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Carbon monoxide asphyxia

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INTRODUCTION

Since the advent of fire, man has been confronted with substances which proved deleterious to his health. Carbon monoxide is the most ancient of poisons derived from this source. Its uses have been most variable, ranging from suicide, homicide, and torture chambers, of the ancient times to its introduction in the law courts in its medico-legal aspect of the modern age.

It has become more prominent in the eyes of the physician and the public with the birth of the machine age. Much has been written about carbon monoxide and investigation of its action has been profuse. Engineers, men interested in certain problems of insurance, men handling compensations for accidents, safety directors and teachers of safety, lawyers, employees of utility companies, many plant physicians, all are concerned with the carbon monoxide problem.

No one who has seen what carbon monoxide can do has any desire to minimize the possible effects of this dangerous by-product of some of our great modern conveniences, but as in the case of other dangerous instruments, it is our task to learn to control the danger, not to abandon use of the instrument.

The use of gas, of gasoline, of oil and of coal is

part of the daily life of well nigh the whole world, and carbon monoxide is the companion of the use of all these. In the modern literature, we find evidences resulting from its improper use, the production of almost any medical condition.

In this review, an attempt is made to correlate the pathological findings of experimentally produced carbon monoxide asphyxia in dogs, rabbits and mice to the pathological picture found at autopsy in known cases of carbon monoxide asphyxia in humans.

In order to understand more thoroughly the effects of carbon monoxide on the tissues of the body, it is desireable to give a brief review of the physiology of respiration, for it is by this means that carbon monoxide enters the body. No attempt will be made to explain or describe the detailed procedures of any experiment. Only the results of these experiments have been taken into consideration, and if the reader is desirous of such information, he is referred to the article from which the information was obtained. Study of this subject has been conducted only for the purpose of obtaining fundamental information on the response of the organism to asphyxial environment.

HISTORY

Human experience dates back to the pre-historic ages when man first came into possession of fire (77). Dr. Lewin (56) states he has traced references to the action of this gas back through the ancient Greek and Latin literature and concludes that this poisoning "of all stands alone in its close relation to the history of the civilization of mankind". Dr. Lewin found a number of carbon monoxide cases described in ancient literature, quotations from which indicate that this poison was a frequent cause of death by accident, by suicide, and used during the second Punic War. About 200 B.C., "the commanders of the allies and other Roman citizens were suddenly seized and fastened in the public baths for guarding, where the glowing fire and heat took their breath, and they perished in a horrible manner".

Julian the Apostate (331-363 A.D.), in one of his satires (56), tells how he was almost suffocated while in winter quarters in Paris. Owing to the severe cold, he had a small fire brought into his room "to prevent so much moisture from exuding from the walls" which affected his head and put him to sleep and he was carried unconscious from the room.

Symphoranus Campegius (56), who lived in the fifteenth century, tells of how two merchants, traveling towards

Lyon in the winter time, who stopped in an Inn for the night, and in order to warm the room, kindled a fire in the fire place and went to bed. The next morning they were found dead. The attending physician attributed the cause of death to the coal vapor.

Plutarch (56) reports that Catalus, after it was decreed by Marius that he should die, shut himself in a room and suffocated himself in the bath with the vapor from many glowing coals. In the year 68 A.D., Seneca, after several attempts at suicide, finally ended his life b charcoal vapor.

The Paris Record (77), for the nine years from 1834 to 1843, show a total of 4,595 deaths due to suicide, of which 1,432 were accomplished by means of carbon monoxide. Suicide by means of charcoal brazier became so popular in France that even writers of fiction made frequent reference to it.

A case of mass poisoning is reported by Valerius (60) as follows: "Hannibal (247-183 B.C.) induced the inhabitants of Nuceria to go out of the city with garments, where upon he prepared baths and allowed them to suffocate in the same through smoke and vapor". At the same time of Cicero (106-46 B.C.), poisoning through smoke as a method of punishment (56) seems not to have been unusual, and in the time of Septimus Sevenus

(Emperor 193-211 A.D.), and Diocletian (Emperor 284-305 A.D.), many of the martyrs died by this means (59), "the greenest possible, most smoke producing wood being used for such purposes".

Lucius Verus, who in 172 A.D., made himself emperor, punished in the following manner. He had a stock erected 80 to 100 feet high on which the condemned were bound one above the other and a fire made "so that the flames killed the lowest, the smoke the next, and anguish those highest up" (90).

The latest method of homicide by means of gas recently made its appearance, according to the public press (26), when a victim was bound and placed near the exhaust pipe of an automobile so that he was forced to inhale the poisonous fumes of the running motor.

Cassius (22), in Medical Questions (130 A.D.), attributed the cause of the untoward effects of charcoal vapors to the action of the dry heat and not to the vapor produced by the glowing coals, and wrongly considered that wood charcoal did not cause headache on account of a certain degree of moisture which it contained.

Marsilius Ficius (65), who lived in the fifteenth century (1433-1499 A.D.), believed that all coals easily caused headache, but that greater bodily harm would be

occasioned by extinguished coals, while Mercurialis (65) was of the opinion that bod coal was the source of the trouble.

During the seventeenth century, the knowledge of carbon monoxide poisoning had been extended, but the conception of the earlier time in regard to the nature of the pernicious substance which was responsible for its ill-effects was accepted unaltered, and even as late as the eighteenth century, death from this cause was sometimes superstitiously attributed to the work of the devil, as in the case of an Augustinian Monk (23) found one morning unconscious in his cell from the fumes of a fire kindled before he went to bed the previous night.

The very important fact that no bad odor warned of danger from this gas was first mentioned by Baconis de Verulamio in 1648, and unlike most of his predecesors, he was careful to speak of "vapor carbonum" instead of "fumes" (1). However Van Helmont (89) was the first investigator to call such fumes "carbon gas". About 1732 Boerhave (15) made probably the first animal experiments with carbon monoxide and found that all red-hot organic matter, as wood and coal, gave off a vapor which would quickly kill an animal shut up in a confined space.

F. de Lassone was the first to make carbon monoxide experimentally by reducing zinc oxide with carbon in 1776,

and it was prepared by Priestly in 1796 by heating iron oxide with charcoal (64). Lavoisier (64) knew that this gas burned to carbon dioxide but was unable to satisfactorily fit carbon monoxide in with his theory of oxidation until, in 1800, Cruickshank (25), showed that the gas was nothing but a "gaseous oxide of carbon".

As late as 1812, the Dictionnaire des Sciences Medicales of Paris (28) stated that "it has not yet been definitely determined to which of these gases (carbon monoxide or hydrogen sulfide) are due the pernicious effects of vapor from charcoal.

INCIDENCE

Rossiter (74) gives the following description of carbon monoxide. It is a colorless, tasteless and odorless gas which has a slight solubility in water, and is lighter than air. It burns forming carbon dioxide. As stated before, its attraction for hemoglobin is about 300 times that of oxygen. It forms no permanent compound with hemoglobin, nor does it produce any lasting deterioration of the oxygen carrying power of hemoglobin. The corpuscles are not destroyed, and the action of an excessive amount of carbon monoxide is that of asphyxia.

Carbon monoxide is found where ever there is incomplete combustion of carbonaceous material. It is found in the exhaust of all internal combustion engines, furnace leaks, expecially open stoves, industrial by-products and poorly ventilated tunnels where autos pass (74). Henderson (45) notes the poisonous effects of smoke in burning buildings, of fumes around furnaces, and from explosions of the "after-damp" of methane and coal dust in mines, and from mine fires of timber and coal. It is also pointed out by several workers that illuminating gas contains a considerable amount of carbon monoxide (11, 17, 30, 45, 61, 75).

White (92) points out that carbon monoxide is

produced during electrical storms and by growing kelp. It is also formed in lime, brick, and charcoal kilns, and also produced on detination of high explosives. It is also found in compartments which have been painted with oil paints and sealed (33). One of the most common places for the presence of carbon monoxide is in garages (30, 75).

It has been found that carbon monoxide in dilution of .05%, if inhaled over a long period of time, may prove dangerous; 0.2% inhaled for four or five hours, 0.4% inhaled for one hour or a few inhalations of two to five percent may cause death. The severity and clinical course depend upon the concentration, duration of exposure, temperature and humidity, physical exertion, health of the individual, admixture of other poisonous gases and individual susceptibility. Atmospheric conditions influence the diffusion of the gas (9, 75).

A high temperature and a high relative humidity cause an increase in the rate of absorption due to increased respiration. Low barometric pressure also increases the rate of absorption. On damp, foggy days, fog acts as a blanket preventing the rapid diffusion of gas, and as a consequence increases the chance of being overcome, whereas on windy days there is a rapid diffusion of gas(74).

The incidence of suicides by use of coal gas, as reported in Scotland in 1914, was six deaths. In contrast to this number, there were ninty-one deaths by this means in 1924 (49).

Some workers have ranked carbon monoxide fatalities second to those of automobile fatalities as the cause of accidental and suicidal death. It has been reported in 1940, that 50,000 deaths from asphyxiation annually occur in the United States of which fifty per-cent are due to carbon monoxide. In New York City, for every seven automobile deaths there are five carbon monoxide deaths. The records of 1936 show a progressive increase of the hazard of both domestic and industrial life of the community(11, 27).

Beck (11) points out that, of a total of 518 gassings, there were 288 from defective domestic appliances accounting for sixty-two fatalities; twenty-three were overcome by bath room heaters, resulting in four deaths; twenty-six were overcome by hot water heaters, with six deaths occurring, and fifty-five by coal or coke stoves and furnaces, accounting for five deaths.

In 1937, a survey was carried on by Helpren (44) in the city of New York. He accumulated the following data:

quite coincidental with the situation of the financial world.

From the Annual Health Bulletin of the city of Omaha for 1941 (6), the following information was obtained: there were ninteen suicides, by what means was not stated. However there were fifty-five attempted suicides by gas, and forty-four attempted suicides by poison, which again shows the preference of gas.

