Anesthesiology
V 35, No 4, Oct 1971

# Literature Briefs

Myron B. Laver, M.D., Editor

*Literature Briefs were submitted by Drs. G. Battit, T. Caldwell, R. Clark, B. Geffin, M. Gold, M. Laver, E. Lowenstein, H. Pontoppidan, and S. Schnider. Briefs appearing elsewhere in this issue are part of this column.*

## CNS Function

**CSF IN DIABETIC KETOACIDOSIS** Cerebrospinal fluid and blood were studied in six patients with ketoacidosis before and four to nine hours after treatment, at the time neurologic improvement began. No alkali was included in the treatment regimen. Initial spinal fluid *p*H was normal or elevated in every patient, and decreased with treatment in four patients. Osmolality was significantly higher in cerebrospinal fluid than in blood before treatment; lactate was above normal initially and did not change with treatment. The concentrations of keto acids and glucose initially were lower in CSF than in blood and decreased with treatment at a rate consistent with slow equilibration. The authors speculate that administration of bicarbonate would aggravate the spinal-fluid acidosis that occurs with treatment, and could interfere with clinical improvement. They consider the increased osmolality before therapy to be a reason for caution against the excessively rapid correction of blood hyperosmolality. (*Ohman, John L., and others: The Cerebrospinal Fluid in Diabetic Ketoacidosis, NEJM 284: 283–290, 1971.*) ABSTRACTER'S COMMENT: Another situation in which correction of blood *p*H appears to be contraindicated.

## Circulation

**HYPOXIA AND CEREBRAL AUTOREGULATION** "Cerebral autoregulation" used to describe two phenomena: 1) the capacity to maintain constant blood flow during changes in arterial perfusion pressure; 2) local adjustments in blood flow in response to tissue metabolic needs. Although losses of autoregulation in hypoxia and hypercapnia have been described, recent studies have demonstrated preservation of autoregulation in response to pressure in brain areas affected by severe ischemia.

The inhalation of 6 per cent $O_2$–$N_2$ served as the hypoxic stimulus in 18 dogs. Cerebral blood flow (CBF) was measured while $Pa_{CO_2}$ was controlled by artificial ventilation. Cerebral arterial perfusion pressure was altered by three mechanisms: 1) pharmacologically, with intravenous Neo-synephrine; 2) by increasing intracranial pressure; 3) by hemorrhage and retransfusion of the animal's blood. The results indicated that autoregulation was not lost until $Pa_{CO_2}$ had been below 25 torr for 4–6 min. Autoregulation was maintained even after hypoxia had produced an increase in CBF and decreased cortical *p*H. This suggests that loss of autoregulation does not occur secondary to parenchymal acidosis or maximal vasodilatation. In response to increased arterial perfusion pressure autoregulation occurred after a transient increase in CBF, whereas autoregulation in response to reduced perfusion pressure appeared instantaneously, without an initial drop in CBF. (*Kogure, K., and others: Effects of Hypoxia on Cerebral Autoregulation, Amer. J. Physiol. 219: 1393 (Nov.) 1970.*)

## Renal Function

**CARBON DIOXIDE AND RENAL BLOOD FLOW** This study was done in dogs under conditions of varying $Pa_{CO_2}$ produced by either diffusion respiration or ventilation with high concentrations of $CO_2$. Other investigators who have studied the effect of $Pa_{CO_2}$ on renal blood flow have not controlled $Pa_{CO_2}$ precisely in a range such as might be expected in living subjects. In general, the results have been confusing, some providing little evidence of renal vasoconstriction in hypercapnia, and others indicating that reduction in renal perfusion is part of a generalized vasoconstrictor response. The present study has attempted to resolve this problem.

