ANESTHESIOLOGY

The Journal of

THE AMERICAN SOCIETY OF ANESTHESIOLOGISTS, INC.

Volume 10 **JULY, 1949** **Number 4**

ANOXIA AND THE CENTRAL NERVOUS SYSTEM
A REVIEW AND CASE REPORT *

DONALD L. BURDICK, M.D., JAMES R. LISA, M.D., AND MIGUEL G. ELIAS, M.D.

New York, N. Y.

Received for publication August 31, 1948

THE untoward reactions to and injurious sequelae of sudden and severe episodes of hypoxia and anoxia have been known for a long time. The causes were little understood. Paul Bert, in 1858, in studying this problem as related to balloon ascensions concluded that the lowered oxygen tension in the rarified atmosphere of high altitudes was responsible for the symptoms (1). The true significance of oxygen lack and the resultant histopathologic changes were not fully appreciated, however, until Haldane's investigations in 1912, the results of which he so tersely summarized by stating that "anoxia not only stops the machine, but wrecks the machinery" (2). Since then much has been accomplished toward clarification of the problem.

Barcroft classified the anoxias into four types: (1) anoxic, (2) anemic, (3) stagnant, (4) histotoxic (3). Nine years later, Krogh demonstrated the increased capillary permeability found especially in stagnant anoxia, and stressed its irreversibility when permitted to persist (4). The asphyxial effects of improperly conducted nitrous oxide anesthesia have been demonstrated by Courville, Waters and his school, White and his associates, Barach and Rovenstine, and others adding further contributions (1, 5, 6, 7). The fundamental physiology of the problem was clearly presented by Chase, who also suggested that a fifth type, "combined anoxia," be added to Barcroft's classification (8).

The pathologic changes produced by experimental methods show marked similarities to those found in clinical reports. Gildea and Cobb, in animals subjected to periods of temporary hypoxia, noted neuromuscular and behavior patterns associated with focal areas of cerebral cortical necrosis (9). Morrison succeeded in producing le-

* From the Department of Anesthesia and Pathology, The Doctors Hospital, New York City, N. Y.

sions of variable severity in monkeys dependent upon whether the oxygen lack was acute, subacute or chronic, mild or severe. These were focal softening of the globus pallidus, necrosis of the thalamic gray matter, plus edema, vascular hyperplasia with endothelial and adventitial proliferation, chromatolysis and vacuolization of cells of the supragranular layer, while ischemia, pyknosis and chronic shrinkage occurred in the cells of the deeper layers. The gray matter of the frontal lobe was most frequently and severely affected, followed by changes in the parietal areas. The occipital lobes showed less damage while the temporal lobes were least involved (10).

Clinically, Courville reported the necropsy findings from 9 fatalities attributable to nitrous oxide anesthesia. Changes were minimal in instances of immediate death with more marked alterations in patients surviving many hours or days. The process varied from spotty degeneration to ischemic malacia. There was marked pial congestion with subpial hemorrhages and arachnoidal thickening. Petechial hemorrhages were scattered throughout the gray matter and lenticular nucleus. The convolutions were flattened and showed cortical softening, with necrosis most advanced in the deeper layers of the frontal cortex. The nerve cells were severely damaged with fragmentation of the neurofibrillar structures. In the lenticular nucleus there was diffuse malacia with focal necrosis and nerve degeneration. The cerebellum was somewhat softened and fragmented in certain instances. The basal ganglia were not noticeably affected (1). Lowenberg and his coworkers reported 4 similar cases (11). Stewart described meningeal congestion with a purplish discoloration of the gray matter, and a degenerative zone approximately 2 mm. in depth extending from the white up into the deeper layers of the gray matter. The corpus striatum and the optic thalamus also were involved. The picture was one of diffuse myelin destruction and glial proliferation, destruction and degeneration of the ganglion cells, congestion and extensive cellular proliferation of the vessels, with an increase in the number of capillaries. The dentate nucleus, pons, cerebellum, white matter and spinal cord were free of lesions (12). Race and Lisa, in 15 cases of combined acute vascular lesions of the brain and heart, encountered a wide variety of cerebral changes. Petechial hemorrhages of the frontal, temporal and parietal lobes, as well as of the pons, medulla and island of Reil, were found in a comparatively young individual surviving only twenty-four hours. Areas of cortical atrophy and softening, which in one instance involved the island of Reil, were encountered in older patients who survived from four to fifteen days after the initial attack. These authors stated that the etiology of such neurologic changes perhaps is best explained as cerebral ischemia incident to the hypotension usually associated with acute cardiac infarction (13).

