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Received Sept. 4, 1968. P.S.E.B.M., 1969, Vol. 130.

Effects of Local Alterations of pCO_2 and pH on Cerebrovascular Resistance in Isolated Dog Heads* (33546)

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The effect on cerebral vascular resistance of changing blood pCO_2 generally throughout the body has been studied extensively in animals and man using a variety of techniques (1–4). When pCO_2 is increased by adding CO_2 to the ventilating gas or by decreasing ventilation, cerebral vascular resistance falls and cerebral blood flow increases (1–4). While evidence indicates that the direct effect of CO_2 on cerebral blood vessels is dilation, there appear to be few definitive experiments showing the effect of locally altering pCO_2 and pH on cerebral vascular resistance. One author stated that the cerebral vasculature of the isolated cat head was largely unresponsive to local changes in pCO_2 and pH unless the alterations were extreme (5). However, this maneuver was a peripheral part of the study and no data were presented.

The present paper describes the effect of locally increasing and decreasing p_aCO_2 and pH by graded increments on the isolated cerebral circulation.

Methods. Adult mongrel dogs of both sexes were anesthetized intravenously with sodium thiopental (30 mg/kg) and heparinized (3 mg/kg).

Dog-pump-head. Each of five dog heads was perfused with blood from another dog (donor) as follows: A Sigmamotor pump was interposed between one carotid artery of the donor animal and two carotid arteries of the head of another dog. Blood returned by gravity from the cannulated jugular veins of the head to a jugular vein of the donor. The external carotid arteries were ligated, the head was severed from its body, and the spinal canal was plugged with bone wax. Wire ligatures prevented bleeding from the cut surfaces of the neck. Carotid artery pressure was measured distal to the perfusion pump with a Statham pressure transducer and recorded on a Schlumberger galvanometer recorder. The donor dog was ventilated with a positive pressure respirator using mixtures of percent CO_2 in O_2 over the range 0–14.5% CO_2. These mixtures were obtained continuously with an anesthetic gas machine. Approximately 10 min were allowed at each different concentration of CO_2. Percentage of CO_2 in the ventilating gas was monitored continuously with a Harvard critical orifice CO_2 analyzer. Cerebral arterial blood pH was measured at 5–10 min intervals with a Beckman model GS pH meter.

Cerebral blood flow was held constant in each experiment. Changes in cerebral artery perfusion pressure therefore indicated changes in cerebral vascular resistance in the same direction.

Oxygenator-pump-head. Six decapitate dog heads were perfused at constant flow with blood from an artificial oxygenator system. A diagram of the preparation is shown in Fig. 1. The system was primed with whole blood from the same dog and circulation was established through the dog's head via both caro-

* This work was supported by a grant from the Defense Research Board of Canada.

