The similarity of circulatory response to low oxygen and sodium cyanide suggests like chemical disturbances in and on the opposite sides of the neurone membranes of the circulatory centers involved in the regulation of circulation.

The inverse relation of carotid and femoral flows suggest again that circulatory adjustments occurred in favor of the brain.

Likewise, the similarity of the circulatory response to the administration of carbon dioxide on the one hand, and to the administration of low oxygen and sodium cyanide on the other, suggests common factors of control. Acidity and state of oxidation in and about the neurone membrane concerned may be the outstanding factors controlling circulation.

The high sensitivity of the circulatory and respiratory centers to changes in oxidation agrees again with their common and coördinated function.

3323

Tissue and Blood Acidity: Coördination of the Dual Function of Hemoglobin During Suspended Ventilation.

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In the paper directly following, on tissue acidity, blood acidity and pulmonary ventilation, we studied the problem of respiratory control, by regulating the shift of ions and acid molecules between the blood and tissues. A direct relation between pulmonary ventilation and blood acidity on the administration of carbon dioxide and sodium carbonate, and an inverse relation on the administration of sodium bicarbonate, were demonstrated. These diametrically opposite relationships were harmonized by referring these effects to changes in acidity of the respiratory center itself. Assuming that the acidity of the cerebro-spinal fluid reflected the changes in acidity of the respiratory center, our results agree with the theory that the acidity of the respiratory center is important in the control of pulmonary ventilation. For carbon dioxide turned the cerebro-spinal fluid acid, and increased ventilation; sodium carbonate turned it alkaline and decreased ventilation; and sodium bicarbonate turned it acid, and increased ventilation.

Changes which occur during suspended ventilation offer another approach to the study of tissue acidity, blood acidity and pulmonary ventilation, by virtue of the changes in the coördination of the dual function of hemoglobin. Changes in acidity of the arterial and venous blood of the dog, resulting from mechanical asphyxia, were studied with the continuous method of recording acidity in the circulating blood and with the hydrogen and quinhydrone electrodes. On administering over-ventilation, sufficient to produce apnea, the duration of apnea, and the relation of blood acidity to the end of apnea, were noted. Mechanical asphyxiation, with the lungs filled with either room air or oxygen, permitted partial control of blood acidity and alveolar and blood carbon dioxide pressure.

In one experiment apnea lasted 65 seconds during mechanical asphyxia, with the lungs filled with room air, and 86 seconds with the lungs filled with oxygen. The increase in acidity of arterial blood was decidedly more rapid when the lungs were filled with oxygen, and pulmonary ventilation began at a greater hydrogen ion concentration. This agrees with the common finding of an inverse relation between pulmonary ventilation and acidity of the blood.

The difference in results, and the significance of these differences with the two types of asphyxia, were considered in relation to variations in the coördination of the dual function of hemoglobin, and the acidity of the respiratory center itself. The low acidity of the arterial blood at the close of apnea, with the lungs filled with room air, was related in part to a disturbance in the coördination of the dual function of hemoglobin, resulting in a probable increase in accumulation of acid in the respiratory center. A highly reduced blood heavily laden with acid, incapable of the normal liberation of oxygen and alkali at the tissues, returns to the lungs with a small increment of carbon dioxide. Failure in oxidation at the lungs leads to retention of carbon dioxide by the blood. A highly reduced and relatively alkaline hemoglobin is in equilibrium with a low alveolar carbon dioxide tension. During mechanical asphyxia, with the lungs filled with oxygen, a highly oxidized blood lightly laden with carbon dioxide, capable of great liberation of oxygen and alkali at the tissues, returns with a large increment of carbon dioxide. Subsequent high oxidation of the hemoglobin at the lungs efficiently expels carbon dioxide. A highly oxidized acid hemoglobin is in equilibrium with a high alveolar carbon dioxide tension.

The relatively greater alveolar and arterial carbon dioxide tension at the end of apnea agrees with the common finding of the inverse relation between pulmonary ventilation and the carbon dioxide tension of the arterial blood.

A relatively high acidity and high carbon dioxide tension of the arterial blood may be indicative of a relatively high efficiency of the transport of acid from the tissues and its liberation in the lungs.

The experiments support the view of the lack of correspondence between changes in acidity in the blood and in the tissues.

The results agree with the theory that the acidity of the respiratory center is important in the control of pulmonary ventilation. They are not in disagreement with a direct effect of oxygen on pulmonary ventilation by changes in the state of oxidation of the respiratory center.

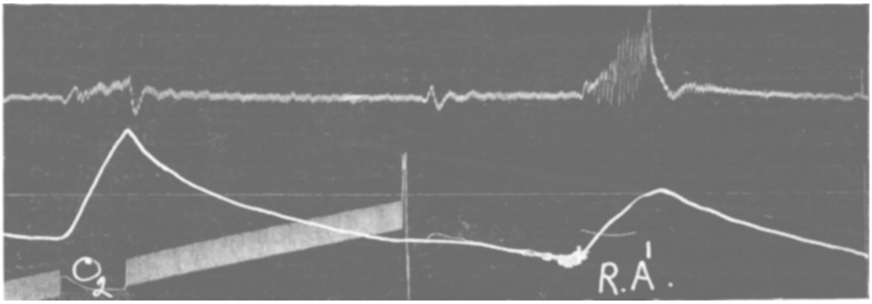

FIG. 1.

Record showing the effects of mechanical asphyxia during artificial ventilation on the acidity of the arterial blood and mean blood pressure. With the lungs filled with oxygen the increase in acidity of the blood is greater than in the second observation, in which the lungs were filled with room air. Note: the increase in mean blood pressure was considerably less.

3324

Tissue and Blood Acidity: Coördination of the Dual Function of Hemoglobin During Low Oxygen Administration.

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This paper deals primarily with effects of low alveolar oxygen on oxidation, and resulting changes in acid metabolism, coupled with the impairment of transport of acid and its elimination in the lungs.

Low oxygen mixtures (3 to 12 per cent) were administered by normal ventilation, which permits control of ventilation by the animal, and by artificial ventilation, which maintains a constant