BRIEFS FROM THE LITERATURE

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Briefs were submitted by Drs. Gerald Allen, C. M. Ballinger, Lee S. Binder, John P. Bunker, M. T. Clarke, J. E. Eckenhoff, Martin Helrich, S. J. Martin, R. E. Ponath, William Rabenn, Alan D. Randall, Lawrence Reichmann, and H. S. Rottenstein. Briefs appearing elsewhere in this issue are a part of this column.

CARBON DIOXIDE Fifteen young mongrel dogs were lightly anesthetized either with pentobarbitone sodium or with one of the inhalants (ether, halothane or cyclopropane). Increasing concentrations of carbon dioxide were then added to the gas mixture in steps of five per cent every five minutes to a maximum of 75 per cent.

The various inhalants differed in the degree to which they reduced the stimulatory effect of carbon dioxide on minute volume. The reduction among the inhalants was most marked with ether and least marked with cyclopropane. Pentobarbitone caused even less reduction. The peak stimulatory response to ventilation was reached when carbon dioxide concentration was about 25 per cent. The increase in minute volume was achieved in some dogs principally by an increase in rate, in others by an increase in tidal volume. A further marked increase in minute volume occurred, if the inhalant was withdrawn at a carbon dioxide concentration of about 20 to 25 per cent. The stimulating effect of carbon dioxide then gradually decreased. At a concentration of about 40 per cent respiratory arrest supervened. If artificial ventilation was then maintained, while the carbon dioxide concentration was further increased, spontaneous respiration then recommenced, usually at a carbon dioxide concentration of 60 to 70 per cent, and at a minute volume which approximated control values. At this stage ("supercarbia") arterial and venous pressures, heart rate and rhythm, and respiratory minute volume remained essentially constant for more than an hour. Cutting of the vagi during this stage in three dogs produced the typical slowing and deepening of respiration.

Slow decrease in the carbon dioxide concentration to complete elimination led to the re-establishment of a normal respiratory pattern, after a short period of stimulation when the carbon dioxide concentration was reduced below 30 per cent (mirror-image of the respiratory response at the onset, when the carbon dioxide had been increased). (*Graham, G. R., Hill, D. W., and Nunn, J. F.: The Effect of High Carbon Dioxide Concentration on Respiration and Circulation, Der Anaesthesist 9: 70 (Feb.) 1960.*)

CARBON DIOXIDE A new carbon dioxide electrode separated from the blood or tissue by a membrane permeable only to carbon dioxide can be calibrated directly to read P_{CO_2}. P_{CO_2} on the surface of the brain in dogs was found to be about 55 mm. Hg. Liver and gut mucosa have high P_{CO_2} (about 80 mm. Hg). The rate of rise of arterial P_{CO_2} during apnea was studied in seven patients and found to average 4 mm. per minute after the initial rise from arterial to mixed venous level. The prominent effects of carbon dioxide on the circulation are three. The myocardium is depressed by high carbon dioxide concentrations and this depression may be partially reversed by adrenalin or noradrenalin, acetylstrophanthidin, or by buffering the *p*H to normal levels. Secondly, high concentrations of carbon dioxide cause direct vasodilitation of smooth muscle. Thirdly, the sympathetic nervous system is stimulated partly mediated through peripheral chemoreceptors, in part directly through the adrenal medulla, and in part through the central nervous system. Increased carbon dioxide also increases the irritability of the ventricle. Withdrawal from high carbon dioxide concentrations usually produces hypotension, which may be a complication in post-

anesthetic periods. Ventilation of one area of the lung decreases if the carbon dioxide concentration in that area is allowed to decrease by occluding its pulmonary blood supply. This may be a homeostatic mechanism to control the distribution of ventilation to those areas of the lung where blood flow is going. The cerebral blood flow is regulated, in part, by the carbon dioxide concentration in arterial blood. Inspiration of seven per cent carbon dioxide doubles the cerebral blood flow and hyperventilation may reduce the cerebral blood flow to 60 per cent of normal. The symptoms of hyperventilation are in part due to hypoxia of the brain, resulting from cerebral vasoconstriction. Carbon dioxide inhalation causes hyperpnea by an elevation of the P_{CO_2} in the respiratory center.