PHYSIOLOGY OF RESPIRATION

One of the most important factors concerned in maintaining the normal functioning of a living organism is that of respiration. Every manifestation of life involves the liberation and utilization of free energy, and in aerobic animals the requisite energy is obtained from the cells in which the oxidative process is concerned. In order to meet these demands, an adequate supply of oxygen must be available at all times. Furthermore, the carbon dioxide formed in intra-cellular oxidations must be removed if the oxidations are to continue unabated. Respiration in the biological sense is the process by which oxygen is supplied to, and carbon dioxide removed from, a living system. In air breathing animals, the medium by which this process takes place, is the tissue fluid and lymph which bathe the cells. The oxygen store of the cellular environment is replenished and the accumulated carbon dioxide is removed by the blood, which establishes contact with the external environment in the lungs. Here another gas exchange takes place between the blood and air, the blood receiving oxygen in exchange for the carbon dioxide received from the tissues. In other words there are two processes of respiration which may be properly termed internal and

external respiration. To insure the adequacy of this exchange the air in contact with the blood in the lungs is renewed by means of appropriate contractions of respiratory muscles, synchronized and regulated through the central nervous system according to the needs of the body.

Ordinarily, the respiratory movements are passive to the organism, requiring the minimal of energy output. In carrying out this action only the diaphragm and external intercostal muscles are involved, producing an enlargement of the thoracic cavity. This is the inspiratory movement which causes the lungs to become filled with air. Expiration follows as an elastic rebound of the diaphragm and abdominal viscera which had become displaced downward and foreward during the process.

During labored breathing, more muscles are called upon, the accessory muscles of respiration, namely, the scaleni, sternocleidomastoidei, pectoralis muscles, external intercostals, levator costarum, serratus posticus inferior, triangularis sterni and the internal intercostals, have their place in expiration. The function of the internal and external intercostals has long been the subject of debate, but recently it has been found that the muscles are activated alternately, the internal with expiration and the external with inspiration (79).

The following data has been gathered from Drinker (30) concerning the diffusion of gas in the lungs. The ultimate air-containing sacules of the lungs are designated as alveoli, and the composition of air in them is roughly as follows: nitrogen, 80%; oxygen, 14%; carbon dioxide, 5.5%. The exchange of gases between the lungs and blood depends upon the partial pressures of these gases in the alveolar air and in the lung blood. At atmospheric pressure, the partial pressures in the alveoli, at body temperature, are as follows: nitrogen, 590 m.m. mercury; oxygen, 100 m.m. mercury; carbon dioxide, 40 m.m. mercury. These figures are for quiet or passive respiration and may be altered to a considerable degree by forced breathing. Nitrogen is simply a dilutent and has no physiological significance. On the other hand, the other two substances are of considerable import. Because the oxygen tension of venous blood is around 35 m.m. mercury, and the corresponding alveolar tension is 100 m.m mercury, oxygen readily diffuses into the blood and visa versa. Thus, by the time the blood leaves the lungs, an approximate equilibrium has been attained, the arterial blood containing ninteen c.c. of oxygen per one-hundred c.c. of blood under a tension of 100 m.m. of mercury. The same condition is observed in the tissues; the oxygen tension is lower than that of the blood, thus

diffusion in the opposite direction takes place. But due to the short circulatory time through the capillaries, not all of the oxygen is able to escape to the tissues and, as a result, the oxygen tension of the venous return is approximately 38 m.m. mercury.

The conditions governing the diffusion of carbon dioxide are similar to those described above. The carbon dioxide tension in the venous blood returning to the lungs is around 46 m.m. mercury, whereas that of the alveolar air is 40 m.m. mercury. Even though the difference in tensions is not very great, the high diffusibility of carbon dioxide and the enormous surface provided in the lungs make it sufficient to accomplish carbon dioxide excretion. Due to the continuous production of carbon dioxide in the tissues, the partial pressure of this gas is between 50 and 70 m.m. mercury, which is some what higher than that of the alveolar air.

Thus far, no mention has been made as to how and what substance is responsible for the transportation of oxygen and carbon monoxide through out the system. According to Bodansky (14), a substance hemoglobin, which is a passive carrier of oxygen and not a catalyst, is responsible for this job. The transportation of oxygen and carbon dioxide depends upon the reversible chemical reaction between hemoglobin and these two gases.

As far as oxygen is concerned, factors influencing its combination with hemoglobin may be enumerated as follows: altitude has no effect upon the affinity of hemoglobin for oxygen; at low oxygen tensions, oxyhemoglobin is more readily dissociated in the presence of salts, especially if the oxygen tension is low. It has been shown that if the temperature is maintained at a constant, say thirty-eight degrees centrigrade, and at an oxygen tension of ten m.m. mercury, the saturation of hemoglobin in the presence of electrolytes may be reduced to less than on-half of what it is in pure solution. But on the other hand, this effect is not obtained at higher pressures where an increase in the combining capacity of hemoglobin is actually indicated at 100 m.m. mercury. A third factor influencing the efficiency of hemoglobin as a carrier of oxygen is carbon dioxide. The effect of carbon dioxide may be referred to the hydrogen-ion concentration changes. The iso-electric point of oxyhemoglobin is 6.6, and of reduced hemoglobin, 6.81. On the acid side of the iso-electric point of hemoglobin, its affinity for oxygen is less than on the alkaline side. Thus with the inpouring of carbon dioxide from the tissues, on the tissue side of the exchange hemoglobin gives up oxygen, and on the lung side, with the elimination of carbon dioxide and with the trend

toward the alkaline side, the relationship between hemoglobin and oxygen becomes altered.

The transportation of carbon dioxide is by several agents. It has been found that seventy per-cent comes from the bicarbonate ions, chiefly in combination with sodium and potassium; ten per-cent comes from the preformed dissolved carbon dioxide, and that twenty per cent comes from the carbomino compound of carbon dioxide with hemoglobin. However, the speed of decomposition is much too rapid to be based merely on a diffusion basis. Work done on this subject resulted in the isolation of an enzyme which speeded up the rate of carbonic acid dehydration 1500 times at thirty-eight degrees centrigrade. Because of this property this substance has been named carbonic anhydrase. In contrast, of the bicarbonate in the plasma the amount of carbon dioxide liberated directly is insignificant, and yet approximately fifty per cent of the total carbon dioxide evolved in the lungs comes from this source.

Now let us examine the role that the central nervous system plays in respiration. According to Schmidt (79), who wrote the section on respiration in the text of Macleod's Physiology, a section of the medulla, known as the formatio reticularis, is the center from which impulses regulating respiration originate. This center

has an automatic rhythm of its own, and can develop such without afferent impulses from the lungs or thorax. In the intact animal, the intrinsic rhythm is greatly modified by afferent impulses, but the fact remains that the respiratory neurons can initiate and maintain a rhythmic discharge of impulses in response to a chemical stimulus. We shall learn presently how carbon monoxide can influence this property.

It is probable that factors such as differences in threshold of different cells to chemical stimuli and a reciprocal innervation of the inspiratory and expirator cell-groups have some concern in the intrinsic rhythm.

Some parts of the center have a lower threshold to chemical stimuli, namely those which innervate the quiet muscles of respiration, for it has been demonstrated that respiration becomes purely inspiratory when a considerable portion of the medulla has become damaged by trauma, oxygen-lack, poisons and depressent drugs.

One of the most valuable regulators of the respiratory center is carbon dioxide. A lack of this respiratory hormone causes a depression of the center, whereas an increase in its concentration causes stimulation. If the concentration is high enough, a condition of hyperpnea developes with a corresponding hyper-ventilation of the lungs resulting in the elimination of carbon dioxide

from the system and the restoration of normal breathing.

There are several reflexes (79) which have considerable control over respiration in the normal animal. The Hering-Breuer reflexes, which have to do with the expansion and collapse of the lung, send inhibitory and stimulative impulses respectively, to the respiratory center via the vagus nerve. This mechanism will not be discussed in detail because I do not believe it concerns carbon monoxide asphyxia to any great extent. However, the reflexes arising from the carotid and arotic sinuses do have an important role in the respiratory behavior of the animal.

These are chemical receptor areas which react to changes in carbon dioxide and oxygen tensions of the arterial blood. They also exert influences on the respiratory center and heart through changes in arterial pressure; namely stimulating these organs when there is a decrease in pressure and inhibiting when there is an increase in pressure. However these chemical receptors are not as sensative to chemical changes as the respiratory center in the medulla, but the part of the carotid and aortic sinuses is to furnish afferent impulses which keep the center active or even increase its activity in the face of abnormal circumstances which depress nerve cells in general and which would otherwise causedepression

or failure of respiration. Such circumstances are anoxemia, great increases in carbon dioxide tension of the blood and poisoning by narcotic drugs and by agents which interfere with the utilization of oxygen by the tissues. The chemical receptors are stimulated only by the most extreme degree of oxygen lack or carbon dioxide excess. They are decidedly less sensative than the cells of the center normally are to changes in carbon dioxide tension or hydrogen-ion concentration of the blood, but are more resistant ot adverse conditions. They are the ultimum moriens of the respiratory regulating system.

Now let us consider the effect of carbon monoxide upon respiration. As pointed out by several workers (18, 27, 29, 40, 45, 74), hemoglobin has an affinity for carbon monoxide from two hundred to three hundred times as great as it has for oxygen. As a result of this union, a substance, carbon monoxide-hemoglobin, is formed which is incapable of carrying oxygen. However, this is not a stable compound (42) and its poisonous action diminishes as the oxygen tension increases, and as pointed out by Henderson (45) and others, hemoglobin is fully restored in three or four hours. In order to substantiate this statement, Henderson (45) gives this simple experiment: A drop of blood from the finger is diluted with water, a drop of very dilute ammonium is added, and the

reddish yellow solution is shaken with air. One-third of the solution is poured off in a test tube, while the remaining two-thirds are shaken with illuminating gas in another test tube. In the course of a few minutes this portion becomes cherry red in color which is characteristic of carbon monoxide hemoglobin. It is now divided into two protions, one of which is stoppered and set aside while the other is shaken vigorously with air. In a few minutes this sample has lost its cherry red tint and has returned to the appearance of normal blood. The mass action of the oxygen of the air has displaced the carbon monoxide from its combination with hemoglobin. To all intents and purposes, the condition of the blood is the same as if it had never been in combination with carbon monoxide.

As carbon monoxide combines with hemoglobin, the oxygen carrying power of the erythrocytes (74, 77) diminishes. At the same time there is an increase in the concentration of carbon dioxide in the tissues, and there results a condition of hyperpnea (77). As was mentioned in the discussion of the respiratory center, increased carbon dioxide tension stimulates the respiratory act. Not only does breathing become more rapid, but also are the heart and pulse increased due to vagal paralysis. These reactions take place however, when the blood

saturation is relatively high with carbon monoxide.