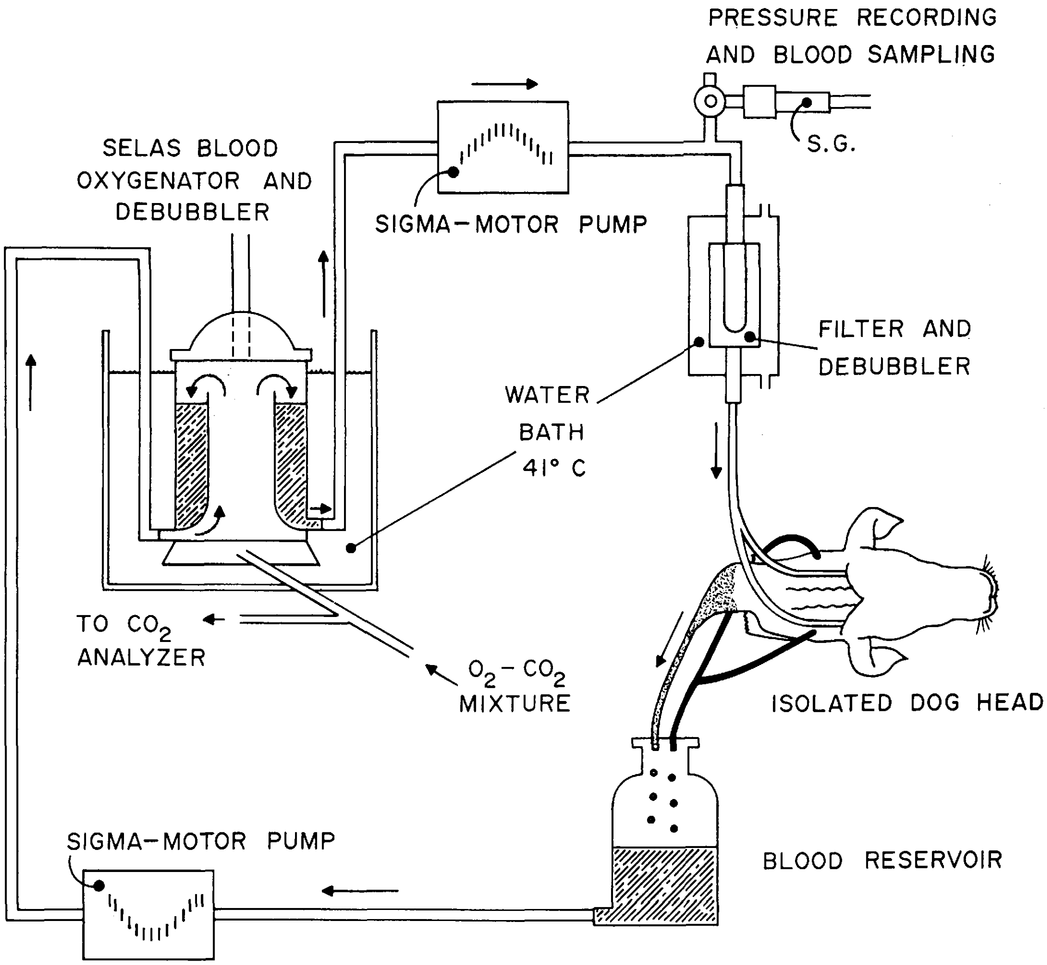

FIG. 1. Diagramatic representation of experimental set-up for oxygenator-pump-head study. S.G. = Statham pressure transducer. Blood flow in direction of arrows.

tid arteries. The external carotids were ligated and the head was removed from its body. Blood from the severed jugular veins and spinal venous sinuses drained by gravity into a reservoir and was pumped (Sigmamotor) to the oxygenator. Oxygenator blood was subsequently returned at constant flow to the isolated head by another pump. The CO_2 concentration in the oxygenator gas was varied and measured as in the preceding group. Carotid arterial blood pH and perfusion pressure were also measured as mentioned previously.

Results. Data from the cross-perfusion head experiments are shown individually in Table I. The most consistent response was a fall in carotid artery perfusion pressure as blood CO_2 concentration was increased and pH decreased; carotid artery pressure most frequently rose when the opposite changes were made. This relationship was not as clear-cut in Expts. 1 and 4 as in the others.

Table II shows data from individual decapitate head experiments in which the CO_2 concentration was altered in an oxygenator system. Increasing and decreasing blood CO_2 concentration in a stepwise fashion consistently caused a fall and rise in carotid artery pressure, respectively. Blood pH changed inversely to CO_2 changes.

Figure 2 shows data from one experiment which illustrates an inverse relationship be-

TABLE I. Effect of CO_2 and pH on Cerebral Perfusion Pressure (flow constant).[a]

Expt. no.	CO_2 (%)	pH	ΔCAP (mmHg)
1	4.0	7.61	0
	0.0	7.68	+26
	14.5	7.22	+11
	0.0	7.78	+43
2	8.4	7.41	0
	0.0	7.68	+50
	10.5	7.31	—60
	0.0	7.70	+20
	11.6	7.27	—20
	0.0	7.70	+19
3	5.0	7.52	0
	6.3	7.48	—3
	0.0	7.62	+14
	8.4	7.32	—22
	3.4	7.50	+20
	11.5	7.20	—18
4	3.8	7.54	0
	0.0	7.61	—27
	13.7	7.01	+22
	0.0	7.74	+10
	3.4	7.31	0
5	3.7	7.48	0
	0.0	7.62	+20
	11.1	7.13	—55
	0.0	7.46	+40

[a] Dog-pump-head preparation: CO_2 = % CO_2 in ventilating gas; ΔCAP = change in carotid artery perfusing pressure from control.

tween changes in blood CO_2 tension and carotid artery perfusion pressure. It is clear from this tracing that relatively moderate changes in p_aCO_2 and pH directly cause profound changes in carotid artery pressure. It is also evident that these changes are readily reproducible in the same head.