The effect of $CO_2$ on renal perfusion was studied using a direct cannulation technique to measure renal blood flow. $Pa_{CO_2}$ was varied from 20 to 120 torr. Measurements were made with $Pa_{CO_2}$ maintained within narrow ranges. Renal vascular resistance, oxygen consumption, and filtration fraction were measured, as was creatinine and p-aminohippurate clearance, while excretion of sodium and potassium was monitored. No real change in renal perfusion occurred until $Pa_{CO_2}$ exceeded 70 torr. A further increase in $Pa_{CO_2}$ was associated with a progressive decrease in renal blood flow, accompanied by similar decreases in glomerular filtration rate, renal plasma flow, and electrolyte excretion. The depressed perfusion which resulted from hypercapnia was preventable by mannitol infusion and by renal nerve blockade. The authors suggest that $CO_2$ has no direct effect on the intrarenal vasculature, and that the vasoconstrictor effect of hypercapnia is secondary to the interaction between $CO_2$ and the sympathoadrenal system. (*Norman, J. N., and others: Effect of Carbon Dioxide on Renal Blood Flow, Amer. J. Physiol. 219: 672 (Sept.) 1970.*)

## Respiration

**2,3-DPG, *p*H AND HEMOGLOBIN–OXYGEN AFFINITY** The influence of *p*H on hemoglobin affinity for oxygen (Bohr effect) is well known. On the other hand, we know now that an intermediate of glucose metabolism, 2,3-diphosphoglyceric acid (2,3-DPG) is present in high concentration in erythrocytes, and has been shown to reduce the affinity of hemoglobin for oxygen. In 1942, Guest showed that diabetic acidosis was associated with low erythrocyte 2,3-DPG. A reduction of the concentration of 2,3-DPG leads to a higher affinity of hemoglobin for oxygen, whereas the decrease in *p*H, mediated through the Bohr effect, leads to a shift of the dissociation curve to the right. The purpose of the present study was to investigate the adaptive response to systemic acidosis or alkalosis of oxyhemoglobin dissociation in normal man and to delineate mechanisms involved in this regulation.

Acidosis was induced acutely in four healthy volunteers with intravenous acetazolamide given in a one-week period. The acidosis was then rapidly corrected and alkalosis induced with sodium bicarbonate injected intravenously. Control values for hemoglobin–oxygen affinity, erythrocyte acid-soluble organic phosphates, plasma and erythrocyte *p*H, blood gases, plasma electrolytes, and hemoglobin were determined, and hematocrit readings were made. Serial values were obtained during acidosis and alkalosis. Arterial blood was obtained for all measurements.

Acute changes in plasma *p*H produced no alteration in erythrocyte 2,3-DPG content, but there were changes in hemoglobin–oxygen affinity, and these correlated with changes in mean corpuscular hemoglobin concentration (MCHC). When acidosis or alkalosis was maintained (usually for four hours) erythrocyte 2,3-DPG content was affected and correlated with the change in hemoglobin–oxygen affinity. An increase in *p*H was countered by an increase in 2,3-DPG; conversely, a decrease in *p*H was associated with diminution of erythrocytic 2,3-DPG. Provided the rate of *p*H change is not too rapid or too great, 2,3-DPG changes counteract the *p*H effect and hemoglobin-oxygen affinity *in vivo* remains unchanged. Approximately 35 per cent of the change in hemoglobin–oxygen affinity which occurs from alteration in erythrocytic 2,3-DPG, can be explained by the effect of 2,3-DPG on erythrocyte *p*H. (*Bellingham, A. J., Detter, J. C., and Lenfant, C.: Regulatory Mechanisms of Hemoglobin Oxygen Affinity in Acidosis and Alkalosis, J. Clin. Invest. 50: 700 (March) 1971.*)

## Endocrine Function

**THYROID ACTIVITY AND CATECHOLAMINE SENSITIVITY** This paper reviews the state of our knowledge of thyroid hormone and its relationship to the action of catecholamines. According to the author, studies of the circulatory effects of hyperthyroidism in relation to catecholamine hypersensitivity published prior to 1960 are inconclusive, because they failed to utilize dose–response curves or their data were insufficient for statistical analysis.

Subsequent studies (1965–1967) found no difference between the responses of hyperthy-