As one may readily see, with hyper-ventilation, carbon dioxide is driven from the system (40), with the development of an alkalosis (8). And as observed by Davis (27), alkalosis causes carbon monoxide hemoglobin to be held with greater tenacity. It was once thought (45) that a condition of acidosis resulted, and there was speculation on the use of alkalies in treatment of this condition.

PATHOLOGY

Lewin (56) claimed that Troja in 1778 first described the cherry red color of the blood in carbon monoxide poisoning and that Peorry in 1826 also called attention to this. Bernard (13) demonstrated this phenomenon in his classes at the College de France from 1847-1857. Profound disturbance of the peripheral nerves and central nervous system following poisoning with charcoal fumes and illuminating gas had been known for a long time. The symptoms are of such diseased conditions as amnesia, localization paralysis, hemiplegia and complete dementia. They may follow the poisoning immediately or may appear many days or weeks later. Such sequences of gas poisoning are rare. Peterson, Haines and Webster (72) summarized the appearance in the human body as follows: bright patches in skin, pulmonary edema and bright red froth in the air passages, gastric and intestinal mucosa may also show small punctiform hemorrhages, multiple punctiform hemorrhages and softening of the cortex and lenticular nuclei, notably the two internal segments, kidney may show fatty degeneration and necrosis in the convoluted tubules. Such changes have been reported as dilatation of the heart with blood changes of progressive pernicious anemia (52), extensive necrosis of the

myocardium (85), unilateral and bilateral gangrene (3, 16, 63), and multiple sclerosis. McCurn and Altschul (5, 62) reported vascular lymphocytic infiltration of the central nervous system in four women who were asphyxiated in a burning theatre.

The conspicuous changes in the brain when death takes place soon after poisoning with illuminating gas or carbon monoxide in some other form are hyperemia, multiple small hemorrhages and the bright pink or scarlet color of the blood. But if persons poisoned live several days bilateral regions of softening are found in the inner segments of the lenticular nucleus, the globus pallidus. Kolisko (51) described such lesions as due to carbon monoxide. He explained this phenomenon on this basis: the long arterioles supplying the lenticular nucleus became dilated resulting in a slowing of the blood current, edema of the brain, pressure below by the dilated, pulsating carotid arteries, and absence of any other blood supply to the globus pallidus. He also believed that the right angle at which the vessels arise from the carotids is an additional factor causing the deplete supply of blood. The dilation and atony of the musculature in the walls of the arterioles were demonstrated by Klebs (50) many years before in the first careful study of experimental carbon monoxide poisoning.

The theory proposed by Heinecke (43) that carbon monoxide acts like a ferment has not found much support. A few have suggested that it may produce encephalitis (55). It was also suggested by a few that it acts as a poison directly on the nerve tissues (82). Haggard (38) in his studies on carbon monoxide asphyxia exposed cultures of nerve tissue of the chick to a concentration of seventy-nin per cent in vitro, as no effect could be observed on the growing cells, he concluded that carbon monoxide has no specific effect on nerve tissue, but acts only through the asphyxia resulting from its combination with hemoglobin.

Haldane suggested that possible carbon monoxide may act on the cellular catalysts, replacing oxygen in this respect (41). Closely related to this theory is the conception that some tissues are particularly susceptible to the action of carbon monoxide, being especially vulnerable because of the physio-chemical characteristics that they possess. This theory advanced by Vogts (89) included the introduction of a new term "patho klise" to define the predilection of the globus pallidus (found few advocates). Recent suggestion is that some parts of the central nervous system are more susceptible to lowered oxygen tension than others (58).

An excellent description of some of these lesions

of the brain was made by Mott (66). He found small hemorrhages in the white substance of the cerebrum due to stasis and thrombosis and there, he said, resulted from the extremely small channels of the vessels, the weakened heart action and the anatomic characteristics of the vessels, their terminality and absence of anastomoses. Each arteriole that perforates the cortex from the lepto meninges, as well as each in the white substance directed outwards, has a brush-shaped set of capillaries altogether separate from other vessels and a separate emergent vein unconnected with adjacent veins. Many authors describe fatty, hyaline and other retrogressive changes in the walls of the blood vessels, for the most part arterioles and capillaries. Such alterations, it is believed, account for the atony of the muscular coats, dilatation of the channels, slowing or cessation of the current of blood and also for the thrombosis observed by many who have studied these alterations of the brain. The opinion has also been expressed that anoxemia, which after all is at the bottom of all the untoward effects of carbon monoxide as a poison, may first so influence the vasomotor centers in the brain that dilatation of the vessels preceeds all the other modifications in their walls or in the circulation through them (32).

Chonnyak (22) demonstrated the effects of carbon monoxide asphyxia by submitting four dogs to an atmosphere containing 0.06% of carbon monoxide by volume for a period of twenty to thirty minutes. Under these conditions a saturation of seventy-five to eighty per cent carbon monoxide-hemoglobin was obtained and resulted in the death of the dogs in that period of exposure. The following conditions were found to be present.

A perineuronal and perivascular edema was found in the cortex. Practically this entire region was markedly damaged except for a few large motor cells. It was also noted that the cells in the deeper layers were damaged more than those of the more superficial layers of the cortex. The cells showed central chromatolysis with swollen and distorted nuclei. The pyramidal cells stained uniformly dark blue. Through out the cortex the capillaries were found to be greatly dilated and blood stasis marked. Occasionally one would see the perivascular spaces infiltrated with leukocytes and occasional areas of hemorrhage, but these would be no larger than would occur by diapedesis. The olfactory cortex showed particularly severe damage; the nerve cells were completely fragmented, the nuclei were greatly swollen, vacuolated and distorted. There was also marked perineuronal and perivascular edema in this region.

In the thalmus, perineuronal and perivascular edema was marked. Some neurons appeared shrunken with slight central chromatolysis. The nuclei were eccentric and distorted and some of the cells were badly fragmented.

The corpus striatum showed severe degenerative changes. There was marked perivascular and perineuronal edema and many of the neurons seemed to have been ruptured; much of the cytoplasm was fragmented and vacuolated. Chromatolysis was marked. The nuclei were swollen, distorted and vacuolated, and in many cases there was very little left of the cell, the nucleus surrounded by a small amount of Nissl staining material. Some nerve cells were uniformly, darkly stained and others appeared to be invaded by stellate cells. The vessels of this area were markedly dilated and stasis marked.

The section in the mesencephalon through the colliculi showed dilatation of the vessels, stasis and marked perivascular and perineuronal edema. The large polygonal shaped cells with large Nissl granules (cells of the tecto-spinal tract), showed relatively little change as compared with the smaller cells which showed chromatolysis and swelling of the nuclei.

In the oculo-motor nucleus there was very little

chromatolysis. A few cells were shrunken and stained a uniform blue. There was some perivascular edema with stasis and dilatation of the vessels, however there was no perineuronal edema noted. On the whole the nucleus did not show much damage.

In the trochlear nucleus most of the cells were unchanged. However there were a few cells which were shrunken and stained uniformly dark blue.

The nucleus rubar appeared normal for the most part. A few cells had dust-like Nissl granules between the nucleus and the periphery of the cell. No perineuronal edema was present.

Most of the cells of the substantia-nigra showed a central chromatolysis. In some cells Nissl granules were found in the periphery. Some of the neurons appeared shrunken. There was slight edema through out. Many of the cells stained a homogeneous dark blue.

The cells of the mesencephalic nucleus of the trigeminal nerve appeared shrunken and stained dark blue. Perineuronal edema was marked.

The interpeduncular ganglion showed marked perivascular and perineuronal edema and chromatolysis.

The nuclei pontis showed marked central chromatolysis. The nuclei were distorted and eccentric. Perineuronal edema was slight.

The nucleus of the abducens nerve showed practically no degenerative change. However some of the cells were shrunken. Perineuronal edema was slight.

The nucleus of the facial nerve showed the same pathology as the nucleus of the abducens nerve.

In the nucleus of the trigeminal nerve, most of the cells showed severe degenerative change. There was much chromatolysis, some of the cytoplasm was fragmented, and the nuclei swollen and distorted. The large polygonal shaped cells of the motor nucleus showed relatively little change.

The cochlear nucleus showed little or no change.

The nucleus of the trapezoid body showed relatively little change excepting a slight perineuronal edema.

In the reticular formation, the vessels were dilated by blood stasis and perivascular edema. There were a few small petechial hemorrhages scattered through out.

The nucleus cuneatus and gracilis of the medulla oblongata may show severe edema. Many of the cells were shrunken and some stained homogeneously dark blue. Many showed chromatolysis with large swollen nuclei, and stasis and perivascular edema with a few small hemorrhages.

The inferior olive showed mainly central chromatolysis and perineuronal edema.

The dorsal motor nucleus of the vagus nerve showed

severe degenerative changes; some of the nerve cells showed complete absence of nuclei and the cell to be greatly shrunken and stained dark blue. Degenerative changes in this nucleus were the most severe found in any center of the brain.

In the nucleus of the hypoglossal nerve, a few cells showed chromatolysis and many were shrunken. Large Nissl granules were found in some cells. There was also evidence of severe perineuronal edema.

The nucleus of the tractus solitarius showed severe degenerative changes. Most cells showed chromatolysis, many were fragmented, nucleus swollen, distorted and stained a uniform blue.

The vestibular nucleus showed relatively little change. Some of the smaller cells showed a slight central chromatolysis with swollen, distorted nuclei. There was some perineuronal edema present.

The nucleus ambigius showed relatively little change, but perineuronal edema was present.

The reticular formation showed occasional petechial hemorrhage.

In the cerebellum, vessels were found to be dilated and packed with erythrocytes. Perineuronal and perivascular edema was also present, and there were occasional areas of petechial hemorrhage. Practically

all the Purkinge cells were shrunken and stained a homogeneous dark blue. Some of the cells in the granular layer appeared to be fused.

Some of the cells in the efferent nuclei showed relatively little change. Many showed central chromatolysis with distortion of the nucleus. A few cells were shrunken and uniformly stained dark blue.

Rossiter (74) points out that degeneration takes place mostly in the white matter due to the lack of venous anastomosis. Anterior horn degeneration and basal ganglia degeneration is quite characteristic. However he states that the most characteristic lesion is a bilateral, ischemic necrosis of the lenticular nucleus, especially the globus pallidus and is due to thrombosis.

