Cerebral Blood Flow and Cerebral Oxygen Consumption During Hypothermia

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Currently there is widespread interest in the physiologic effects of cold, and in the use of hypothermia with surgery (1, 2). Although no gross neurologic derangements have been observed following the application of this technique in man and experimental animals (3, 4), it seemed appropriate that a special study be made of the effects of hypothermia on cerebral physiology. Cerebral blood flow, cerebral oxygen consumption, cerebral vascular resistance, as well as systemic blood pressure and pulse rate were investigated.

METHODS

Nineteen mongrel dogs, weighing between 8.5 and 12.9 kg and unselected as to age and sex, were used in this investigation.

Cerebral Blood Flow. The nitrous oxide and dye dilution techniques for measuring cerebral blood flow (5) were considered not applicable to this study because they do not allow the continuous observation of changes in flow; and they require the taking of numerous blood samples which would distort the blood volume so as to invalidate the results of the experiment. Accordingly, we adopted a direct method in which the arterial blood flow to the brain was isolated and measured by a continuously indicating magnetic rotometer (6).

The common carotid arteries were mobilized bilaterally and all branches except the internal carotid arteries were ligated and divided. The eyes were enucleated and the anastomotic, ophthalmic, and ethmoidal arteries were coagulated (7). The vertebral arteries were ligated at their origin and exposed up to their entrance into the sixth cervical vertebra. Cannulae in the carotids directed flow from the heart into the rotometer, from whence it was distributed to the brain through cannulae placed cephalad in both carotid and vertebral arteries.

Cerebral Oxygen Consumption. A catheter was placed in the superior sagittal sinus from which venous blood samples were obtained. Samples of arterial blood were collected from one of the cannulae in the carotid arteries. Arterial and venous oxygen contents were determined by the method of Holaday and Verosky on the Kopp Natelson microgasometer (8). The brain of each animal was weighed and the observed cerebral blood flow converted to ml per 100 gm of wet brain weight. Arteriovenous oxygen differences were computed in volume per cent. Cerebral oxygen consumption was calculated as the product of the cerebral blood flow and the arteriovenous oxygen difference.

Systemic Blood Pressure and Pulse Rate. A bellows manometer recorded systemic blood pressure and pulse rate continuously through a large bore catheter which had been threaded into the aorta through a femoral artery.

Experimental Procedure. The animals were anesthetized with intravenously administered pentobarbital, 30 mg/kg. Following induction of anesthesia, a cuffed endotracheal tube was inserted and the dogs were placed on an automatic positive-negative respirator which delivered 100% oxygen at a rate of 24 respirations/min. The positive pressure phase of the respirator was adjusted between 7 and 11 mm Hg in order to maintain a tidal volume of approximately 200 ml. The maximum negative pressure was 4 mm Hg. The animals were then prepared as described above and heparinized. Temperature readings were obtained from a mercury laboratory thermometer placed 200 mm into the esophagus. Control readings of cerebral blood flow, blood pressure and pulse rate were obtained during a 30-minute period. At the end of this time, arterial and venous blood samples were drawn for analysis of respiratory gases. The dogs were then immersed to the shoulders in ice water. Cerebral blood flow, blood pressure, and pulse rate were recorded at 2-minute intervals during the cooling period. Further arterial and venous blood samples were obtained when the esophageal temperatures reached 30° and 26°C, respectively.

RESULTS

Cerebral Blood Flow. Observations on 10 dogs were obtained. Body temperature during the control period was usually between 35 and 36°C. To facilitate comparative analysis of the data, values at 35°C, interpolated where necessary, were designated as 100% at the control level. The blood flows of individual animals were plotted against temperature (fig. 1). The carbon dioxide contents of arterial and venous bloods were also determined and their differences calculated. They showed greater variability but were in general agreement with the arteriovenous oxygen difference.
The cerebral blood flow varied proportionately with the change in temperature. The average decrease in cerebral blood flow per degree decline of temperature between 35 and 25°C was 6.7% of the control flow. The standard deviation of the observed slopes is 1.38%/degree C; and the standard error of the estimated mean slope is 0.43%/degree C.

Systemic Blood Pressure and Pulse Rate. Observations of systemic blood pressure on eight dogs were made (fig. 2). Recordings were not obtained in two experiments because of mechanical difficulty with the bellows manometer. Mean blood pressure was calculated from the formula: Mean B.P. = diastolic pressure plus one-third pulse pressure. The average mean blood pressure varied with changes in temperature. It declined 4.8 mm Hg/degree temperature reduction between 35 and 25°C. However, the relationship of blood pressure to temperature change was not as constant as that observed for cerebral blood flow. The standard deviation of the observed slopes is 1.8 mm Hg/degree C and the standard error of the estimated mean slope is 0.63 mm Hg/degree C.

