoglobin levels greater than 3.3%.[4]

The Committee on Toxicology stressed that individuals with compromised cardiovascular status (eg, as a result of atherosclerosis) may be at increased risk for angina or sudden cardiac death. The committee recommended that individuals exposed to these levels in militarily unique circumstances such as submarine service undergo careful physical examinations and refrain from smoking when exposed to these levels.[4]

The Committee on Toxicology reviews available scientific data and develops recommended exposure levels for use by its sponsoring organizations. The council was established by the National Academy of Sciences to assist the academy in preparing its advice to the federal government. The council has now become the principal operating agency of both the National Academy of Engineering and the National Academy of Sciences. Both organizations provide services to the government, the public, and the scientific and engineering communities. The Council is administered by both organizations and the Institute of Medicine.[4]

Military Standards

A militarily unique standard (Military Standard [MIL-STD]-1472C, Paragraph 5.13.7.4.1, *General*) has been promulgated for Department of Defense (DoD) use. The standard states that personnel will not be exposed to concentrations of toxic substances in excess of the DoD Occupational Safety and Health standards or specialized standards applicable to militarily unique equipment, systems, or operations.[40] With specific reference to carbon monoxide, MIL-STD-1472C, Paragraph 5.13.7.4.2, *Carbon Monoxide*, states

> that carbon monoxide in personnel areas shall be reduced to the lowest level feasible. Personnel shall not be exposed to carbon monoxide in excess of values which will result in carboxyhemoglobin levels

in their blood greater than the following percentages: 5 percent [carboxyhemoglobin] (all systems design objectives and aviation system performance limits); 10 percent carboxyhemoglobin (all other system performance limits).[40]

The pharmacodynamics of carbon monoxide intoxication have been discussed earlier in this chapter. Because many factors (in addition to absolute exposure level) influence the formation of carboxyhemoglobin, no one exposure level can directly be related to the 5% and 10% carboxyhemoglobin levels that are published in MIL-STD-1472C. Further complicating this dilemma is the large degree of variability of factors that relate to carbon monoxide exposure in military situations. Factors such as the duration of exposure, the rate of rise of carbon monoxide levels, and intermittent changes in levels are highly variable and, to some degree, influence carboxyhemoglobin formation.

Considerable time and effort have been spent attempting to resolve this dilemma. The goal has been to find and validate—over a wide range of exposure scenarios—a reliable predictive model for carboxyhemoglobin levels. In 1965, Coburn, Forster, and Kane evaluated major physiological variables that influence and determine the concentration of carboxyhemoglobin in humans.[34] In their experimental design, they developed equations using groups of normal subjects, male volunteers who breathed 100% oxygen for extended time periods, and patients with conditions known to contribute to elevated endogenous production of carbon monoxide. The Coburn-Forster-Kane equation resulted from these experiments.

Although it was first developed to calculate the endogenous production of carboxyhemoglobin, the Coburn-Forster-Kane equation is clinically useful when calculating carboxyhemoglobin levels following exogenous exposures.[4,34,55] The equation is based on parameters such as the

- ambient concentration of carbon monoxide,
- barometric pressure
- alveolar ventilation,
- comparative affinity of carbon monoxide for hemoglobin (a relative affinity of 218 is used in this formula),
- ambient concentration of oxygen,
- carbon monoxide diffusion across the alveolar membrane,
- rate of endogenous carbon monoxide production, and
- duration of exposure.[4,34]

Military Handbook 759A, paragraph 3.7.5, "Evaluation of CO Toxic Hazard," specifies the use of the Coburn-Forster-Kane equation:

> The prediction of carboxyhemoglobin blood content is determined by the following empirical equation:
>
> $$\text{carboxyhemoglobin}_t = \%\ (\text{carboxyhemoglobin}_0(e^{(-t/A)}) + 218(1-e^{(-t/A)}) \bullet (1/B + \text{ppm carbon monoxide}/1316)$$
>
> where *carboxyhemoglobin*$_t$ is the predicted carboxyhemoglobin in the exposed individual; *carboxyhemoglobin*$_0$ is the amount of carboxyhemoglobin usually found in non-smoking adults; *t* is the exposure duration in minutes; and *ppm carbon monoxide* is the carbon monoxide exposure in parts per million of contaminated atmosphere; *A* and *B* are constants which are obtained from [Table 11-3] and depend on the estimated physical activity level [of] the individual during the exposure. This equation accounts for the minute respiratory volume of contaminated atmosphere actually respired by an exposed individual whose level of physical activity is either estimated or specified. For combat vehicle crewpersons, the specified work effort level scale required to be substituted in the equation is 4 for periods of weapons fire and 3 for intermediate periods. The equation also accounts for the elimination of carbon monoxide by the body.[56]

The equation is equally applicable to short-term, high-level exposures and low-level, long-term exposures.[56] The equation is considered to be a reliable tool and has demonstrated good correlation with experimental values under a variety of conditions.[37] With respect to potential exposure of soldiers and the de-

TABLE 11-3

WORK-EFFORT CONSTANTS FOR THE COBURN-FORSTER-KANE CALCULATIONS

Work-Effort Scale	Work-Effort Description	A Value	B Value
1	Sedentary	365	939
2		211	1,623
3	Light work	155	2,211
4		119	2,874
5	Heavy work	97	3,536

Source: Military Handbook 759A. *Human Factors Engineering Design for Army Materiel (Metric)*. Redstone Arsenal, Huntsville, Ala: US Army Missile Command, Standardization Division; 30 June 1981. Table 3-5.