Strecker, Taft and Wylie (84), in the study of two cases of asphyxia by illuminating gas gave the following autopsy report of the pathological conditions found in the central nervous system. These are very similar to the pathological changes that were demonstrated by Channyak in the above paragraphs in his experiment on artificial asphyxiation in dogs.

The gross examination in these two cases revealed no specific changes on the outer surfaces of the brain. In one case, there was considerable atherosclerosis of

the basal vessels. In the other case, the frontal sections showed small softened areas in the globus pallidus on both sides. The corpus denatum on both sides was also degenerated. There was generalized atrophy with a consequent wide space about the crura.

The significant microscopic sections were similar in both cases and varied mainly in degree. In the first case, the softened areas seem grossly appeared as broken down tissue infiltrated with large, compound, granular cells. There were also many miliary softenings found only in this specimen, which was found to be the case of longer duration of asphyxia. In case two, changes in the basal gray matter were present but had not gone to cystic softening, as was found in the first case.

The most outstanding alteration was present in the white matter through out, in which there was wide diffuse infiltration by various types of glial elements, mainly large protoplasmic forms and focally many endothelial forms of the compound type, which were shown by the Scharlach Red stain to be filled with fat. These fat laden cells appeared in the perivascular spaces as well as interstitially. The alterations in this type of poisoning are generally considered to be due to anoxemia.

The diffuse reaction in the white substance has seldom been reported. It is apparently the result of a

severe alteration in the myelin, a definite myelinopthy, which leads to marked disturbance of function and when sufficient in degree is unrecoverable.

Structures endowed with a rich blood supply, such as the myocardium and central nervous system and that normally utilize more oxygen than those less aoundantly supplied; consequently, in states of anoxemia the damage to tissue in these organs is relatively more pronounced (8).

It has been shown that there is a definite relationship between anoxemia and cardio-vascular disease. Keefer and Resnik (48) stated an opinion that anoxemia is a constant factor in angina pectoris and it is possible to demonstrate anoxemia in all cases. Elliott (31) reported a case of angina pectoris with severe anemia in the presence of healthy coronary arteries and aorta, and expressed the belief that the occurrance was more than just a coincidence. Cabot (19) and Allbutt (4) also reported cases of angina pectoris in which the coronary arteries were patent and the angina syndrome was attributed to pernicious anemia or general anemia.

Kroetz (53) stated that the classic anoxemia lesions in the heart are hemorrhage, necrosis, and processes of granulation and regeneration, and that their co-existance with similar lesions in the brain adds to their significance.

The lesions affecting the heart have certain predilection; these are in the papillary muscles of the mitral valve and in the wall of the left ventrical. Gey (35) substantiates this view through his observations on several patients who died of carbon monoxide poisoning. Lewis, White and Meekens (57) state that the nuitritional changes resulting from these lesions not only affects heart muscle, but also the bundle of His, producing auriculo-ventricular block. Green and Gilbert (36) were able to produce in man, by oxygen deprivation, diminished conductivity of the auriculo-ventricular nodes as well as the bundle of His.

Stearns, Drinker and Shaughnessy (83) have shown in a series of electrocardiograph studies on cases of carbon monoxide asphyxia that there is an abnormality in the "T" waves or in the level of the "S-T" segment. In four cases that they studied, they were able to show a paroxysmal auricular fibrillation, one transitory intra-ventricular block, two ventricular, premature contractions and one premature auricular contraction.

Beck (10) also states that thrombi commonly occur in the small vessels, however the large vessels are not exempt, as many cases of coronary thrombosis have been reported.

Haggard (40) states that oxygen deficiency caused

by carbon monoxide even in advanced asphyxia is not in itself suffient to cause impairment of the auriculo-ventricular conduction. Following respiratory failure, however, the increased anoxemia from this cause speedily results in the development of heart block through its various stages. He states that by restoring respiration and rapidly eliminating the carbon monoxide by means of inhalations of carbon dioxide and oxygen, cardiac conduction is restored to normal, following the development of the block. He was able to demonstrate the variations in EKG records, involving the "R" and "T" waves and also a complete auriculo-ventricular block, a condition resembling auricular fibrillation or flutter, in animals subjected to an atmosphere of carbon monoxide.

Yant et al (94) studied the blood chemistry changes which resulted from comparatively rapid asphyxia by atmospheres deficient in oxygen, and compared these results with those found in a carbon monoxide atmosphere. They found that in a condition of decreased oxygen tension, there was a marked hyper-glycemia and a hyper-uricemia, and that the N.P.N. and urea were only slightly increased. The total and pre-formed creatinine remained practically normal; and the inorganic phosphorous was somewhat increased. There was also found to be an increase in the hydrogen-ion concentration and a marked

decrease in the carbon dioxide content of the blood, and a decrease in the carbon dioxide capacity of the plasma.

The red blood cells increased in one case in their series of four dogs, and showed no significant change in two. They also found that the white blood cells and the polymorphonuclears increased, while the lymphocytes decreased.

The following charts will give a more accurate summary of the results obtained in this experiment.

BLOOD CHEMISTRY CHANGES RESULTING FROM COMPARATIVELY RAPID ASPHYXIA BY ATMOSPHERES DEFICIENT IN OXYGEN

Dog No.	Duration of exposure				
	Minutes	Seconds	Normal	Death	Change
				SUGAR	
39	28	35	96.7	254.2	+157.5
40	11	4	108.7	147.3	+ 38.6
41	21	--	149.7	570.5	+420.8
42	14	40	87.2	166.5	+ 79.3
				UREA	
39	28	35	21.2	27.2	+ 6.0
40	11	4	29.1	30.6	+ 1.5
41	21	--	32.4	32.9	+ 0.5
42	14	40	32.2	36.0	+ 3.8
				URIC ACID	
39	28	35	0.69	3.4	+ 2.7
40	11	4	0.70	3.6	+ 2.9
41	21	--	0.70	4.7	+ 4.0
42	14	40	0.64	4.0	+ 3.4
				N.P.N.	
39	28	35	29.8	39.3	+ 9.5
40	11	4	33.3	37.2	+ 3.9
41	21	—	42.5	42.9	+ 0.4
42	14	40	44.1	49.8	+ 5.7

Dog No.	Duration of exposure Minutes	Seconds	TOTAL CREATININE (1) Normal	Death	Change
39	28	35	3.9	3.7	- 0.2
40	11	4	4.1	4.0	- 0.1
41	21	--	3.1	3.3	+ 0.2
42	14	40	3.0	3.8	+ 0.8
			PREFORMED CREATININE (1)		
39	28	35	1.2	1.2	0.0
40	11	4	1.2	1.3	+ 0.1
41	21	--	1.1	1.2	+ 0.1
42	14	40	1.2	1.3	+ 0.1
			INORGANIC PHOSPHOROUS IN PLASMA (2)		
39	28	35	5.3	6.5	+ 1.2
40	11	4	5.2	5.3	+ 0.1
41	21	--	4.1	5.6	+ 1.5
42	14	40	24.8	25.2	+ 0.4

* (1) Expressed in milligrams per 100 c.c. of blood.
(2) Expressed in milligrams per 100 c.c. of plasma.

Dog No.	Dur. of Exp. Min.	Sec.	Percentage Oxygen in Blood (3) Normal	Intermediate	Death	Change
39	28	35	23.42	3.45 (4)	0.72	-22.70
40	11	4	20.00	----	1.69	-18.31
41	21	--	22.70	2.97 (5)	0.85	-21.85
42	14	40	21.92	----	0.31	-21.61
			PERCENTAGE CARBON DIOXIDE IN BLOOD (6)			
39	28	35	39.10	21.34 (4)	16.90	-22.20
40	11	4	45.10	----	26.01	-19.09
41	21	--	42.56	20.61 (5)	9.77	-32.79
42	14	40	35.11	----	25.46	- 9.65
			HYDROGEN-ION CONCENTRATION EXPRESSED AS pH.			
39			7.15	7.09 (4)	6.98	-0.17
40			7.22	---	7.20	-0.02
41			7.21	7.05 (5)	6.88	-0.33
42			7.16	---	7.06	-0.10

Dog No.	Duration of Exposure Minutes	Seconds	PERCENTAGE CARBON DIOXIDE CAPACITY OF PLASMA (6) Normal	Death	Change
39	28	35	45	19	-26
40	11	4	53	36	-17
41	21	--	47	16	-31
42	14	40	40.5	28.5	-12

* (3) c.c. of gas in 100 c.c. of blood.

(4) Taken after fifteen minutes exposure.

(5) Taken after thirteen minutes exposure.

(6) c.c. gas in 100 c.c. of plasma.

Dog No. 39

	Normal(1)	At Death (2)
Hemoglobin	105	(3)
Red Blood Cells	7,040,000	7,030,000
White Blood Cells	8,450	13,100
Polymorphonuclears	31	52
Lymphocytes	61	39
Lymphoblasts	4	3
Eosinophils	3	2
Endothelials	1	3

Dog No. 40

	Normal (1)	At Death (2)
Hemoglobin	89	90
Red Blood Cells	8,300,000	(3)
White Blood Cells	11,550	(3)
Polymorphonuclears	71	(3)
Lymphocytes	25	(3)
Lymphoblasts	(4)	(3)
Eosinophils	1	(3)
Endothelials	3	(3)

Dog No. 41

	Normal (1)	At Death (2)
Hemoglobin	101	100
Red Blood Cells	6,280,000	5,730,000
White Blood Cells	11,700	16,500
Polymorphonuclears	59	67
Lymphocytes	40	29
Lymphoblasts	(4)	(4)
Eosinophils	(4)	1
Endothelials	(4)	1

Dog No.42

	Normal (1)	At Death (2)
Hemoglobin	98	(3)
Red Blood Cells	6,190,000	7,350,000
White Blood Cells	13,900	15,400
Polymorphonuclears	71	80
Lymphocytes	28	17
Lymphoblasts	(4)	(4)
Eosinophils	(4)	(4)
Endothelials	1	3

(1) Normal sample taken before exposure.

(2) Taken just at time of occurrence of death. See table three for duration of exposure before the occurrence of death.

(3) Not determined.

(4) Not found in the 300 cells counted for the differential determination.

