The human brain uses the same amount of oxygen per minute at an inspired Po_2 of 2000 mmHg (oxygen breathing at 3.5 ata) as in air breathing at sea level (156 mmHg inspired Po_2) (Fig. 6) [10]. Failure of brain oxygen metabolism begins when mean brain capillary oxygen tension falls below about 50 mmHg [22]. Above this level, metabolism is remarkably unaffected by even massive increases in arterial or mean brain oxygen pressure. It is assumed that if an exposure to high oxygen pressure is prolonged to the degree that extreme oxygen poisoning occurs, brain and other tissue oxygen metabolism will be found to be decreased by the disruptive, toxic effect of hyperoxygenation.

C. Hyperoxygenation and Respiratory Control Functions

The suppression of carotid and aortic body impulse generation by hyperoxia leads to the well-known fall in ventilation induced by oxygenation in certain hypoxic and narcotized states. Hyperoxygenation—as by oxygen administration at pressure of 1 or several atm—induces two other, less prominent physiologic effects on respiratory control mechanisms. One is distinguishable from the rapidly expressed decrease in chemoreflex influence and appears to be a suppression of central mechanisms of respiratory control, leading to a decreased respiratory reactivity to carbon dioxide (Fig. 7) [23-25]. The other, generated by the diminished hemoglobin reduction in the presence of large supply of oxygen in physical solution, derives from the previously described failure of base release by hemoglobin in the tissue capillary and consequent rise in carbon dioxide pressure (and $[H^+]$) in the central tissues [5,10]. These three different effects on respiratory control are concurrent in stable states of hyperoxygenation. It is to be expected that while the composite influence of oxygen is respiratory stimulation in normal individuals, as it is in environmental hypoxia (Fig. 8a and 8b) [24], the effect of hyperoxygenation in narcotized or otherwise depressed and hypoxic patients will be gross depression of respiration with rise in carbon dioxide tension in arterial blood as well as in brain tissue.

D. Cardiovascular Effects of Hyperoxygenation

Oxygen pressures above normal have been found to induce vasoconstrictor effects in many organs studied, including brain and eye, kidney, heart, and general systemic circulation. Specialized vascular tissue, represented by the ductus arteriosus, prominently contracts on exposure to oxygen even at oxygen pressures less than 1 ata [26], and this contraction is probably an important mechanism in normal closure of the ductus and of the umbilical vessels.