The electrotlyte composition of the cerebral spinal fluid in the fourth ventricle plays a role in the control of respiration, slightly acid solutions stimulating and slightly alkaline solutions depressing ventilation. Carbon dioxide present in the brain contributes to the narcosis produced by nitrous oxide inhalation. The average nitrous oxide concentration required to produce loss of consciousness varied from 30 to 60 per cent when alveolar carbon dioxide was varied downward from nine to three per cent. *(Severinghaus, J.: Carbon Dioxide Tension and Perfusion in Tissue, Der Anaesthesist 9: 50 (Feb.) 1960.)*

CARBON DIOXIDE Experiments are shown which demonstrate the respiratory driving action of hydrogen ions in cerebrospinal fluid. A specific action of carbon dioxide at this location can be excluded. The action of cerebrospinal fluid hydrogen ions is not direct effect on centers but an influence on intracranial efferents to the centers. It can be eliminated by procaine introduced into the cerebrospinal fluid. *(Loeschcke, H. H.: Relationship Between Carbon Dioxide and Respiration, Der Anaesthesist 9: 38 (Feb.) 1960.)*

CARBON DIOXIDE Adjustments of body stores of carbon dioxide were studied during voluntary hyperventilation for one hour at a constant rate by trained subjects. Carbon dioxide was eliminated at an average of 161 ml. per mm. Hg decrease in mixed venous tension. Increasing the respiratory minute volume by about 50 per cent for one hour resulted in elimination of 1.5 to 2.5 liters of carbon dioxide in excess of the metabolic production. *(Vance, J. W., and Fowler, W. S.: Adjustment of Stores of Carbon Dioxide during Voluntary Hyperventilation, Dis. Chest. 37: 304 (March) 1960.)*

HYPERCAPNIA Progesterone is capable of lowering the arterial P_{CO_2} in patients with emphysema and hypercapnia. This hormone will aslo lower the alveolar P_{CO_2} in normal subjects. If one assumes that the action of progesterone causes a small but definite degree of hyperventilation, then it is of interest that this increase in ventilation is sufficient to cause a fall in arterial P_{CO_2} in patients with severe obstructive diseases and hypercapnia. Voluntary hyperventilation is incapable of lowering the arterial P_{CO_2} in patients with emphysema. The effect of progesterone on ventilation is not solely the effect of progestational activity. The ethinyl group inactivates the respiratory effects seen with progesterone itself and alterations of the molecular structure at other sites can abolish the effect. Conclusions on the mode of action of progesterone are not possible from this study. It lowers the arterial P_{CO_2} without altering the ventilatory response to carbon dioxide. Other areas of the brain, possibly the hypothalamus, may represents the site of action. *(Tyler, J. M.: The Effect of Progesterone on the Respiration of Patients with Emphysema and Hypercapnia, J. Clin. Invest. 39: 34 (Jan.) 1960.)*

HYPERCAPNIC ACIDOSIS Experiments were designed to investigate the effects of tris-hydroxymethyl-amino methane (T.H.A.M.) on hypercapnic acidosis in dogs. High degrees of hypercapnic acidosis were induced in the animals using the technique of earlier diffusion respiration experiments. Treated dogs were administered .34 mM. of T.H.A.M./kg./min. during a 60-minute period of apneic oxygenation. In the untreated dog, the *p*H decreased from 7.41 to 6.45; arterial P_{CO_2} increased from 38 to 346 mm. Hg; arterial oxygen saturation dropped from 100 to 54 per cent; total catecholamines increased from 1 to 44 micrograms per liter. In the dogs