The controlled experiments were preformed under identical technique except that the dogs breathed normal air for a period of fifteen hours. Briefly, the results of the controlled experiments show no significent changes in the blood chemistry and support the conclusion that the changes found in the animals exposed to atmospheres containing carbon monoxide were not significantly influenced by experimental technique other than carbon monoxide.

In summary, the results found in animals exposed to carbon monoxide atmosphere are very similar to the results

found when the animals were exposed to atmospheres deficient in oxygen. The most important changes were a marked hyper-glycemia and hyper-uricemia, a slightly increased non-protein-nitrogen and urea; the total and pre-formed creatinine remained practically normal and the inorganic phosphorous increased. There was found to be an increase in the hydrogen-ion concentration and a marked decrease in the carbon monoxide capacity of the plasma and a lesser though distict decrease in the carbon dioxide content of the blood. Blood counts showed a slight but insignificant tendency toward an increase in hemoglobin, erythrocytes, leucocytes and polymorphonuclears. The lymphocytes as before showed a slight decrease. There was no significant change observed in the number of endothelials and eosinophil cells.

At the time of death, it was found that the carbon monoxide saturation of the blood varied from 83 to 90 percent, and that the oxygen saturation of the venous blood at death ranged from 0.0 to 5.6 c.c. per 100 c.c. of blood. The following graphics give a more minute description of the blood changes found during carbon monoxide asphyxia.

BLOOD CHEMISTRY CHANGES RESULTING FROM COMPARATIVELY RAPID ASPHYXIA BY ATMOSPHERES CONTAINING CARBON MONOXIDE

Milligrams in 100 c.c. blood

Dog No.	Duration of Exposure	Normal	At Death	Change
			SUGAR	
29	22.5 Minutes	102.0	360.0	+258.0
30	30.5 "	89.4	186.0	+ 96.6
31	22 "	78.1	241.0	+162.9
			UREA	
29	22.5 Minutes	32.4	34.3	+ 1.9
30	30.5 "	27.0	27.3	+ 0.3
31	22 "	27.8	26.6	- 1.2
			URIC ACID	
29	22.5 Minutes	0.8	5.1	+ 4.3
30	30.5 "	1.1	5.9	+ 4.8
31	22 "	1.1	4.9	+ 3.8
			N.P.N.	
29	22.5 Minutes	32.0	39.9	+ 7.9
30	30.5 "	26.3	34.9	+ 8.6
31	22 "	37.2	34.6	- 2.6
			TOTAL CREATININE	
29	22.5 Minutes	5.2	5.8	+ 0.6
30	30.5 "	4.0	4.5	+ 0.5
31	22 "	5.0	4.6	- 0.4
			PRE-FORMED CREATININE	
29	22.5 Minutes	1.4	1.8	+ 0.4
30	30.5 "	1.3	1.3	+ 0.0
31	22 "	1.5	1.4	- 0.1

Milligrams in 100 c.c. plasma

			INORGANIC PHOSPHOROUS	
29	22.5 Minutes	6.0	(1)	(1)
30	30.5 "	5.0	7.5	+ 2.5
31	22 "	5.5	6.8	+ 1.3
			OXYGEN IN 100 C.C. BLOOD	
29	22.5 Minutes	13.5	.00	- 13.5
30	30.5 "	(1)	1.13	(1)
31	22 "	10.76	0.39	- 10.37

Dog No.	Duration of Exposure	Normal	At Death	Change
		CARBON DIOXIDE, C.C GAS IN 100 C.C. BLOOD		
29	22.5 Minutes	45.65	31.72	- 13.93
30	30.5 "	(1)	34.19	(1)
31	22 "	47.64	33.41	- 14.23
		CARBON DIOXIDE CAPACITY OF PLASMA PER C.C GAS IN 100 C.C. PLASMA		
29	22.5 "	52.5	28.0	- 24.5
30	30.5 "	52.5	36.0	- 16.5
31	22 "	52	25.0	- 27.0
		HYDROGEN-ION CONCENTRATION EXPRESSED AS pH		
29	22.5 "	7.26	6.88	- 0.38
30	20.5 "	7.37	7.25	- 0.12
31	22 "	7.28	7.15	- 0.13

CARBON MONOXIDE AT DEATH

Dog No.	c.c./100 c.c Blood	Carbon Monoxide, c.c./100 c.c. of Blood	Percentage Saturation of Hemoglobin
29	17.40	19.28	90
30	17.48	20.27	86
31	12.47	15.04	83

	Normal	At Death
	Dog No. 28	
Hemoglobin	85	(3)
Red Blood Cells	4,500,000	(3)
White Blood Cells	9,600	11,200
Polymorphonuclears	72	(3)
Lymphocytes	24	(3)
Endothelials	2	(3)
Eosinophils	1	(3)
	Dog No. 29	
Hemoglobin	78	80
Red Blood Cells	4,200,000	4,400,000
White Blood Cells	10,050	11,500
Polymorphonuclears	68	70
Lymphocytes	30	28
Enothelials	2	(4)
Eosinophils	(4)	2

	Dog No. 30	
	Normal	At Death
Hemoglobin	70	72
Red Blood Cells	3,800,000	4,000,000
White Blood Cells	11,050	12,000
Polymorphonuclears	74	80
Lymphocytes	23	18
Endothelials	2	2
Eosinophils	1	(3)

* (1) Normal sample taken before exposure.
(2) Taken just at time of occurrence of death. See table Five for duration of exposure before the occurrence of death.
(3) Not determined.
(4) Not found in the 300 cells counted for the differential determination.

The following observations were made by Nasmith and Graham (67) in their study of experimental carbon monoxide asphyxia on a number of guinea pigs which were placed in such an atmosphere that would produce a carbon monoxide hemoglobin of twenty-five per cent. At different intervals, erythrocyte and leukocyte counts were made and the hemoglobin content determined concommitantly. In order to obviate a large error in the leukocyte count, the animals would not be fed for fifteen hours prior to the determination, for it was found that feeding produced a leukocytosis. All hemoglobin estimations were made after the animal had been free in the air for a period of one and one-half hours, after which time it was found that the blood, with a twenty-five percent carbon monoxide hemoglobin, would be completely free.

taking place only more rapidly in the gas. Even when compensation has taken place, this process is more rapid.

From what has been said, it is clear that the effects of chronic carbon monoxide poisoning is similar to that which occurs at high altitudes. In the latter case, nucleated red cells are not found, but this may be due to the fact that ascent is not as rapid or high enough. The similarity is obviously explained by the view that a lack of oxygen is the chief cause in both cases of the changes in the blood picture.

In cases of carbon monoxide poisoning of guinea pigs, a leukocytosis takes place which varies in intensity with the strength of the saturation of the blood with the gas. In acute poisoning, the total count may or may not increase for three or four hours, but the differential count alters from the beginning. The change in oxyphil granular cells is particularly note worthy; they increase from twenty-three to eighty-nine per cent, while the eosinophils totally disappear when the animal has been removed from the atmosphere of gas for four or five hours, but return six or seven hours later. In chronic poisoning, the eosinophils steadily increase and remain, until death, on a higher level than normal.

From the results obtained by the author, it seems quite apparent that the lack of oxygen does produce

auto-intoxication and therefore gas poisoning is really due to a toxemia caused by the lack of oxygen; the carbon monoxide itself being merely the substance which prevents the oxygen from reaching the tissues. The lack of oxygen means a deranged metabolic activity and that certain excretory products usually eliminated as certain definite chemical compounds either must accumulate as some incompletely formed excretory product or abnormal constituents are evolved, both of which act as poisons. Such extraordinary products may be nitrogenous and poisonous in nature and prove positively or negatively chemiotactiv to the oxyphil-granular forms according to the quantity of poison formed.

The higher the saturation and the longer the time involved, the greater will be the damage to the body cells at large, and to those of the central nervous system in particular. It is probably this reason that cases of poisoning produced by rapid saturation of the hemoglobin with carbon monoxide, and continued only for a short time, recover rapidly when fresh air and artificial respiration are used as a means of eliminating the gas.

Williams and Smith (93) brought about an adaptation of mice to an atmosphere of carbon monoxide which would cause a sixty to seventy per cent saturation which is

Of the twelve guinea pigs offered for the experiment, not one died from the effects of carbon monoxide. Most of them gained weight, and after the first few days, appeared to be as active as those controls living in free air.

It was supposed that the animals would show signs of anemia when only seventy-five per cent of their total hemoglobin could be utilized, but this was not the case. On the second day, the blood showed a degeneration of erythrocytes, and on the third day normoblasts appeared in the blood stream. In a few days, there appeared a steady rise in the erythrocyte count which indicated that the gas was causing a proliferation of erythroblasts and that compensation was taking place. After a period of three or four weeks, the animals attained their maximum of erythrocytes for that saturation, and the counts thereafter remained fairly constant. With compensation, it was noted that degeneration of the red blood cells gradually disappeared and that the leukocytosis, which was present at first, gradually disappeared and the count became constant but at a level slightly higher than normal. The normoblasts disappeared in a few days as did the poikilocytes.

As the erythrocytes of normal blood are being used up and replaced continually, so this process is constantly

just sub-lethal for exposure of one hour, by gradually increasing the daily exposure from an initial ten minutes to one hour in three weeks.

They found that the fragility of the red blood cells to hypo-tonic salt solutions showed no change until after the gasing had been continued for two hundred days. In those small groups which were exposed for more than two hundred successive days, there was only a slightly increased fragility exhibited over non-gased litter mates.

It was found that the hematocrit readings for rats exposed for two hundred days was increased from 58.3 to 75 per cent. The cell percentage correlated directly with the hemoglobin percentage; the mean hemoglobin difference between gased and controlled rats ranged from 2.66 to 3.70.

Williams and Smith (93) also observed that daily exposure to carbon monoxide proved deleterious to the well being of the animals. Body weight was always found to be lower in the gased rats than in their non-gased litter mates. It is also noticed that the appetite was decreased and that muscular and tissue turgor was reduced. The hair became unkempt and a typical alopacia ensued, the old hair being retained and the new hair scanty. No predisposition to infection was incurred.

The lungs of the gased rats at autopsy appeared normal except for occasional ephasema and excess red blood cells.

