COMPARISON OF VENTILATION RESPONSES TO HYPERCAPNIA AT NORMOTHERMIA AND HYPOTHERMIA DURING HALOTHANE ANAESTHESIA*

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VENTILATION RESPONSES of animals to hypercapnia have been studied by several investigators with different results. Cranston and his co-workers[1] compared the ventilation of anaesthetized normothermic and hypothermic dogs during inhalation of 6 per cent carbon dioxide in air and concluded that during hypothermia the response was not different from that observed during normothermia. Salzano and Hall,[2] on the other hand, reported (in dogs anaesthetized with dial) a markedly depressed slope in the ventilation response at 29°c to inhalation of 4 per cent and 5.5 per cent carbon dioxide in air. Regan and Eger[3] confirmed Salzano's data during their study using constant-depth halothane anaesthesia. In none of the previous studies were respiratory effects of hypercapnia investigated at lower temperatures.

In the present study, observations were made at 37°c, 28°c, and 25°c and the levels of respired carbon dioxide were 10 per cent and 15 per cent at which some reversal of carbon dioxide response was evident.

METHOD

Five unpremedicated mongrel dogs weighing 10 to 16 kg were studied. Anaesthesia was induced with thiopental sodium 15 mg/kg. After intubation, anaesthesia was maintained by a high flow technique with halothane from a copper kettle vaporizer and mixture of approximately 50 per cent oxygen in air, so that the Pa_{O_2} tension was maintained above 250 mm of mercury. Animals breathed spontaneously throughout the experiments.

End-tidal carbon dioxide concentration was continually monitored with a Godart infra-red analyzer. Femoral artery and vein were cannulated. Arterial blood samples were taken for measurement of pH, Pa_{CO_2}, and Pa_{O_2} and correction factors applied.[8,9] Blood halothane level was measured by gas chromatographic technique after extraction with heptane. Range was 20 ± 2 mg/100 mls.

Expired gas volume was measured with a continuous flow spirometry technique (Figure 1) described by Nunn[5] as well as others.[6]

Volumes were converted to conditions of ambient pressure, body temperature and saturated water vapor (BTPS).[7] Oesophageal temperature was continuously

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CONTINUOUS FLOW SPIROMETRY TECHNIC

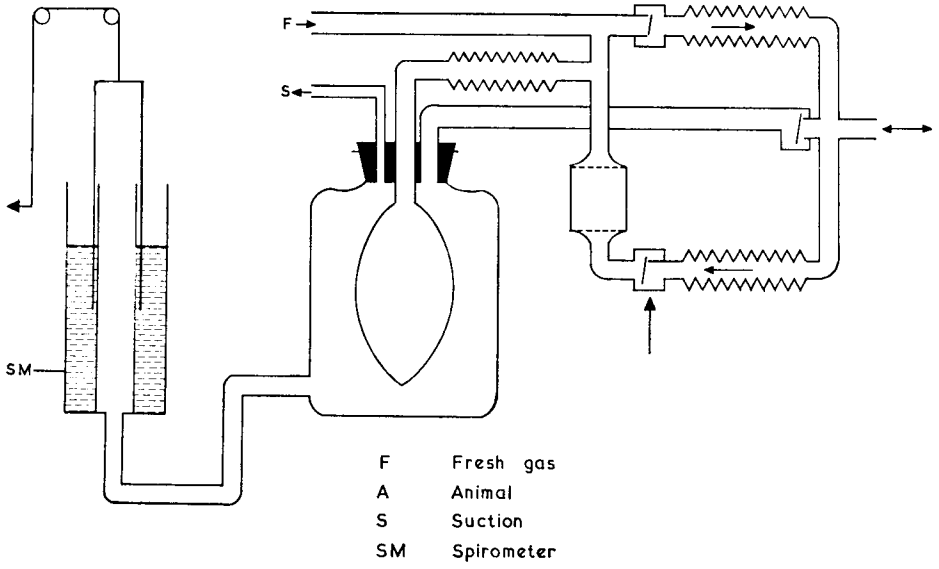

FIGURE 1

measured with a thermistor-probe electrode and Yellow Springs telethermometer.

Response to hypercapnia was recorded at two levels of 10 per cent and 15 per cent increased carbon dioxide. After a period of steady-state the resting ventilation was recorded, correlated with a sample of arterial blood for pH, $Paco_2$, and Pao_2. Inspired carbon dioxide tension was then increased by removing the carbon dioxide absorber and by adding the desired percentage of carbon dioxide. The end-tidal carbon dioxide tension was maintained constantly for at least 15 minutes. Arterial blood was withdrawn during the last minute of ventilation at this arterial carbon dioxide tension ($Paco_2$), and minute ventilation (VE) again recorded. This was then repeated at each new level of carbon dioxide.