The results of acute oxygen lack vary greatly. The rapidity of onset, the type or types of anoxia, the duration of the hypoxic state,

the amount of available oxygen, the age and physical status of the patient, all bear on the final outcome. The latter may be complete recovery, with variable degrees of sequelae, or immediate or eventual death. The following case is illustrative of the results of an acute anoxic insult superimposed upon preexisting cardiovascular disease in a mildly anemic patient.

REPORT OF CASE

The patient, a 65 year old white man, was admitted to the hospital with the diagnosis of phlebothrombosis of the right leg. The past history revealed hypertensive cardiovascular disease and moderate arteriosclerosis of several years' duration. There had been a recent mild attack of decompensation.

Physical examination demonstrated that the patient was slightly orthopneic, obese, mentally clear and alert. Temperature and respirations were normal. Blood pressure was 170 mm. systolic and 100 mm. diastolic. The heart was enlarged. There was radial arteriosclerosis and slight hepatomegaly. The right leg showed a tender right calf, absent dorsalis pedis pulsation and a negative Homans' sign. Electrocardiograms revealed moderate left ventricular preponderance, auricular fibrillation, ventricular extra-systoles, ventricular rate 350, auricular rate 80. There was a mild anemia (hemoglobin 12 Gm., erythrocytes 4,140,000). There were no other pertinent findings.

Bed rest resulted in improvement until the fifth day when edema of the leg increased and Homans' sign became positive. Deep femoral ligation was decided upon. Premedication was morphine sulfate 0.015 Gm., atropine 0.0004 Gm. In the operating room the blood pressure was 200 mm. systolic and 118 mm. diastolic, the pulse 100 and respirations 28. Operation was begun with local infiltration. The patient complained bitterly, was uncooperative and general anesthesia was requested. Anesthesia was induced with nitrous-oxide oxygen, followed by ether maintenance with the absorption technic. Shortly after induction, the blood pressure fell to 130 mm. systolic and 70 mm. diastolic, pulse remained at 100 and respirations rose to 36. The surgical procedure was completed in forty-five minutes, at which time the blood pressure was 120 mm. systolic and 68 mm. diastolic and respirations were 40. The pulse at 90 was thready and weak and the patient, although awakening, was considered to be in poor condition. Oxygen therapy was instituted at once.

Massive hemorrhage from the wound was discovered approximately one hour later, and his condition rapidly became critical. A right-sided hemiplegia was noted. Plasma infusion was started, morphine sulfate 0.01 Gm. given for restlessness and he was returned immediately to surgery. The skin was cold and ashen, pulse questionably at 160 and blood pressure questionable at 60 mm. Nitrous-oxide 70 per cent, and oxygen, 30 per cent, were administered for two minutes, followed by 100 per cent oxygen. Infusion and transfusion by vein and sternal marrow were begun. The wound was explored rapidly and the bleeding vessel ligated. Pulse and blood pressure became imperceptible. At the end of one hour the pressure returned at 90 mm. systolic and 70 mm. diastolic and the pulse to 130. With gradual return to consciousness an aphasia was evident. Two hours later he was returned to bed with blood pressure at 150 mm. systolic and 90 mm. diastolic, pulse 100 and respirations 28. The aphasia persisted.

Oxygen and other therapeutic measures were continued through the postoperative period. During the two hours immediately following the surgical procedure the blood pressure rose to 240 mm. systolic and 110 mm. diastolic, the pulse slowed to 70 to 80, respirations were 9 to 12 and Cheyne-Stokes in type. Six hours later respirations were normal. Restlessness continued, hemiplegia and motor aphasia persisted, oliguria developed with a slight nitrogen retention with blood urea nitrogen of 37 mg. per 100 cc., and the blood pressure reading remained high with a definite pulse deficit. The temperature gradually rose to 104.2, coma developed and the patient died forty-eight hours after the initial operation.

Autopsy performed eighteen hours after death showed the following pertinent findings. The brain weighed 1350 Gm. The left cerebral hemisphere felt cystic, the right normal. On section, the former consisted of a shell of cortical gray matter, occipital pole, wall of lateral ventricle and basal nuclei. The white matter was replaced by a fluid gray tissue of the consistency of thin soup. The preserved shell of gray matter was sprinkled with small foci of degeneration and petechial hemorrhages. The right hemisphere, pons, medulla and cerebellum appeared normal.

