Reports of Scientific Meetings

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Aspen Conference on Research in Emphysema

Presentations of the 14th annual conference, held June 9–12, 1971, in Aspen, Colorado, were devoted to the topic, “Acid–Base Blood Gas Transport and Regulation.” The scientific sessions were of great breadth, and presented many new concepts and diverse opinions. The meeting was of inestimable value in bringing together interested workers, who met both formally and informally. Fortunately, this conference will be the subject of a forthcoming Proceedings.

The first group of papers concerned acid–base regulation. Dr. Ralph Dell introduced the concept that during acute hypercarbia there is a loss of blood bicarbonate into the interstitial fluid, a loss which does not occur in vitro. A mathematical model which predicts changes in plasma bicarbonate and whole-blood base excess as functions of P_{CO_2} was presented. The model identified interstitial fluid volume, blood volume, hemoglobin concentration, and movement of bicarbonate from intracellular to extracellular fluid as being the major determinants of the final equilibrium concentration of bicarbonate and base excess. Dr. Ernest B. Brown also stressed the importance of differences between the in-vitro (approximately 10 sylkes *) and in-vivo (approximately 29 sylkes) buffer slopes. In addition, he pointed out that cardiac output may increase during acute hypercarbia, a hemodynamic change which will increase venous oxygen saturation. The change in venous bicarbonate concentration resulting from the Haldane effect will be shared with the entire extracellular fluid compartment, and therefore venous values should be used to construct the in-vivo nomogram. However, in experiments designed to test this hypothesis, differences between arterial and venous slopes over a wide range of changes in carbon dioxide tension were neither statistically significant nor of a degree to be of practical importance in evaluating acid–base disturbances. It is popular with some writers to express acid–base status in terms of hydrogen ion concentration rather than pH. Dr. Robert Davis presented his “Gibbsian” view, which states that the idea of discarding pH in favor of hydrogen ion “concentration” is without justification. A substance contributes to the free energy of a system in proportion to its chemical potential; this is a logarithmic function of the activity of the substance. Since pH has a logarithmic relationship to hydrogen activity, it is the best statistical variable for describing the mean free energy contributed by hydrogen ions to a physiologic system.

The next session dealt with oxygen transport and was opened by Dr. Clement A. Finch. His discussion pertained to various responses which collectively provide an integrated defense against hypoxia. Vasodilatation occurring in tissues with an inadequate oxygen supply results in redistribution of blood, while increased amounts of erythrocyte 2,3-diphosphoglycerate (2,3-DPG) decrease erythrocytic oxygen affinity. The latter response facilitates oxygen delivery and occurs with decreased hemoglobin concentration, arterial oxygen saturation and cardiac output, and an increased concentration of reduced hemoglobin in venous blood. These two mechanisms act promptly with little expense of energy. A more sluggish response is the elevated hemoglobin concentration which is mediated by erythropoietin. Cardiac output will also increase, but does not appear to respond until other compensatory mechanisms have failed. Mechanisms for increased 2,3-DPG formation during hypoxia were discussed by Dr. G. J. Brewer, who proposed that the significant regulatory factor is the rate of glycolysis. This is controlled by phosphofructokinase activity (activation of phosphofructokinase indicates increased intra-

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cellular pH). Blood obtained from hypoxic patients has decreased concentrations of glucose-6-phosphate and fructose-6-phosphate, while the fructose-1,6-diphosphate concentration is increased, findings which indicate activation of phosphofructokinase. Thus, alkalosis resulting from hypoxia-induced hyperventilation activates phosphofructokinase which, in turn, leads to enhanced glycolysis and an increased erythrocytic concentration of 2,3-DPG. The resulting decreased erythrocytic oxygen affinity aids in oxygen unloading to tissues, which compensates for hypoxia. The question whether decreased erythrocytic oxygen affinity is always advantageous was discussed by Dr. Natalio Banchero, who compared oxygen transport in a llama (P20 = 23 torr) and in a sheep (P20 = 41 torr). Although the low oxygen affinity found in the sheep might facilitate oxygen release to tissue, it also hinders oxygen uptake in the lung. The net result depends on the degree of hypoxia, which determines where one is operating on the hemoglobin-dissociation curve. Thus, when the sheep and llama were compared at a barometric pressure of 335 torr, the sheep were cyanotic, hyperventilated markedly, and often appeared to be unconscious for brief periods. The llamas tolerated chronic hypoxia well while operating in the middle steep portion of the hemoglobin-dissociation curve and showed no signs of discomfort. Anemia might be expected to have profound effects on oxygen transport which necessitate activation of compensatory mechanisms. Dr. Gerd Cropp reported that erythrocyte 2,3-DPG is elevated within minutes after the oxygen-carrying capacity of blood is lowered in the dog. When the anemia is mild, adequate oxygen delivery is maintained without increased cardiac output. In severe anemia, the requirements for increased cardiac output are lessened by the rightward shift of the hemoglobin-dissociation curve resulting from increased 2,3-DPG concentrations.