The ventilation response to carbon dioxide was repeated at two levels of hypothermia, 28°C, and 25.3°C. Hypothermia was induced by surface cooling with ice. Observations were made after 15 minutes stabilization at the desired temperature. The animals were rewarmed and further observations recorded on return to 28°C and 37°C.

RESULTS

Table I summarizes the results. Resting minute ventilation (VE) fell progressively from 3.02 litres per minute at 37°C to 1.7 litres per minute at 28°C and to 1.32 litres per minute at 25.3°C and rose to 2.5 litres per minute on rewarming to 37°C. It is also interesting to note that despite the decrease of ventilation at 28°C

SUMMARY OF RESULTS (TABLE I)

VENTILATORY RESPONSE TO CO_2 (10% and 15%) DURING NORMOTHERMIA AND HYPOTHERMIA IN 5 DOGS

Mean ± Standard Deviation

	TEMPERATURE ^0C				
	37 ± 0.5	28 ± 0.4	25.3 ± 0.2	28 ± 0.2	37 ± 0.5
Resting VE (L/m.)	3.02 ± 0.26	1.7 ± 0.29	1.32 ± 0.08	2.4 ± 0.3	2.5 ± 0.21
Resting $PaCO_2$ (mm. Hg.)	39.9 ± 0.89	30.8 ± 1.6	31.2 ± 2.2	32.5 ± 1.72	41.5 ± 1.5
Resting pH (units)	7.335 ± 0.02	7.42 ± 0.01	7.41 ± 0.05	7.415 ± 0.02	7.33 ± 0.03
Base Excess (mEq/L)	-4.4 ± 0.8	-3.76 ± 0.97	-3.3 ± 2.7	-3.5 ± 1.7	-4.6 ± 1.1
Mean CO_2 response slope (L/min/mm.Hg.)	0.23 ± -0.04	0.045 ± 0.01	0.022 ± 0.01	0.061 ± 0.02	0.24 ± 0.04