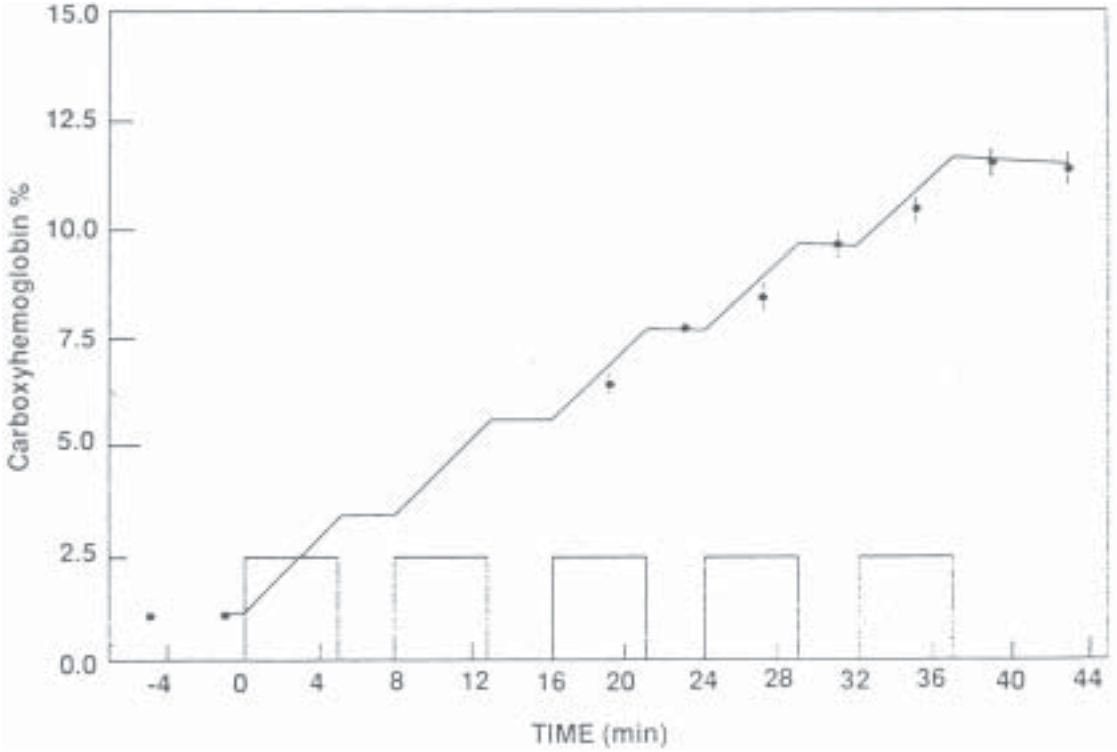

Fig. 11-10. Excellent correlation can be seen between calculated (—) and measured (•) levels for intermittent exposures (boxes along X axis). Subjects were exposed to 1,500 ppm of carbon monoxide for 5 minutes followed by a 3-minute rest. Source: adapted from Tikuisis P, Buick F, Kane DM. Percent carboxyhemoglobin in resting humans exposed repeatedly to 1,500 and 7,500 ppm CO. *Journal of Applied Physiology*. 1987;63:820–827.

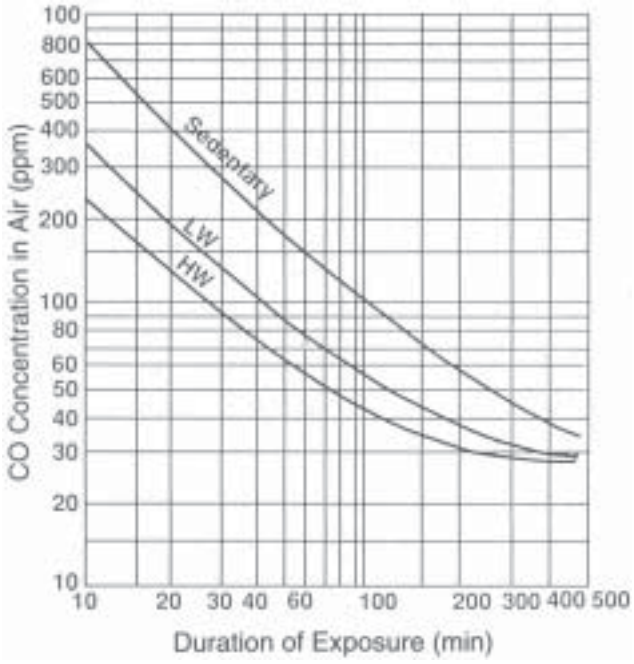

Fig. 11-11. The predictive relationship between the level of work effort, ambient carbon monoxide concentration, and duration of exposure to achieve a cumulative level of 5% carboxyhemoglobin. Source: US Department of Health, Education, and Welfare. *Criteria for a Recommended Standard .... Occupational Exposure to Carbon Monoxide*. Washington, DC: National Institute for Occupational Safety and Health and US Government Printing Office; 1972.