It was also found that reproduction became impaired, as the period of gasing lengthened. As has been pointed out by other workers (8,11,74,93), sterility results from prolonged or chronic carbon monoxide poisoning. Histological examination of the testes and epididymis of gased rats showed some sperm cells to be present, but that the weight of the testes of these rats was from one-half to one-third that of the control. Histological study of the ovaries of gased females showed the Graffian follicles and corpora lutea to be of normal appearance, however the size of these organs seemed somewhat reduced.

CLINICAL RECOGNITION

Studies of carbon monoxide asphyxia reveal that disease of the central nervous system, cardio-vascular and gastro-intestinal systems are much more common in persons whose occupations expose them to this gas over considerable periods of time.

For a practical classification of carbon monoxide poisoning, Beck (8) gives the following groups:

1. Simple Anoxemia. Represented by the acute cases of asphyxiation and the milder chronic forms, i.e., recovery without any delayed or residual manifestations. The symptoms are; headache, vertigo, paresthesias, stupor, dullness, vomiting, weakness, ataxia, yawning, dyspnea, palpitation, tremor, flushing, anorexia, myalgia, neurolgia, etc.

2. Hematologic Syndromes. Polycythemia (common) and the anemias (rare).

3. Cerebrospinal Syndromes. Carbon monoxide anoxemia permanently affects the central nervous system. Chronic encephalitis with Parkinsonian like syndrome come in this category. Chronic encephalitis and hypopituitarism, and multiple sclerosis are also included.

4. Cardio-vascular Syndrome. Persons suffering from myocardial disease are susceptable to carbon monoxide poisoning. Angina pectoris is often associated with anemia.

5. Respiratory Syndrome. Does not produce severe inflammatory reaction in the lungs such as result from irritative gases. However hoarsness and coryza and respiratory distress are frequent symptoms, and must be differentiated from tuberculosis and other chronic lesions.

6. Gastro-intestinal Syndromes. Cardiospasm and pylorospasm combined with other gastric disturbances often lead one to suspect an ulcer. The tendency to entero-spasm associated with abdominal cramp and severe constipation often suggests the possibility of perforation or intestinal obstruction.

Acute poisoning symptoms appear almost instantaneously and without warning the victim may loose consciousness. The rapidity with which symptoms develop depends upon the volume, intake and susceptability of the individual. Owing to the loss of consciousness, death often results from a fall. If poisoning is slow, a characteristic train of symptoms usually develops; dizziness, yawning, frontal headache, blurring of vision, weakness of the extremities with tremulousness, especially in the knees and unsteadiness of gait. Nausea and vomiting sometimes occur. The pulse is slow, blood pressure increased, the respiratory rate increased and the temperature normal. There is palpitation, throbbing of the arteries and veins and dilatation of the cutaneous vessels with flushing of the skin and dilatation of the pupils. Later great muscular weakness with tendency to syncope, stupor, mental confusion and delirium. Glycosuria frequently occurs, pulse rate increases, blood pressure falls and temperature may show a slight elevation. Profound coma finally supervenes in which the patient dies unless treatment is

promptly instituted (9, 74, 75).

McGurn (61) states that these gases, carbon monoxide and illuminating and coal gas, are capable not only of producing many diseases and conditions peculiar to them selves, but also of simulating nearly every disease known to modern neuro-pathology as well as many of the so-called idiopathic and functional abnormalities. In his artical he gives a complex list of symptoms presumably due to carbon monoxide which simulate almost any disease.

Repeated inhalations of very minute quantities of carbon monoxide, are far more dangerous to the future health of the individual than one exposure where the patient is rendered fully unconscious (70).

In a most detailed study of daily exposures to small amounts from automobile exhausts, Sayers and Yant (74, 75) and others found that two parts of carbon monoxide in ten thousand parts of air cause frontal headache after three and one-half hours in six per cent of test subjects, and that after a period of five hours., twenty-two per cent of the test subjects experienced this symptom. It was also noticed that with slight exercise, the number of headaches increased after an exposure of a given length of time, that is, eight per cent of the test subjects experienced frontal headache

after three and one-half hours and twenty-eight per cent experienced frontal headache after five hours exposure to 0.02 per cent carbon monoxide. Vertigo was reported in as short a time as one hour and increased to ten per cent in three and one-half hours. It is also significant to observe that there were no cases of occipital headache reported even after six and one-half hours of exposure to this mixture of carbon monoxide in air. It was found too that the saturation of blood with carbon monoxide practically attains an equilibrium value in that time, somewhere between twenty-eight and thirty per cent, and this is insufficient to produce occipital headaches except in cases of hyper-sensitivity or strenuous exercise.

In the experiments using three parts of carbon monoxide to ten thousand parts of air, frontal headaches were reported after an exposure of two and one-half hours. Exercise caused a greater number of headaches to be experienced in a number of test subjects. Vertigo to the most part occurred after approximately three hours, and after a period of three and one-half hours there was a distinct occurrance of occipital headaches with a few subjects. The equilibrium of carbon monoxide hemoglobin at this concentration is reported to be between thirty-eight and forty per cent, the major portion

being attained at the end of four or five hours.

With a concentration of four parts of carbon monoxide to ten thousand parts of air, frontal headaches occurred after one and one-half hours of exposure and with exercise increased to thirty-four per cent at the end of two and one-half hours. Occipital headaches, and vertigo and a feeling of muscular weakness occcurred with a few subjects at the end of two and one-half to three hours of exposure. The equilibrium value at this concentration is somewhere between forty-four and forty-six per cent and the rate of saturation is said to be very fast.

The general health and the physical condition of the subjects, which in this experiment were medical students, were not in any way impaired. As far as blood pressure, pulse, body temperature and respirations are concerned, there were no changes of any significance.

In the blood studies, there was found to be a distinct increase in hemoglobin which was due, probably to compensation. There was also a distinct increase in the number of erythrocytes and leukocytes, however there was no change in the differential count in any case.

The urine examinations in each of the test subjects was negative. No albumin or sugar, which is often reported, was found, and there were no changes in the

specific gravity of the hydrogen-ion concentration.

Franklin (33) points out that confusion and collapse are likely to occur at blood saturation levels of forty to fifty percent and that syncope, increased respiration and pulse and coma with intermittent convulsions and sometimes Cheynes-Stokes respirations occur at saturation of fifty to sixty percent. At saturations of seventy to eighty per cent, the pulse becomes weak and respirations slow, with respiratory failure and death, and with saturation over eighty per cent, is rapidly fatal.

According to Rabinowitz (73), the early appearance of decubitus ulcers is diagnostic of carbon monoxide poisoning. The author cites three cases of carbon monoxide poisoning, all of which demonstrated early bed sores. He attributes this to the fact that carbon monoxide is attended by a great decrease of tissue respiration, and that a severly poisoned individual, lying on his back for a considerable time, will have ulcers formed over the scapular, sacral and heel areas, resulting from pressure together with the above factor or tissue asphyxia. He claimed that the early appearance of bed sores in a previously comatose or still stuporous individual is almost pathognomonic of carbon monoxide poisoning, as it is not found as early in other conditions.

As has been stated by many authors, the absolute diagnosis of carbon monoxide poisoning is dependent upon the finding of the gas in combination with hemoglobin at the time of asphyxiation. There are several tests which may be used to determine its presence in the blood stream.

Katayamas is one of the best tests for this purpose as it will detect as little as a ten per cent saturation. It is quite a simple procedure to follow. Ten c.c. of water are placed in two test tubes; five drops of suspected blood are added to one test tube and five drops of normal blood are added to the other. Then five drops of orange colored ammonium sulfide are added to each, mixed thoroughly and then each mixture is made faintly acid with acetic acid. If carbon monoxide hemoglobin is present, a rose red color will develope, whereas the control will be a dirty greenish brown (86).

The Hoppe-Syeler's is less sensitive than the one above, but is much simpler and may be carried out at the scene of the accident if necessary. The procedure is as follows: place three c.c. of water in a test tube, add three drops of blood and one drop of five per cent sodium hydroxide, mix gently and let stand one hour. Carbon monoxide hemoglobin is more or less pink while normal blood give a greenish brown color.

Carbon monoxide has a characteristic spectrum, and when present in a sufficient amount, thirty per cent or more, is readily identified with the ordinary pocket spectroscope (86).

Carbon monoxide indicators are now available on the market, which indicate by direct reading the percentage of carbon monoxide present in the blood or in the air (33).

Another method of determining the amount of carbon monoxide in the blood, both qualitative and quantitative, involves the comparison of a small amount of blood similarly prepared with a set of color standards (76).

The standards are made up by drawing five c.c. or more blood to which 0.05 grams of potassium citrate or 0.02 grams of sodium fluoride are added for each ten c.c. of blood. This amount is divided into two equal parts, one of which is immediately diluted, one to ten with distilled water; the other is saturated with three to five per cent of carbon monoxide, and then diluted one to ten with distilled water. From these two solutions, mixtures are made up which total one c.c., but vary in carbon monoxide hemoglobin from zero to one hundred per cent in steps of ten. To each standard prepared, a one c.c. mixture consisting of equal parts

of a two per cent fresh pyrogallic acid solution and a solution of two per cent tannic acid. The tubes should be sealed immediately, and done so properly, will remain permanent for several weeks. The color develops in the standard tubes within fifteen minutes.

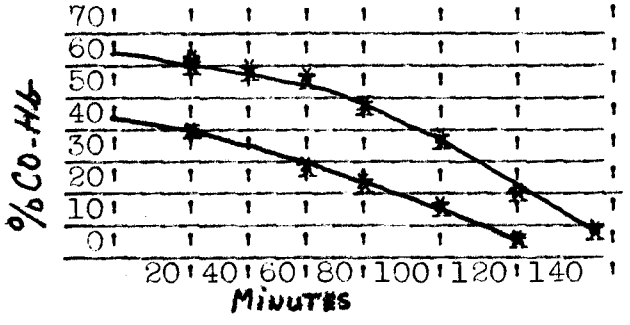
In making the test for carbon monoxide in the blood of a suspected victim, 0.1 c.c. of blood from the finger is used. The same constituents are used in making this test as were used in making the standards, including the type of test tube. The contents are thoroughly mixed and allowed to stand ten minutes, at the end of which time, comparisons are made with the standards. Thus knowing what amount of carbon monoxide hemoglobin each standard tube contains, quantitative and qualitative estimations can readily be determined.

