

8326 P

Studies in Water Balance. 2: Anoxemia Factor in Water Intoxication.

HARRY A. DAVIS. (Introduced by E. B. McKinley.)

From the Department of Surgery, University of Chicago, and the Department of Pathology, The George Washington University.

The mechanism of death in intoxication by water is obscure. There is invariably a marked dilution of the blood and certain workers^{1, 2, 3} believe that the profound disturbance in the isotonicity of the body fluids which occurs is the cause of death. Others⁴ attribute the symptoms to a loss of chloride ions with a resulting alkalosis. Rowntree⁵ has pointed out that an oedema of the brain is always present and that, usually, this is the only lesion found in animals dying from the administration of excessive quantities of fluid. The oedema of the brain substance is accompanied, paradoxically enough, by a diminished secretion of cerebrospinal fluid and empty cerebral ventricles. A similar type of cerebral oedema occurs in carbon monoxide poisoning in which an anemic anoxemia is present. In view of this fact, an investigation was undertaken to determine the rôle played by anoxemia in the production of symptoms of water intoxication.

Twelve healthy dogs weighing 8 to 19 kg. were used. Isotonic sodium chloride solutions (0.9%) and isotonic (5%) glucose solution were administered by vein in amounts from 2,000 to 4,500 cc. Metabolic readings were taken before, during and after each experiment at intervals of 10 minutes. Hemoglobin determinations were made by the Newcomer⁶ method before and during the administration of fluid. Blood was withdrawn from the femoral artery and vein under oil and the oxygen content was estimated by the Van Slyke⁷ manometric gas analysis apparatus at standard intervals.

The following changes occurred during the administration of isotonic fluids. The respiration increased in rate from 20 to 40 and even to 60 respiratory excursions per minute. As the fluid intake increased the breathing became deep, irregular and dyspnoeic in

¹ Misawa, H., *Jap. J. M. Sc. Tr.*, VIII, 1927, 1, 355.

² Helwig, F. C., Schutz, C. B. and Curry D. E., *J. A. M. A.*, 1935, 104, 1569.

³ Kylin, E., *Z. f. d. ges. exper. Med.*, 1928, 63, 606.

⁴ Smith, F. S., Deamer, W. C., and Phatak, N. M., *J. Clin. Invest.*, 1933, 12, 55.

⁵ Rowntree, L. G., *J. Pharmacol. and Exp. Therap.*, 1926, 29, 135.

⁶ Newcomer, H. S., *J. Biol. Chem.*, 1923, 55, 569.

⁷ Van Slyke, D. D., and Cullen, G. E., *J. Biol. Chem.*, 1917, 30, 289.

type. Later the breathing became shallow. The pulse rate increased from 100 to 150 and even to 200 beats per minute. In the early stages the blood pressure increased 20 to 30 mm. of Hg., but in the later stages it fell below the original level.

In the early stages the oxygen consumption rate increased 50% to 600% or more above the initial level. Later the metabolic rate fell below the original level. The hemoglobin of the blood became much diluted until a critical point was reached which varied from 20% to 50%. In those animals which survived, the dilution of the blood did not go beyond the critical point. However, when this point was passed, the animal invariably died.

The oxygen content of the blood from the femoral artery fell from a normal 18 to 20% to 10% and even to 6% in the later phases of the experiment.

Oxygen Content of Venous Blood. The initial values of 13.5% to 15% fell to 6% and finally to 3% in fatal cases. In the later stages of the experiment the oxygen content of the venous blood rose especially when a considerable amount of fluid had collected in the interstitial tissue spaces.

These experiments suggest that the administration of fluids produces an early anemic anoxemia due to a dilution of the hemoglobin of the blood. Later, as fluid accumulates in the interstitial spaces around the arterioles and capillaries, the transfer of oxygen from the blood to the tissues is impeded and a histotoxic form of anoxia is superadded. Landis⁸ has shown that anoxemia increases the permeability of the capillaries to fluid, and it is possible that the cerebral oedemas of water intoxication and of carbon monoxide poisoning are explainable upon this basis. It was noted in these experiments that anoxic symptoms occurred more readily with isotonic glucose than with isotonic sodium chloride solutions. This is in agreement with the work of Loeb⁹ upon the relationship between electrolyte concentration and cell respiration.

Summary. The correlation of the changes in blood oxygen content, oxygen consumption rate and hemoglobin dilution during the administration of excessive amounts of fluid seems to indicate that the symptoms of water intoxication are those, in part, of an anoxemia.

⁸ Landis, E. M., *Am. J. Physiol.*, 1917, **30**, 289.

⁹ Loeb, J., *Pflüger's Arch.*, 1903, **97**, 394.