velopment of military items, the exposure magnitude, frequency, and duration of exposure to carbon monoxide are not restricted as long as the criteria of MIL-STD-1472C, 2 May 1981, are met.[40,56]

The applicability of the Coburn-Forster-Kane equation to the intermittent, episodic, peak-and-valley carbon monoxide exposure profile of the exposed military individual has been questioned. However, through an intermittent series of questions and evaluations, the equation was determined to be both applicable and predictive of actual carboxyhemoglobin level following exposures.[24] The authors of an independent study calculated predicted cumulative carboxyhemoglobin levels following intermittent exposures.[55] Figure 11-10 is adapted from that study, which has been useful in clarifying this relationship, and reflects the cumulative amount of carboxyhemoglobin following repetitive, intermittent exposures to 1,500 ppm of carbon monoxide. The study also evaluated the predictive capability using shorter-term, higher-concentration exposures (7,500 ppm) and demonstrated similar predictive success.

Figure 11-11, which has been reproduced from the NIOSH criteria document for occupational exposure to carbon monoxide,[32] incorporates the Coburn-Forster-Kane variables to develop families of curves. Because these curves incorporate the level of exertion, healthcare workers can quickly assess the work-effort level of a job and estimate the permissible duration of exposure at a given ambient carbon monoxide exposure concentration to achieve a 5% carboxyhemoglobin level.

MEDICAL SURVEILLANCE

Employees who routinely are exposed to carbon monoxide at potentially hazardous levels should be carefully evaluated prior to exposure. In addition to being given a careful medical history, review of medical systems, and medical examination, the employee should be advised of the insidious hazard posed by carbon monoxide exposure. Proper engineering controls and necessary PPE should be provided and properly maintained for each employee. Exposures to hazardous levels should be prevented when possible and documented in the medical record if significant exposures occur.

Employees should have a preplacement examination to detect preexisting conditions that may increase the risk of carbon monoxide toxicity and to establish a baseline for future monitoring. Medical histories that could contribute to susceptibility include smoking, coronary artery disease, anemia, chronic obstructive pulmonary disease, cerebrovascular disease, and/or disorders of the CNS. Employees who are either pregnant or considering pregnancy should be advised of the increased fetal susceptibility (the fetus can be exposed in utero if external exposures are uncontrolled), encouraged to quit smoking, and informed concerning methods to minimize exposure potentials.

The physical examination provided for preplacement, periodic, and termination examinations should emphasize the cardiovascular system, the pulmonary system, and the CNS. A complete blood count baseline should be obtained, and subsequent analyses obtained if they are clinically indicated.

Employees whose occupations include the potential for daily exposures to carbon monoxide above the acceptable action level should be offered periodic medical examinations. In addition, a medical evaluation is indicated following an acutely hazardous carbon monoxide exposure (a situational exposure) or on termination of employment. In situational exposures, a venous blood sample should be obtained for carboxyhemoglobin measurement as soon as possible following the exposure. A determination of end-alveolar carbon monoxide, as an indirect measurement of carboxyhemoglobin, may be used when blood carboxyhemoglobin determinations are not available,[16] although this is less preferable. Workplace carbon monoxide concentrations should routinely be documented by the industrial hygienist; levels above the action level should be referred to the healthcare provider as a stimulus for surveillance evaluation.

The occupational medicine physician should perform and document evaluations of the patient's mental, baseline neurological, and visual or ophthalmological status. One useful tool is the carbon monoxide–neuropsychological screening battery. This test, which can be administered easily by healthcare providers, evaluates the following functions, which carbon monoxide disrupts most commonly:

- short-term memory (for events that occurred 1–24 h ago),
- concentration (ability to concentrate to perform simple tasks),
- visual spatial ability (ability to distinguish among several objects placed close to each other),
- agnosia (lack of sensory ability to recognize objects), and
- aphasia (a weakness in or loss of the ability to understand ideas by reading, writing, or speaking).[57]

SUMMARY

Exposure to carbon monoxide can cause acute clinical illness. Military exposures to the chemical occur in homes, vehicles, and weapons systems. The profile of exposure during the performance of military duties is typically episodic, with high peak exposures followed by prolonged periods of limited, minimal exposure.

Although the primary effect of carbon monoxide poisoning appears to be the consequence of hypoxia associated with the production of carboxyhemoglobin, cellular enzyme systems are also adversely affected by carbon monoxide poisoning. Individuals with coronary heart disease appear to be at excess risk of adverse effect, such as myocardial infarction, following acute exposures. Chronic ophthalmological and neurological sequelae have been reported following carbon monoxide exposure. Timely diagnoses and implementation of appropriate methods to improve tissue oxygenation, such as hyperbaric oxygen treatment, are beneficial in the reduction of mortality and morbidity following carbon monoxide intoxication.

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