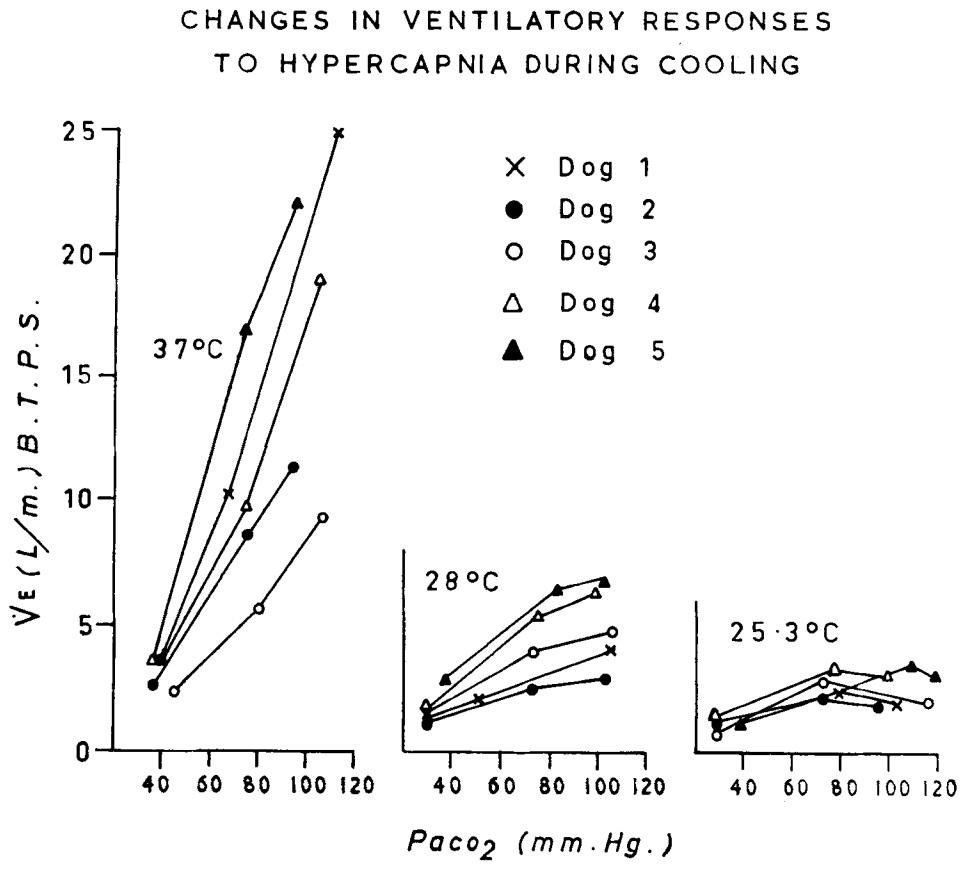

FIGURE 2

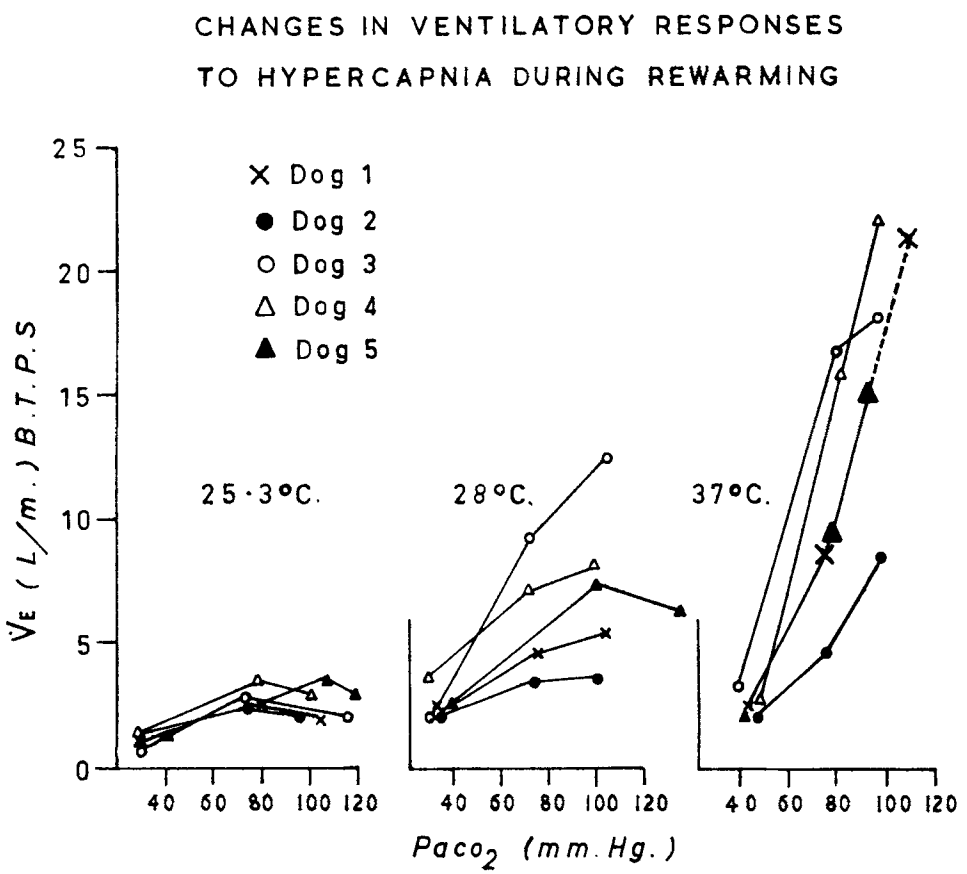

FIGURE 3

and 25.3°C; resting $Paco_2$ fell from 39.9 mm of mercury at 37°C to 30.8 mm of mercury and 31.2 mm mercury at 28°C and 25.3°C respectively. Arterial pH rose during cooling from 7.335 at 37°C to values between 7.41–7.42 at lower temperatures and fell to 7.33 on rewarming to 37°C. The mean base excess was maintained between –3.3 and –4.6. The mean slope of the ventilatory response curve to CO_2 also decreased progressively during cooling (from 0.23 litres per minute per mm of mercury at 37°C; to 0.045 litres per minute per mm of mercury at 28°C and to 0.022 litres per minute per mm of mercury at 25.3°C and rose again after rewarming to 0.24 litres per minute per mm of mercury at 37°C. The depression of ventilatory response is well demonstrated in Figures 2 and 3.

Mean resting ventilation fell to 57 per cent at 28°C, and to 43 per cent at 25.3°C of the normothermic ventilation, while resting $Paco_2$ declined simultaneously by 22 per cent.

DISCUSSION

There is a progressive reduction in ventilatory responsiveness to carbon dioxide as body temperature is lowered. This is reversible by rewarming.

VENTILATION RESPONSE AT 10% AND 15% CO_2. IN DOG ONE

			% CO_2	10%	15%
COOLING	37°C.	$\dot{V}E$	2.9	10.1	26.2
		$PaCO_2$	39	69	110
	28°C.	$\dot{V}E$	1.2	2.1	4.0
		$PaCO_2$	29	51	105
	25.3°C.	$\dot{V}E$	1.3	2.5	1.4
		$PaCO_2$	29	79	103
REWARMING	25.3°C.	$\dot{V}E$	1.3	2.5	2.0
		$PaCO_2$	29.	79	103
	28°C.	$\dot{V}E$	2.1	4.6	5.4
		$PaCO_2$	30.5	72	103
	37°C.	$\dot{V}E$	2.6	8.6	21.4
		$PaCO_2$	41.5	76	112