Figure 3 illustrates the effect of local alteration of blood pH on cerebral resistance in the decapitate head experiments shown in Table II. This figure shows that whenever pH was lowered, perfusion pressure also fell, i.e., all pressure points fell in the lower right quadrant, indicating a fall in cerebral vascular resistance. Increasing the pH in the same experiments resulted in a rise in perfusion pressure, depicting an increase in resistance.

Discussion. This study indicates that the effect of locally increasing p_aCO_2 is a fall of cerebral vascular resistance and vice versa. Thus, when p_aCO_2 was increased in decapitate heads perfused with blood from an artificial oxygenator, there was a consistent fall in cerebral vascular resistance. This fall of vascular resistance was probably due to active vasodilation of blood vessels since it occurred in the face of a fall in transmural pressure. While blood viscosity alterations cannot be ruled out, the literature provides no evidence indicating a significant effect of CO_2 on viscosity. It should also be mentioned that ex-

TABLE II. Effect of CO_2 and pH on Cerebral Perfusion Pressure (flow constant).[a]

Expt. no.	CO_2 (%)	pH	ΔCAP (mmHg)
6	7.8	7.11	0
	0.0	7.49	+45
	14.0	6.88	—57
	0.0	7.49	+47
	10.4	6.98	—41
	0.0	7.40	+61
7	3.6	7.25	0
	0.0	7.40	+19
	4.2	7.18	—17
	0.0	7.39	+20
	4.2	7.25	—16
8	0.4	7.82	0
	4.8	7.21	—15
	0.0	7.62	+175
	3.8	7.26	—45
9	7.0	7.19	0
	0.0	7.49	+80
	4.5	7.20	—144
	0.0	7.52	+114
	2.5	7.39	—60
10	0.0	7.80	0
	5.0	7.17	—35
	0.0	7.80	+85
	4.5	7.20	—58
	0.0	7.75	+58
	5.2	7.28	—35
11	2.1	7.43	0
	0.0	7.82	+8
	4.5	7.23	—41
	0.0	7.85	+41
	5.6	7.23	—35
	0.0	7.79	+51
	5.1	7.11	—30

[a] Oxygenator-pump-head preparation: CO_2 = % CO_2 in ventilating gas; ΔCAP = change in carotid artery perfusing pressure from control.

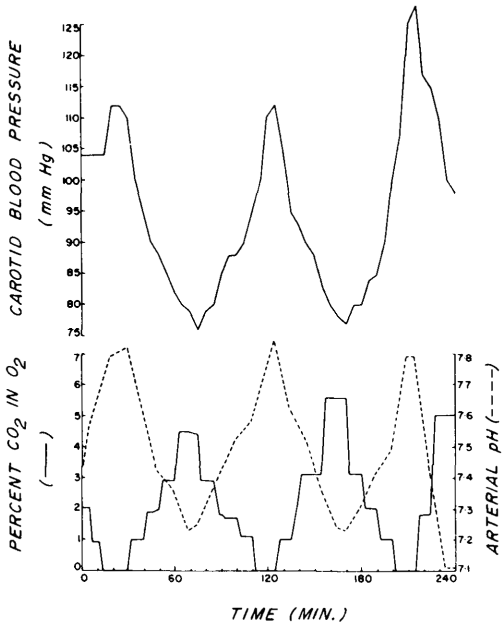

FIG. 2. Representative tracing on one experiment from oxygenator-pump-head study. Percent CO_2 in O_2 = CO_2 in oxygenator gas mixture.

tracranial vessels of the head could be involved in the overall response, and even though the external carotid arteries were ligated, this factor cannot be ruled out. Data from this study extend the brief observation of Geiger and Magnes who mentioned that a local increase in pCO_2 caused a fall in cerebral resistance in the isolated cat head (5). However, in their experiments extreme changes were required to appreciably affect cerebral resistance and no data relative to this point were presented.

Results from this study are also consistent with findings in intact animals and man in which pCO_2 is changed generally throughout the body. It has been established using a variety of techniques that increasing blood pCO_2 generally in animals or man results in a fall in cerebral vascular resistance and vice versa (1–4). The present study shows that this could, to a large extent, result from a direct action of CO_2 and/or H^+ on cerebral vessels independent from any remote action (6, 7) of these changes. Whether the effect of changing p_aCO_2 results from an action of CO_2 or H^+ on cerebral vascular smooth muscle was not considered and is beyond the scope of this study.