The heart weighed 600 Gm. Its arteries were pipestem in character with marked atherosclerosis producing narrowed lumina which were free of occlusion. Many minute hemorrhages and infarcted areas were scattered throughout the muscle of the left ventricle and the interventricular wall.

Microscopy revealed that the pia-arachnoid of the left hemisphere was extremely edematous. The cortical gray and subcortical white matter showed necrosis, collapsed vessels with pale cells and frayed walls.

The diagnosis was hypertrophy of the heart; severe arteriosclerosis of the coronary arteries; multiple acute miliary infarctions of the heart; arteriosclerosis of the aorta and iliac arteries with mural thromboses; recent thrombosis of the right iliac artery and vein; recent bilateral ligation of the femoral veins; arteriolarnephrosclerosis; cerebral arterioselerosis and recent malacia of left cerebral hemisphere.

COMMENT

In the case reported the patient was mildly anemic with little cardiac reserve. Massive hemorrhage precipitated a relatively long period of anemic anoxia, with an accompanying stagnant anoxia from prolonged hypotension. The resultant hypoxia probably was the cause of the restlessness which was aggravated rather than helped by sedation, since it actually would decrease oxygen intake. The time element between the onset and control of bleeding was seemingly sufficient to initiate the irreversible damage to brain and heart which were found at autopsy.

SUMMARY

The isolated existence of one type of anoxia for any considerable period of time probably is rare if not impossible. An acute onset of one form may establish a cycle of events which will rapidly initiate other forms of oxygen want. Prompt institution of therapeutic measures to restore as rapidly as possible a normal physiologic state is imperative

if a vicious cycle is to be avoided or broken if once established. The recognition of the combined forces of anoxia should be emphasized if all possible means for restoration to the normal are to be employed. The term "combined anoxia" as suggested by Chase seems fully warranted. A case is reported which demonstrates the unfavorable outcome of acute anoxia due to sudden hemorrhage.

REFERENCES

1. Courville, C. B.: Untoward Effects of Nitrous Oxide Anesthesia, Pacific Press Pub. Assoc., 1939.
2. Haldane, J. S.: Respiration, New Haven: Yale University Press, 1922, p. 118.
3. Barcroft, J.: Anoxemia, Lancet 2: 485 (Sept.) 1920.
4. Krogh, A.: The Anatomy and Physiology of the Capillaries, New Haven, Yale University Press, 1929.
5. Waters, R. M.; Wineland, A. J., and Seevers, M. H.: Carbon Dioxide and Oxygen Problems in Anesthesia, Anesth. & Analg. 10: 10–20 (Jan.) 1931.
6. White, J. C.; Verlot, M.; Selverstone, D., and Beecher, H. K.: Changes In Brain Volume During Anesthesia: The Effects of Anoxia and Hyperapnia, Arch. Surg. 44: 1–21 (Jan.) 1942.
7. Barach, A. L., and Rovenstine, E. A.: The Hazard of Anoxia during Nitrous Oxide Anesthesia, Anesthesiology 6: 449–461 (Sept.) 1945.
8. Chase, H. C.: Anoxia—Its Surgical Significance, Surg., Gynec. & Obst., 73: 105 (Aug.) 1941.
9. Gildea, E. F., and Cobb, S.: The Effects of Anemia on the Cerebral Cortex of the Cat. Arch. Neurol. & Psychiat. 23: 876 (May) 1930.
10. Morrison, L. R.: Histopathologic Effect of Anoxia on the Central Nervous System, Arch. Neurol. & Psychiat. 55: 1-34 (Jan.) 1946.
11. Lowenberg, K.; Waggoner, E. W., and Zbinden, T.: Destruction of the Cerebral Cortex following Nitrous Oxide-Oxygen Anesthesia, Ann. Surg. 104: 801 (Nov.) 1936.
12. Stewart, J. D.: Cerebral Asphyxia during Nitrous Oxide and Oxygen Anesthesia, New England J. Med. 218: 754 (Sept.) 1938.
13. Race, G. A., and Lisa, J. R.: Combined Acute Vascular Lesions of Brain and Heart, Am. J. M. Sc. 210: 732–737 (Dec.) 1945.