Of those functions studied, the pulse rate was affected the most constantly by temperature; it decreased linearly with temperature decrements between 35 and 25°C. This has been reported consistently by others (6-11).

Cerebral Oxygen Consumption. Observations on cerebral oxygen consumption of four dogs were made (table 1). The effect of temperature on the average cerebral blood flow and oxygen consumption of these animals is shown in figure 3. Cerebral blood flow and oxygen consumption varied in the same direction and to the same degree with decreases in temperature, while arteriovenous oxygen differences remained almost unchanged.

DISCUSSION

The many transcranial anastomoses in lower animals (12, 13), make the accurate determination of cerebral blood flow difficult (14). However, in the course of the present investigation, a preparation was developed in which no arterial flow could be found outside of the brain and upper cervical cord except for small muscular branches of the vertebral arteries, as confirmed by arteriograms. It is known that the blood vessels of the skin, subcutaneous tissues, and muscles constrict severely during the application of cold. If the flow through...
TABLE

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<tr>
<th></th>
<th>CBF (ml/100 gm/min)</th>
<th>A-V Diff., O₂ Vol. %</th>
<th>O₂ Consumption, ml/100 gm/min</th>
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<tr>
<td></td>
<td>35°C</td>
<td>30°C</td>
<td>26°C</td>
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<td><strong>Dog 7:</strong> wt. 8.5 kg; brain wt. 69.0 gm</td>
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<td></td>
<td>46.4</td>
<td>29.0</td>
<td>10.9</td>
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<td><strong>Dog 13:</strong> wt. 8.6 kg; brain wt. 69.5 gm</td>
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<td>47.0</td>
<td>32.7</td>
<td>20.3</td>
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<td><strong>Dog 14:</strong> wt. 11.7 kg; brain wt. 89.0 gm</td>
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<td>52.7*</td>
<td>34.8</td>
<td>21.3</td>
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<td><strong>Dog 16:</strong> wt. 8.8 kg; brain wt. 71.0 gm</td>
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<td>49.3*</td>
<td>32.4</td>
<td>17.5</td>
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<td><strong>Means and standard errors of means</strong></td>
<td>49.1</td>
<td>±1.34</td>
<td>32.2</td>
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* Interpolated.

The muscular branches of the vertebral arteries were of an appreciable magnitude, a sudden drop in flow through the rotometer following immersion in ice water should have been observed. This was not seen. It is concluded, therefore, that the error introduced by these extraneous vessels into the estimation of the volume of the cerebral circulation cannot be appreciable and that this method is valid for the determination of cerebral blood flow.

Difficulties encountered in the earlier experiments in this series resulted in preparations in which the flow through various combinations of vessels was metered, viz. external carotid retrograde flow, as well as internal carotids and vertebrals; two carotids, one vertebral; one carotid, two vertebrals; two carotids, no vertebrals. Although the magnitude of the flow rates differed in each of these preparations, when they were compared in terms of percentage decrement of flow per unit decrease in temperature, the resultant slopes were almost identical. Hence, it is further concluded that this method of measurement is also valid for the determination of relative changes of cerebral blood flow, even when other circulatory beds are included.

It has been shown in vitro that cerebral oxygen consumption varies as a constant function of temperature (15). The in vivo determinations presented herein are in agreement with this. In the heart, another ‘vital organ,’ it has been shown that coronary blood flow and oxygen consumption maintain the same relationship to temperature (16-18). It is of interest that the decrease of cerebral blood flow parallels the decrease of oxygen consumption with the result that the arteriovenous oxygen differences remain almost constant. Since the systemic blood pressure varied considerably during these experiments, it seems likely that cerebral vascular tone was regulated by some function of the respiratory gas tensions in the brain at all temperatures down to 26°C.

FIG. 3. Solid circles joined by solid lines represent mean cerebral blood flows of four animals at 35, 30, and 26°C. Open circles joined by broken lines represent mean cerebral O₂ consumption of the same animals. Vertical lines represent standard error of each mean.
SUMMARY AND CONCLUSIONS

Cerebral oxygen consumption varies proportionately with body temperature during hypothermia. Cerebral blood flow varies proportionately with temperature to the same extent as does cerebral oxygen consumption, such that arterio-venous oxygen differences are unchanged. Therefore, hypothermia probably produces no hypoxia of brain tissue so long as adequate respiratory and cardiac functions are maintained.

The authors wish to thank Dr. J. Lawrence Pool for the invaluable advice and criticism which he so kindly tendered throughout the course of these experiments.

REFERENCES