TREATMENT

Henderson and Haggard (46) found that asphyxia depressed the oxidative metabolism and production of carbon dioxide, and even when the victim is removed from the poisonous atmosphere, the breathing lacks its normal stimulus and remains at a very low level for an hour or more. The elimination of carbon monoxide at that time is therefore very slight even though the body is surrounded by air and the condition of asphyxiation continues within the tissues.

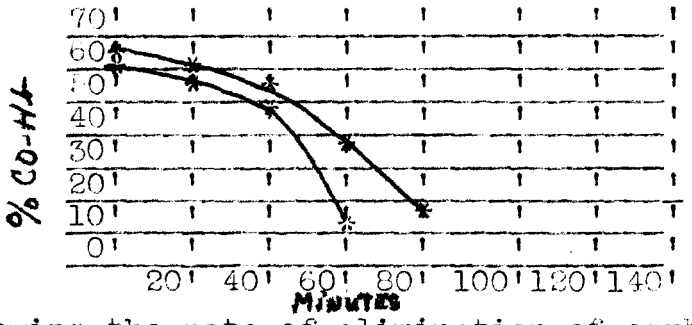
In studying the elimination of carbon monoxide from the blood in animal experimentation, three comparisons were made: A. air, B. oxygen, C. carbon dioxide-oxygen mixtures. The following graphics disclose their findings:

Table I



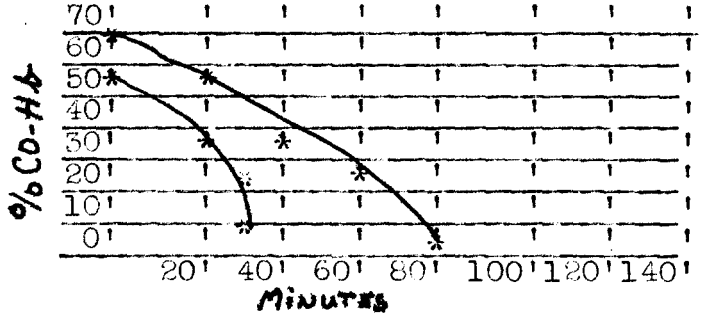
Showing the rate of elimination of carbon monoxide from the blood of profoundly asphyxiated, but there after untreated animals.

Table II



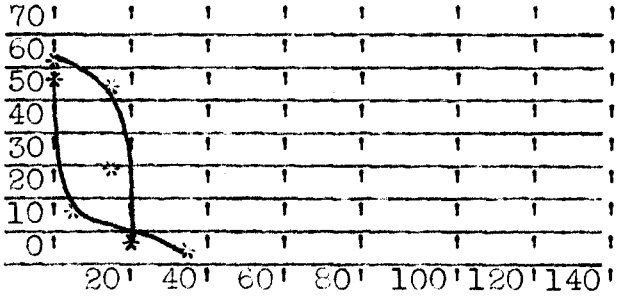
Showing the rate of elimination of carbon monoxide from the blood of animals under inhalation of oxygen.

Table III



Showing the rate of elimination of carbon monoxide from the blood of animals while breathing air and carbon dioxide.

Table IV



Showing the rate of elimination of carbon monoxide from the blood of animals under inhalation of oxygen and ten per cent carbon dioxide.

(Vertical numbers indicate the percentage of hemoglobin combined with carbon monoxide.

Horizontal numbers indicate the time in minutes.)

In summary, they found that air did not increase the rate of elimination, and that oxygen had only a slight effect, for it was not adequately inspired. Inhalations of carbon dioxide diluted with air has an immediate effect. It augments breathing, and hastens the elimination of carbon monoxide. Inhalations of carbon dioxide and oxygen is far more effective than either gas alone; for the augmented breathing allows the oxygen to effect a rapid displacement of carbon monoxide from the blood. It was found too, with this mixture, that functional respiration was correspondingly accelerated.

The value of carbon-dioxide as a means of eliminating inert gases from the blood stream is demonstrated by the experiments of Underwood and Diaz (87). In their experiments, radon gas was used. They determined the value of the elimination constant under different conditions and found it to be the same in all cases. It was not influenced by variations in pulse rate, cardiac out-put, or pneumothorax. However hyperventilation will cause a drastic change in the constant, and that the administration of carbon dioxide will speed up the process of pulmonary elimination of the gas from the blood stream.

Sayers and Yant (78, 81) also advocate the use of carbon dioxide inhalations as a means of eliminating carbon monoxide from the blood stream. They state that a five percent carbon dioxide mixture in oxygen, if given immediately, will greatly lessen the number and severity of symptoms of carbon monoxide poisoning as well as decrease the possibility of serious sequelae. In their estimation, all industries which have such a hazard should be equipt with respirators and inhalators, and employees should be trained in their use so that resusitation may be affected immediately.

Burmeister (18) studied the use of preserved living erythrocytes in the resuscitation of rabbits

and dogs after experimental asphyxiation by means of illuminating gas. He points out that between the years 1864 and 1900, blood transfusion was tried as a means of resuscitation, but it carried a high mortality rate. He attributed the failure of this method of treatment to faulty technique and lack of a sufficient quantity of transfused blood. The mortality rate at that time averaged fifty to one hundred per cent.

In the rabbit experiment, twenty animals were used of which twelve were transfused. All the animals were asphyxiated to the point where respiration and heart beat were not perceptible. It is interesting to note that artificial respiration was used along with the transfusion. It is assumed that the control animals died although no mention was made to this effect. Autopsy showed no pathology outside of a cherry-red appearance of the tissue.

In the dog experiment, of the fifteen dogs transfused, twelve recovered without apparent ill after effects. Two died without regaining consciousness and one developed symptoms quite typical of the manias sometimes seen in humans after acute asphyxiation. Here again, artificial respiration and intra-cardial injections of epinephrine were used as adjuncts.

Transfusions, venisection, and intravenous injection of salt solutions were used by several men (84) as methods of resuscitation.

In 1933, the use of methylene blue became the vogue of treatment. Its use was advocated by several workers who had experimental evidence of its efficacy.

Brooks (17) provides the experimental evidence for this method of treatment. She chose rabbits for her experimental subjects. A 0.03 per cent solution of methylene blue dissolved in a physiological saline solution was given intravenously. The amount used was one cubic centimeter per kilogram of body weight. This was injected one minute after the animal was removed from the gas chamber. The control animals were either injected with normal saline solution or not injected at all. The disappearance of carbon monoxide hemoglobin and the reappearance of oxyhemoglobin was followed by spectrophotometric readings of blood samples taken by heart punctures. The results are given in the following table:

Minutes	Percentage Oxyhemoglobin	
	Controls	Methylene blue
0	26	26
1	43	76
3	54	96
11	63	100
21	82	100

This shows the rapid change from carbon monoxide hemoglobin to oxyhemoglobin in the case of the treated animals as compared with the slower change for the controls. In her opinion, these results show definitely that methylene blue changes carbon monoxide hemoglobin into oxyhemoglobin in the blood stream and not into met-hemoglobin.

The clinical evidence for support of this treatment is given by Geiger (34), Bell (12) and Nass (68). Each of these men give case histories of patients found unconscious as a result of carbon monoxide asphyxiation. In each case, the amount of one per cent methylene blue solution injected intravenously was approximately fifty cubic centimeters. However, it is interesting to note that carbon dioxide and oxygen mixtures were used as an adjunct to this treatment. The spectacular results which were obtained almost immediately after the intravenous injection of this solution, were attributed to this therapy.

However, there are those workers (39, 47) who disagree with the methylene blue therapy. They state that the use of this substance is based upon a misconception of the physiology of carbon monoxide poisoning. They point out that its action is not upon the tissue ferments, as is the action of cyanide for which methylene

blue is used as an antidote. In this type of poisoning. the cyanide combines with the methemo-globin, formed by the reaction of methylene blue with hemoglobin, thus taking up the free cyanide in the blood stream and preventing it to act as a poison on the tissue ferment. It is also pointed out that met-hemoglobin is not capable of carrying oxygen, and by its introduction into the blood stream in the presence of carbon monoxide hemoglobin, only adds to the deleterious affect of anoxemia. These statments are corrobrated by experimental evidence. They also believe that the stimulus received from "counter shock" may have been more beneficial than the methylene blue injections in the experiments of Brooks.

It was observed by Schmidt (80) that the respiration of nerves is inhibited in the dark by carbon monoxide and oxygen mixtures; the degree of inhibition depending upon the partial pressure of carbon monoxide and upon the condition of diffusion in the nerve. In contrast to this condition, it was observed that light markedly decreases this inhibition. As a result of this finding and from the observations of others(2), that light causes the dissociation of the compound formed by carbon monoxide and hemoglobin, especially the visual part of the violet part of the spectrum, sunshine would be a beneficial adjunct to other measures.

Barker (7) gives hydrochloric acid as an example of intravenous treatment for carbon monoxide asphyxia. He cites a case in which he used this therapy, injecting ten c.c. of 1:1500 solution, and obtained marked results within five minutes.

In addition to any therapy which might be used, it is well to treat the shock which the victim is usually suffering, and to keep the patient confined to his bed for several days (33, 34).

COMPLICATIONS - CLINICAL CASES

McGurn (62) cites two cases simulating multiple sclerosis, which he believed to be caused by carbon monoxide poisoning. Case One is concerned with a young man of twenty-six years of age who had a history of working about a faulty furnace in the basement of his home. As a consequence, a considerable amount of gas was inhaled over a long period of time. His first symptoms were dizziness and head ache. Shortly afterwards he had a vomiting attack which lasted several hours. He also became cyanosed and developed an unsteady gait.

Four days after the exposure the patient was able to move one leg with difficulty; his feet felt numb, with little feeling in the soles of his feet. The numbness extended half way to the knees and it was difficult for him to place his right foot in a desired position. About this time diplopia was present and a physician was called. Anti-luetic treatment was instigated. In the meantime, however, the furnace was still leaking gas.

His condition gradually became worse, and the mercury and potassium iodide treatment gave no results. Several consultants were called, and the consensus of opinions was that this was a case of cerebrospinal lues,

although no history of venereal disease could be obtained.

At the end of two years the patient was confined to a wheel chair. At this time there was marked exaggeration of the knee jerks, and ankle clonus, patellar clonus, Oppenheimer's and Babinsky's signs were positive. There was also marked atrophy of the muscles of the back, thighs, legs and arms; there were areas of anesthesias widely distributed over the body; orientation was poor, with complete loss of sense of position of each foot and leg. There was no loss of sphincter control although sexual power was greatly diminished.