A number of papers examined oxygen transport at an organ level. Dr. James Metcalfe reported that blood flow, arterial oxygen content, tissue oxygen consumption, and blood oxygen affinity are so regulated in resting mammals that mixed venous oxygen tension is maintained at approximately 35 torr. Dr. Peter Cohen briefly discussed factors regulating cerebral blood flow, which include PaO2, PaCO2, blood pressure, temperature, age, and state of cerebral function. He indicated that hyper-ventilation may compromise cerebral perfusion in man when PaO2 is less than 20 torr; the resulting decrease in oxygen delivery could be overcome when the subjects breathed oxygen under hyperbaric conditions. Dr. Harry Wallman indicated that hypocarbia could not elicit maximal cerebral vasoconstriction, since developing tissue hypoxia and lactate acid accumulation counteracted vasoconstriction. He presented additional data suggesting that cerebral oxygen requirements might decrease during anesthesia, while cerebral blood flow usually increased as anesthesia was deepened. As a result, the ratio of cerebral blood flow to cerebral oxygen uptake rose as the concentration of anesthesia was increased. In a most provocative paper, Dr. G. H. Gurtner demonstrated that under conditions of little or no gas exchange, the partial pressure of carbon dioxide is higher in the alveolar gas than in mixed venous blood. This is explained by a rapid movement of hydrogen ions from blood buffer toward a negatively-charged capillary wall, with a slower repulsion of bicarbonate away from the wall, resulting in transient production of carbon dioxide near the wall. The alveolar capillary membrane and alveolus are then in equilibrium with the higher carbon dioxide tension near the wall rather than with the bulk capillary carbon dioxide tension. There are important implications of this finding in terms of the distribution of weak acids and bases between cerebrospinal fluid and blood.

Several exciting papers were presented in a session devoted to regulation of ventilation. Dr. A. Guz proposed the concept that the tachypnea and breathlessness which exist in certain clinical conditions not necessarily associated with hypoxia may be mediated by afferent vagal stimulation. Thus, the tachypnea of chemical pneumonitis may be relieved with vagal block. Although vagal block has no effect in normal man, the results of vagal stimulation may be demonstrated during administration of carbon dioxide. As ventilation is stimulated by hypercarbia, tidal volume increases to a point where the Hering-Breuer reflex becomes important. At this stage, vagal block results in an increased tidal volume and
decreased respiratory frequency. Dr. Guz also presented data showing that phrenic block in man increases the breath-holding time, but has no effect on the ventilatory response to carbon dioxide. The conclusion is that although peripheral and central chemoreceptors have a significant role in mediating pulmonary ventilation, information concerning ventilatory movement fed back to the central nervous system via cavity-volume changes transduced by chest wall and diaphragm proprioceptors and lung-volume changes sensed by pulmonary stretch receptors must also be considered in the overall picture of ventilatory regulation. The effects of exercise on ventilation were discussed by Dr. John B. Weil, who demonstrated that very mild exercise is capable of producing substantial increases in hypoxic and hypercapnic ventilatory drives. The effect is not attenuated by beta-adrenergic blockade and may be mediated by alpha-sympathetic activity. In the conditioned athlete, reduction of both hypoxic and hypercapnic drives is significant and is closely related to this level of physical fitness as measured by maximum oxygen uptake. Dr. Weil also studied the attenuation of hypoxic drive resulting from chronic hypoxia. He examined subjects who came to live at high altitudes in the third and fourth decades of life and found that both hypoxic and hypercapnic ventilatory drives were depressed in relation to the time spent at high altitude. Subjects spending 25 years or longer at high altitudes had values resembling findings in high-altitude natives.

In a session examining regulation of tissue utilization of oxygen, Dr. Norman H. Edelman examined the effects of decreased oxygen delivery (expressed as the product of arterial oxygen content and organ blood flow) on oxygen utilization in the brain and muscle. Muscle oxygen consumption began to decrease when arterial oxygen was 40 torr, while cerebral oxygen utilization was not affected until oxygen tension was less than 25 torr. On the other hand, while systemic hypoxia was accompanied by increased cerebral blood flow, little change in muscle blood flow was observed. When both flow and oxygen content were considered, it was observed that oxygen consumption decreased as a single function of oxygen delivery in both muscle and brain. The dependence of oxygen consumption upon oxygen delivery was further confirmed in hypoperfusion studies in which oxygen consumption decreased progressively with flow when flow to each tissue was reduced below 50-90 per cent of control values. The possibility that cerebral oxygen extraction is more efficient during hypoxia was suggested by the observation that cerebral venous oxygen tension could be reduced to only 10-15 torr during hypoperfusion, whereas during systemic hypoxia it could be lowered to 3 torr.

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