BRIEFS FROM THE LITERATURE

JOHN W. PENDER, M.D., *Editor*

Briefs were submitted by Drs. C. M. Ballinger, Lee S. Binder, John P. Bunker, T. H. Cannard, M. T. Clarke, Cody Eames, J. E. Eckenhoff, Martin Helrich, J. R. Householder, S. J. Martin, Alan D. Randall, R. W. Ridley and H. S. Rottenstein.

CEREBRAL BLOOD FLOW Cerebral perfusion is controlled by regulation of perfusion pressure and by cerebral vascular resistance. Until recently, it was believed that cerebral vessels did not possess significant capacity for intrinsic control of vascular tone so that perfusion passively followed changes in arterial blood pressure. Recent quantitative studies in man have demonstrated that—within a wide pressure range—cerebral blood flow is independent of changes in arterial blood pressure. Only in marked hypotension is cerebral vasodilatation inadequate; and when cerebral blood flow falls to about 60 per cent of the control value, clinical signs of cerebral hypoxia become evident. Vascular reactivity to pressure changes appears to be unaffected by sectioning the vagus, cervical sympathetics, sinus and aortic nerves, or to local application of sympathomimetic drugs. Thus active regulation of cerebral vascular tone to pressure change may be a kind of autoregulation, possibly due to a direct effect of pressure change on vascular smooth muscle. Another impeding factor is local vasomotor activity of intracranial vessels. This activity is influenced largely by chemical or humoral factors. Carbon dioxide causes pronounced cerebral vasodilatation. Inhalation of 5 per cent carbon dioxide increases cerebral perfusion by about 50 per cent while 7 per cent carbon dioxide causes an increase of about 100 per cent. Conversely, hypocapnia produced by marked hyperventilation decreases blood flow to about 60 per cent of normal. This is the same low critical level as was found associated with clinical signs of cerebral hypoxia in severe hypotension. Although it is generally believed that the partial pressure of carbon dioxide is the important variable, no clear cut data are available to distinguish the action of carbon dioxide tension from that of associated changes in bicarbonate. Inhalation of air mixtures of low oxygen tension causes dilatation whereas oxygen tensions at 3 to 4 atmospheres cause a moderate vasoconstriction. Thus oxygen seems especially important in the homeostatic regulation of cerebral perfusion in the face of severe anoxia. Consciousness is lost when the oxygen tension of cerebral venous blood reaches 15–20 millimeters of mercury, and at this level, abnormal cortical electrical activity also starts abruptly. The same critical level of cerebral venous oxygen has been found to limit the vasoconstriction of hypocapnia in animal experiments. The effect of *p*H and of nervous influences is not clear. The influence on cerebral blood flow and oxygen uptake of physiological variables such as exercise, apprehension and sleep, pathologic variables such as coma, hypertensive encephalopathy and cerebral arteriosclerosis, and drugs such as depressants, convulsants and hormones is analyzed. Drugs which cause a depression of consciousness, *e.g.*, barbiturates, all cause a reduction in cerebral oxygen uptake proportional to the degree of cerebral depression. Surgical anesthesia reduces cerebral oxygen uptake by about 40–50 per cent. (*Lassen, N. A.: Cerebral Blood Flow and Oxygen Consumption in Man, Physiol. Rev. 39: 183 (April) 1959.*)

CEREBRAL CIRCULATION Carbon dioxide is a more powerful cerebral vasodilator and can produce greater increases in cerebral blood flow than any other chemical agent yet studied. Thiopental anesthesia and old age tend to lessen this effect. Therapeutic effects of carbon dioxide rebreathing, particularly in presence of hypoxemia, are discussed. The effects of most general anesthetic agents with the exception of ether, which has a specific vaso-

dilator effect on the cerebral vessels, are probably chiefly secondary to their effects on blood pressure, cerebral metabolic rate, and respiratory gas tensions in the blood. Similarly, the effect of morphine in increasing cerebral blood flow (and hence elevating CSF pressure) is mediated by hypoxia and carbon dioxide retention secondary to respiratory depression. Homeostatic mechanisms for protection of cerebral blood flow and their modification by drugs are discussed. (*Sokoloff, L.: The Action of Drugs on the Cerebral Circulation, Pharm. Rev. 11: 1 (March) 1959.*)

CUTANEOUS CIRCULATION The controls acting on cutaneous circulation are adjusted primarily toward regulation of body temperature. Other reactions are due to direct sensitivity of cutaneous vessels to temperature and to vasoactive substances in a similar fashion as other vessels, or on the availability of their innervation to excitation by other than thermal stimuli. Thermal conductance and total cutaneous blood flow increase very little until the ambient temperature has risen to 28 C. Above 28 C. thermal conductance and cutaneous blood flow increase almost linearly with temperature. The dominant arteriomotor innervation appears to be arteriodilator. Vasodilatation of the hands (and feet), however, begins at an ambient temperature of 22 C. and is about one-third complete at 28 C. This is adjusted chiefly by variations in the activity of the arterio-constrictor innervation. The cutaneous venomotor innervation can greatly alter the blood capacity of the skin. Adjustments in cutaneous venomotor tone may be an important compensation for deficits in circulating blood volume. Since the cutaneous venous system is distended early in response to heat, mobilization of blood contained in the skin would be favored by cool surroundings. Sympathetic denervation probably exerts its principle vascular effect in the skin only on the veins and on palmar and plantar blood flow. (*Hertzmann, A. B.: Vasomotor Regulation of Cutaneous Circulation, Physiol. Rev. 39: 280 (April) 1959.*)

PULMONARY CIRCULATION The effect of hemorrhage to the extent of one-third of the estimated blood volume was studied in dogs anesthetized with pentobarbital. Reduction in blood flow resulted in continuous decline in systemic arterial blood pressure. Pulmonary arterial blood pressure, however, stabilized after an initial decline, dropping only slightly thereafter. Respiratory dead space increased following hemorrhage. This was accompanied by the appearance of a marked carbon dioxide tension gradient between the arterial blood and the end-tidal gas, indicating development of a significant "alveolar" dead space. Restoration of blood volume resulted in a rise in pulmonary blood pressure which was initially above the control level. The respiratory dead space decreased toward its control volume and the carbon dioxide tension gradient was reduced. With intermittent positive pressure ventilation, reduction of pulmonary blood flow may lead to complete closure of portions of the pulmonary bed. Following restoration of blood flow, there is some delay before these vessels again reopen. (*Gerst, P. H., Rattenborg, C., and Holaday, D. A.: The Effects of Hemorrhage on Pulmonary Circulation and Respiratory Gas Exchange, J. Clin. Invest. 38: 524 (March) 1959.*)

PULMONARY HYPERTENSION The pulmonary vascular bed is a complex system with fluctuating pressure and flow. Alterations in cardiac rate and stroke volume, changes in intrathoracic pressure associated with respiration and possible alterations in resistance to air flow all may affect the pressure-flow ratio across the pulmonary vascular bed without active changes in the caliber of the pulmonary vessels. Pulmonary vessels are constricted by serotonin, and the increase in pulmonary artery pressure seen with hypoxia may be due to a direct affect of lowered oxygen tension on the smooth muscle fibers. In patients with pulmonary hypertension associated with congenital heart disease, breathing mixtures low in oxygen increases the resistance while breathing oxygen decreases it. Also pulmonary hypertension is reduced when acetylcholine is injected into the pulmonary artery. An even greater reduction occurs when oxygen and acetylcholine are used simultaneously. Tone in pulmonary vessels has been demonstrated in every condition in which pulmonary hypertension occurs. The manner in which this tone is maintained is unknown. (*Shepherd, J., and*