At the end of three and one-half years, scanning speech and nystagmus had developed. The patient was entirely bed-ridden and had lost considerable weight, from 168 pounds to 102 pounds. The patient died six years later, but in the meantime serological tests had developed to the stage that it was possible to disprove the opinion that his condition was due to syphilis.

The second case was that of a young man, age twenty-six, who gave an almost identical history as the first.

This patient complained of dizziness, vomiting spells and an unsteady gait. A definite history of exposure to furnace gas for a considerable length of time

was obtained. Upon examination, it was found that the knee jerks were markedly exaggerated and that pain and tactile sensations were lost over the feet, legs, arms and that part of the back below the fifth lumbar segment. However the pupils reacted to light and accommodation, but there was some irregularity and a hippus movement was present.

One day when the physician was called, the patient was found crying out in pain (headache) and was suffering from visual hallucinations. His face was flushed and the pupils fixed. The odor of furnace gas was very strong in the room. The windows were thrown open immediately, and within the next twenty-four hours, his condition had improved greatly.

As time went on his general condition became worse, he lost strength rapidly, spastic and ataxic gait grew more and more noticable. Frequent fibrillary twitchings of the facial muscles, hands and arms developed, and sphincter control also was lost.

There were times when these symptoms seemed to improve, but there would be exacerbations of the old complaints with development of new. Visual and speech defects soon made their appearance. Serological examination was negative through out the course of the disease.

Although scanning speech, nystagmus and muscular contractions were still lacking, there could be no reasonable doubt regarding the carrectness of the diagnosis, while it would seem that the prognosis must be similar to that of Case One.

Kurlander (54) reports a case of leg paralysis following asphyxiation by illuminating gas in a young man of twenty-one years. Three days after the exposure, he complained of anesthesia and paralysis of the right leg and foot. In addition to this, there was found an area of induration over the right tuberosity of the ischium which was painful and progressively increased in size.

A biopsy was taken of this area. The report stated that it was an inflammatory mass and not a malignant growth as was suspected.

Complete flaccid paralysis of the right foot and leg with characteristic toe drop and complete anesthesia corresponding to the distribution of the peroneal nerve developed. The tips of the great and second toes became gangrenous.

Four months later the degree of paralysis had not progressed or regressed, but the area of anesthesia seemed to extend over a slightly lesser area. The authors diagnosis was that of a peripheral neuritis, and

implied that the prognosis was favorable because of the peripheral involvement. He states that paralysis of cerebral origin is apt to remain permanent.

Grinker (37) cites a case of Parkinsonism in a fifty year old woman following an acute exposure to carbon monoxide. The patient recovered within a few hours and appeared physically and mentally normal. However, one month later the patient became apathetic, acted queerly and had poor orientation. She was sent to a state hospital for further observation.

At the time of her admittance to the state hospital, the physical findings were negative. However, she would lie motionless and rigid for hours. The expression on her face was mask-like. The palpebral fissures were widely open and blinking was infrequent. There was no paralysis noted but muscle tone was markedly increased. She presented the symptoms of a catatonic nature. Her speech was slow and answers to questions were given only after long pauses; she finally became mute. Death occurred with pulmonary edema two months after her exposure to carbon monoxide.

An autopsy was done. Symmetrical, yellow, brown necrotic areas were seen in the globus pallida extending from the anterior tip to the center of the ganglia.

Another case of peripheral neuritis and Parkinsonism (71) in a thirty year old woman, who, previous to her exposure to carbon monoxide, did not give a history of pain, paresthesias or motor weakness. However, it was reported that she was a heavy consumer of alcoholic beverages, partaking on the average of one gallon of whisky per week. Whenever she would go on one of these debaches, she would experience visual hallucinations.

When she recovered consciousness, she acted very queerly, being completely disoriented and incontinent. She was removed to a state hospital for observation. Examination revealed a posture and rigid attitude of Parkinsonism; the associated movements of both arms were absent; a cog-wheel phenomenon in both arms was present but more pronounced in the right. There was a right foot drop with weakness of extension and flexion in the right leg. The knee jerks were increased but equal; a transitory left ankle clonus was present and the right ankle jerk was absent. There was a typical extensor response of all the toes to plantar stimulation with slight fanning on the left, and no response on the right. A bilateral Hoffmann was present. The right upper abdominal was absent. There was an absence of faradic response in all muscle groups of the right leg and foot. Numbness was also present in the posterior

Bell (12) cites a case of decerebrate rigidity which developed after asphyxiation by illuminating gas.

Wechsler (91) reports an unusual case of partial cortical blindness with preservation of color perception. This is very unusual because color vision is usually the first to be lost and the last to be regained.

The patient was a thirteen year old boy who was over come by smoke. Examination revealed the speech to be unintelligible and dysphasic. There was aprexia in execution of skilled acts; intellectual deterioration and emotional inadequacy and lack of insight. Before the accident the boy had been considered a superior student in school.

It was concluded that the boy suffered from a brain lesion in which the cortex was extensively affected, while the subcortical and basilar structures were involved to a lesser extent. The loss of vision aside from early temporary retinal hemorrhages, was recognized as cortical because of the preservation of pupillary reflexes and absence of optic atrophy. The probable bilateral hemianopia and the defect in the upper fields was correlated with occipital, i.e., calcarine disease.

Dancy and Reed (26) report a condition which developed from carbon monoxide asphyxiation which resembled a hebephrenic schizophrenia. One other case was cited

which resembled general paresis.

Cohen (23) reports a case history of a middle aged man who developed speech perseveration and astasia-abasia after attempting suicide by inhaling automobile exhaust. It is important to note here that the man was in coma seventy-two hours, and when he regained consciousness, was demented and confused.

When examined at a state hospital four weeks later, the general physical was negative, however a coarse tremor of the tongue was noted, most of the reflexes were hyperactive.

Mental examination revealed a somewhat excited and apprehensive, confused and completely disoriented mind. His memory was very poor. He seemed quite apathetic, very distractable, and did not appear to have any insight. His speech was slurred, monotonus, and rapid. He seemed to comprehend questions but his answers were merely repetitions of the last word or two of the question.

He was able to move his limbs, but when he tried to stand or walk, fell in a heap to the floor.

The neurological symptoms on the whole were attributed to basal ganglia, particularly to the corpus striatum. There was also cerebral damage as was demonstrated by defects associated with memory disturbances

and dementia. The astasia-abasia was regarded as a hysterical inclusion within the picture of organic brain damage.

Nichols and Keller (69) point out that changes in the nervous system can be wide spread and not limited to the globus pallida. They report a case that had severe visuo-motor incoordination. He showed loss of the ability to perform certain skilled acts, and the function of written speech was returned only after a carefully planned retraining program.

Davis (27) states that in persons serviving exposure to carbon monoxide, the most frequent cause of death is the development of a broncho-pneumonia.

Beck and Suter (10) report two cases with symptoms of coronary thrombosis and angina pectoris. These patients were relieved of their symptoms after they were removed from an atmosphere of carbon monoxide. Each gave a history of chronic exposure to the gas from defective heating stoves.

More recent reports of these two men (11) have shown conditions resembling pernicious anemia, epilepsy, tetany and cardiospasm, coronary thrombosis, heart block, encephalitis with Parkinsonism and a case of hypothyroidism all resulting from exposures to carbon monoxide.

CONCLUSIONS

In retrospect, we see that the destruction caused by carbon monoxide asphyxia is not due to any specific toxin or toxins liberated into the blood stream, but mainly caused by anoxemia. It has been demonstrated that hemoglobin has a greater affinity for carbon monoxide than it has for oxygen and that the partial pressures of the two gases determine the amount of saturation of the hemoglobin.

The combination of carbon monoxide and hemoglobin does not form a stable compound, for it can be completely eliminated from the blood stream within a few hours.

The presence of this substance in the body produces a change in the amount of some of the elements of the blood stream, but as pointed out, these are immediately returned to normal limits as soon as it is eliminated from the body.

In the case of chronic carbon monoxide asphyxia, there is a tendency towards compensation demonstrated by a polycythemia and an increase in the amount of hemoglobin. However this is not a true compensatory action because certain normal functions are replaced by abnormal ones. There is to a certain extent, a loss of

the libido, a loss of muscular power, a feeling of lassitude and the production of many other minor complaints.

In prolonged or severe asphyxiation, considerable damage is done to the central nervous system and brain. Hemorrhage, perineuronal and perivascular edema and necrosis are the outstanding results. Certain structures, such as the cortex, corpus striatum, globus pallida and respiratory center are predilected by anoxemia. This appears so because of the blood supply to these organs. There is no collateral circulation, and if so, very poor, to these structures. Their function depends entirely upon an adequate blood and oxygen supply.

Another organ which seems to be affected to a certain degree is the heart. Conditions of angina, incomplete and complete heart block, coronary thrombosis, and myocardial failure have been reported, both experimentally and clinically. However, these conditions have been considered transitory and do not have a lasting effect.

Symptoms of carbon monoxide for the most part are not of a characteristic nature. If the process of asphyxiation is slow, dizziness, yawning, frontal headache, vision disturbances, muscular weakness, nausea and vomiting may be experienced before complete unconsciousness overcomes the victim. The after effects of

asphyxiation depend upon the degree of cerebral damage. The symptoms of cerebral pathology are not classical, but vary in degree and nature, depending upon the degree and the location of the damage. The effects of cerebral damage are lasting, because of the lack of regenerative power of these structures.

Treatment of carbon monoxide asphyxia for the most part is prophylactic. All possible means of exposure must be eliminated, especially in those industries in which employees are subjected to an atmosphere of carbon monoxide. In the home, appliances which produce the gas, or which depend upon illuminating gas for their function, should be checked periodically to see if they are functioning properly.

Treatment of a person asphyxiated by carbon monoxide should consist of (1) removal from the gas atmosphere, (2) artificial respiration augmented by inhalation of a mixture of carbon dioxide and oxygen, and (3) treatment of shock. The individual should be placed in bed for a few days and observed. Complications which arise must be treated accordingly.

The diagnosis of carbon monoxide asphyxiation can only be made by a history of exposure and the positive finding of carbon monoxide hemoglobin in sufficient quantity to produce deleterious effects.

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