Table IIa

Our findings (Tables IIa and IIb) agree generally with those of Salzano,[2] Takeshi,[10] Regan and Eger,[3] who observed diminished ventilatory responses to carbon dioxide at 28°c. In the latter study, initial normothermic and subsequent hypothermic slope values were higher than those observed in the present study and probably reflect differences in anaesthetic techniques and agents. Our results differ from those of Cranston *et al.*[1] who could demonstrate in anaesthetized dogs no difference in response at 37.5°c and 26°c. However, their animals were premedicated with morphine and initial slopes were low. Subsequent depression from hypothermia was perhaps, therefore, minimal and difficult to demonstrate.

We observed variable responses among the animals at isothermic levels. This may relate to differing anaesthetic depths attained in each animal.

The fall in mean resting ventilation observed at 28°c was found to be 57 per cent of the normothermic ventilation and agrees with Spurr and his co-workers,[10] who reported approximately 55 per cent reduction for a similar fall of body temperature.

It should be noted that an enriched inspired oxygen concentration was used during this study. Thus, arterial oxygen tension Pao_2 was kept above 250 mm of mercury at all temperature levels. This more or less eliminated the hypoxic respiratory drive from peripheral chemoreceptors, although Hornbein and his associates have demonstrated slight activity even at this level of Pao_2.[11] Moreover, this high Pao_2 was perhaps partly responsible for the depressed slope of ventilatory response to CO_2 observed. Evidence from Cunningham and his co-workers[12]

VENTILATION RESPONSE AT 10% AND 15% CO_2. IN DOG FIVE

			% CO_2	10%	15%
COOLING	37°C.	$\dot{V}_E$	3·6	17·0	22·0
		$PaCO_2$	40	73	95
	28°C.	$\dot{V}_E$	2·8	6·4	6·6
		$PaCO_2$	37	84	103
	25·3°C.	$\dot{V}_E$	1·4	3·6	3·0
		$PaCO_2$	40	105	120
REWARMING	25·3°C.	$\dot{V}_E$	1·4	3·6	3·0
		$PaCO_2$	40	105	120
	28°C	$\dot{V}_E$	2·5	7·4	6·2
		$PaCO_2$	39	100	135
	37°C.	$\dot{V}_E$	22·0	9·0	15·0
		$PaCO_2$	42	80	95

Table IIb.

indicates that in awake man the slope may be depressed 10–20 per cent by elevating Pa_{O_2} from 100 to 350 mm of mercury, with little further change between 350 and 600 mm of mercury. However, this should not have contributed to the change in slopes observed under the conditions of this study since the Pa_{O_2} was kept above 250 mm of mercury at all temperature levels.

At resting ventilation, the Pa_{CO_2} was maintained at a lower level during hypothermia, even though ventilatory responsiveness to CO_2 challenge was markedly depressed.

The probable explanation for this disparity may be related to recent observations of Mitchell and his co-workers[11] who have located paired areas sensitive to H^+ ion on the ventrolateral aspect of medulla of the cat. There is reason to believe that these areas are major sites of medullary chemo-sensitivity, and they have been termed intracranial chemoreceptors. Perfusing them with acidic solution of cerebrospinal fluid (CSF) caused hyperpnoea and with alkaline solution hypopnoea. Flooding these areas with cold solution of CSF depressed ventilation immediately. This suggests that the feeble ventilatory responsiveness to CO_2 during hypothermia may result from cold depression of these intracranial chemoreceptors.

Summary

Ventilatory responses of dogs to hypercarbia were measured during normothermia and at two levels of hypothermia. A technique of continuous spirometry

was used to determine the minute ventilation. Minute ventilation and resting control $Paco_2$ fell with decreasing body temperatures. In addition, a progressive decrease was observed in ventilatory responsiveness to inhalation of increased carbon dioxide. In this study the resting ventilation maintained the $Paco_2$ lower during hypothermia even though ventilatory responsiveness to carbon dioxide challenge was markedly depressed.

Résumé

Nous avons mesuré, durand la normothermie et sous deux différents niveaux d'hypothermie, les réponses ventilatoires à l'hypercarbie chez des chiens. Nous avons employé une technique de spirométrie continuelle pour déterminer la ventilation minute. A mesure que s'baissait la température corporelle, s'abaissaient également la ventilation minute et le contrôle de la $Paco_2$ de repos. De plus, nous avons observé une diminution progressive de la réponse ventilatoire à l'inhalation d'un taux accru de dioxyde de carbone. Durant cette étude, la ventilation de repos a maintenu la $Paco_2$ plus basse durant l'hypothermie même si la réponse ventilatoire au dioxyde de carbone était fortement déprimée.

Acknowledgments

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