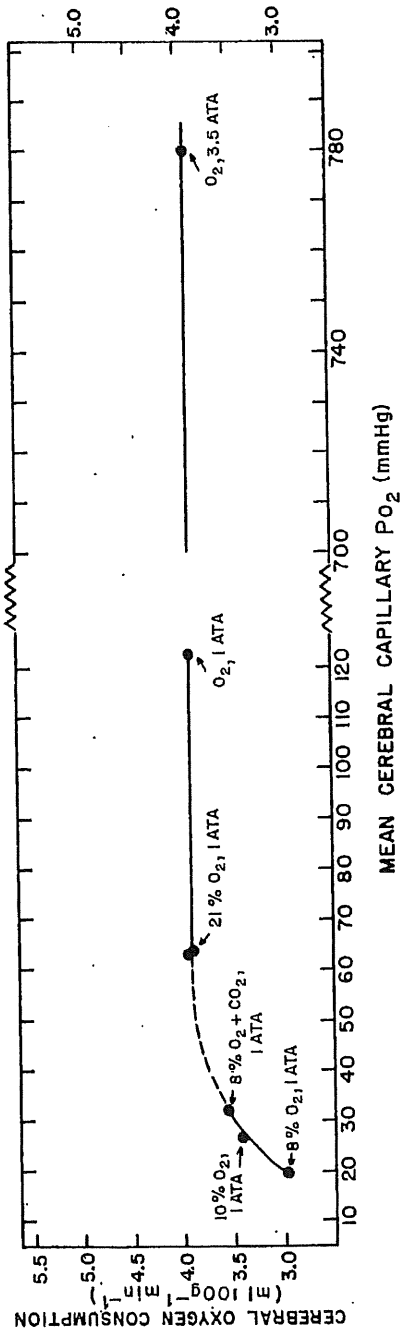

FIGURE 6　Relations between cerebral oxygen consumption ($CMRO_2$) and mean cerebral capillary P_{O_2}. The rate at which brain oxygen is used declines as mean brain capillary P_{O_2} is lowered, and this decline becomes rapid below about 40 mmHg. The dashed portion of the curve points out that no information is yet available to indicate the level of P_{O_2} at which decline in $CMRO_2$ begins. Oxygen breathing does not alter $CMRO_2$, even to 3.5 ata inspired P_{O_2}. The observation that mean brain capillary P_{O_2} during pure oxygen breathing is only about 120 mmHg despite nearly 600 mmHg arterial P_{O_2} and 780 mmHg despite an arterial P_{O_2} greater than 2000 mmHg [10,11] shows the importance of considering the rate of blood flow through a tissue in attempts to improve tissue oxygenation. When the hypocapnia normally accompanying 8% oxygen is prevented by artificially maintaining normal arterial P_{CO_2}, mean brain capillary P_{O_2} is maintained by the higher blood flow above the P_{O_2} associated with 10% oxygen breathing. Preventing hypocapnia during anoxemia thus minimizes anoxic depression of brain metabolism [21]. Mean cerebral capillary P_{O_2} is estimated by integration from values for arterial and internal jugular venous oxygen content, capacity, and tension.

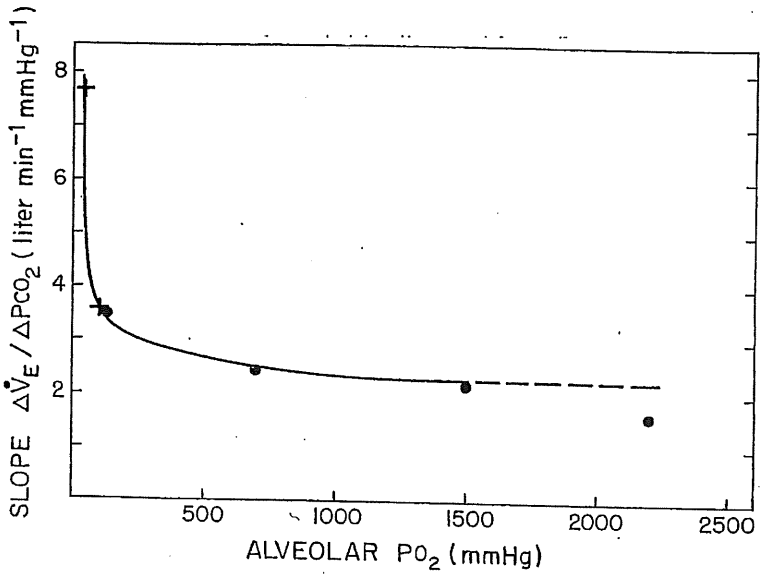

FIGURE 7 Depression of respiratory reactivity to carbon dioxide at increased inspired PO_2. The well-known increase in "sensitivity" to CO_2 in hypoxia [25] is shown as +, along with progressive decrease of reactivity as inspired oxygen pressure is raised to 1, 2, and 3 ata. The depression is greater than what can be accounted for by suppression of peripheral chemoreceptor discharge [5,24].

In spite of what appears to be a specific vasoconstrictor influence of oxygen on the ductus arteriosus, the vascular constriction in other structures is evidently based on more than a direct influence of oxygen itself on the contractile process in smooth muscle. The influences of hyperoxia on vessels of the brain will be emphasized here, because appropriate investigation has been carried out in man, and because the interplay of mechanisms involved can help in appraising oxygen effects in other vascular beds.

Brain Circulation

In the human brain, the vessels dilate in prominent hypoxia, most likely through loss of smooth muscle capacity to sustain contractile tone, and in passive response to the blood pressure within them. Except in severe hypoxemia, this vascular bed appears to be almost entirely controlled by the level of carbon dioxide in arterial blood entering the bed [24,27]. Restoring the normal oxygenation of the vessels restores tone and normal contractile state. However, imposing even several atmospheres of increased arterial PO_2 further contracts brain vessels only if concurrent fall in arterial carbon dioxide pressure occurs [5,24,28].