Autoregulation of blood flow (tendency for blood flow to remain constant despite changes in perfusion pressure) has been demonstrated for the cerebral vascular bed (8). It has been suggested that one of the mediators of this response is CO_2 (8). Thus, lowering perfusion pressure would increase p_aCO_2 and decrease resistance and raising perfusion pressure would lower p_aCO_2 and increase resistance. For this hypothesis to be workable it must be demonstrated that CO_2 is in fact locally active in the cerebral vasculature. The present study lends support to the hypothesis that CO_2 could be one of the factors involved in local regulation of cerebral blood flow.

Finally, this study shows that the local effect of increasing p_aCO_2 in the cerebral vasculature is similar to its local effect in most peripheral organs. Hence, locally increasing p_aCO_2 and decreasing pH causes, in the steady-state, a fall in resistance in the hindlimb (9), forelimb (10), kidney (10), coronary (10), and intestinal (9) vasculatures.

Summary. The local effects of graded increases and decreases of p_aCO_2 and pH on cerebral vascular resistance were determined in isolated dog heads. Two preparations were

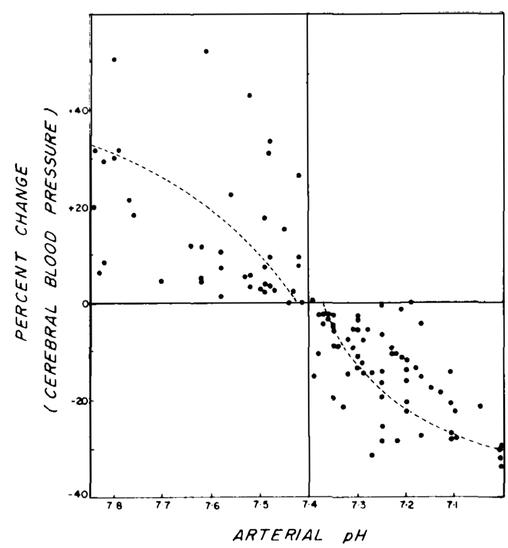

FIG. 3. Plot of all pressure points in oxygenator-pump-head study at different blood pH's.

utilized: In the first series, a donor dog was included in the extracorporeal circulation to supply blood to the constant flow perfused, decapitate head; in the second series, the donor dog was replaced with an oxygenator-reservoir system. Results indicate that the direct effect of increasing paCO_2 and decreasing pH is a fall of cerebral vascular resistance and vice versa.

The authors express their appreciation to Dr. Francis J. Haddy for critically reviewing the manuscript.

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Received Sept. 10, 1968. P.S.E.B.M., 1969, Vol. 130.

Comparative Immunology: Natural Hemolytic System of the Spiny Lobster, *Panulirus argus** (33547)

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The phylogenetic development of immunity has come under increased study in recent years. The attention of our laboratory and others (1–8) was directed toward the study of immune mechanisms in animals at various levels of the phylogenetic tree. Recent work involved a number of invertebrate species as well as the lower vertebrates. It is hoped by such studies to gain insight into the evolution of various factors in mammalian immunity such as complement systems and the immunoglobulins.

Our present work deals with a marine invertebrate, the West Indian spiny lobster *Panulirus argus,* which possesses a natural hemolytic system for sheep erythrocytes, a natural hemagglutinin for various species of red blood cells, and an inducible bactericidin for gram-negative enteric bacteria (9). The present paper is a preliminary report of studies designed to characterize the naturally occurring hemolysin of the lobster in order to further define its biochemical and evolutionary significance.

Materials and Methods. Specimens of the West Indian spiny lobster, *Panulirus argus,* were collected in the waters surrounding Bimini, Bahamas and maintained in hardware cloth cages in 26–28° tidal sea water at the Lerner Marine Laboratory. The animals, weighing 300–500 g, were bled from the pericardial sinus with an 18-gauge needle inserted between the cephalothorax and abdomen. Lobsters bled in this manner yielded 15–30 ml of hemolymph which was collected directly into saturated sodium citrate to prevent

* Supported by Public Health Service Research Grant AI-02693 from the National Institutes of Health. A portion of the work was done at the Lerner Marine Laboratory, American Museum of Natural History under support of the Office of Naval Research, ONR-552-07.

[1] Recipients of Public Health Service Training Grant AI-00293 from the National Institutes of Health.

[2] Recipient of Public Health Research Grant AM-03555 from the National Institutes of Health.