

## EFFECTS OF VAGAL BLOCKADE ON RESPIRATORY WORK IN THE HYPOTHERMIC ANIMAL

F. G. HALL, PH.D., AND JOHN SALZANO, PH.D.

THERE is a paucity of information relative to the qualitative physiologic function of respiratory regulatory reflexes during reduced body temperature. The role of the Hering-Breuer vagal afferents during normal body temperature has been studied by many investigators.<sup>1-5</sup> It is generally concluded that pulmonary ventilation with room air at normal body temperature is most economical when the vagi are intact. Severinghaus and Stupfel<sup>6</sup> found that dead space increased during hypothermia. They suggested that this was related to decreased vagal responses.

The present investigation was undertaken to determine the influence of vagal blockade on respiratory work during hypothermia. A comparison with the effects observed in the normothermic state was also made.

### METHODS

Eight mongrel dogs ranging in weight from 12.7 to 19.6 kg. (average, 17.1 kg.) were used. Each dog was anesthetized with 55 mg./kg. of Dial in Urethane, intraperitoneally.

Observations were made during maintenance of normal body temperature, during hypothermia and during maintenance of normal body temperature after hypothermia. Temperatures were measured from thermocouples located in the rectum, esophagus and inferior vena cava. The voltage output of the rectal and blood thermocouples was read on a Leeds-Northrup Type K2 potentiometer and converted to degrees centigrade by appropriate conversion tables. The temperature from the esophagus was measured by a Yellow Springs Tele-thermometer.

**Vagal Blockade.** The temperature of a restricted length (13 mm.) of each vagus nerve was regulated by being placed in silver-lined grooves of hollow brass blocks

through which water was circulated. This apparatus has been described in a previous publication.<sup>3</sup> The blocks were located in the third and fourth cervical region and carefully oriented with minimal nerve displacement and trauma. Water was pumped (3 liters/minute) from either an ice bath or a warm bath at 38° C. to cool or warm the nerves as desired. Each block was insulated to prevent temperature changes in the surrounding tissues. The average temperatures of the grooves of the blocks were 37.1° C. and 1.2° C. during circulation of warm water and ice water, respectively. When the vagi were cooled it was impossible to demonstrate any sign of conduction across the block when tested by electrical stimulation. Rewarming the vagi always resulted in recovery of the measured variables to control levels indicating that no apparent injury to the nerves was caused by the cold blockade.

**Recording.** Intrapleural pressure and respiratory tidal volumes were recorded simultaneously on a Miller oscillograph. Intrapleural pressure changes were measured and referenced to atmospheric pressure with a Harvard 107 pleural cannula inserted in the fourth intercostal space. The cannula was connected to a 0.2 psi Statham transducer. Tidal volumes were measured from respiratory patterns recorded with a 160 liter tank attached in series with the tracheal cannula. The exchange of gas produced pressure variations within the system which were measured with a 0.05 psi Statham transducer. Pressure variations were calibrated in terms of volume by ventilating the tank with a Palmer resuscitator pump.

Each experiment was conducted as follows: The animal was anesthetized and hair shaved from abdominal and thoracic areas. The animal was placed on a V-shaped aluminum trough suspended above a large metal tank. Thermocouples and intrapleural cannula were inserted as well as a specially constructed tracheal cannula. Vagi were dissected free

Accepted for publication January 19, 1960. The authors are in the Department of Physiology and Pharmacology, Duke University Medical Center, Durham, North Carolina.

TABLE 1

EFFECT OF VAGAL BLOCKADE (COOLING) ON RESPIRATORY WORK DURING NORMOTHERMIA, HYPOTHERMIA AND REWARMING ANIMALS TO NORMOTHERMIA

	Normothermia (37° C.)		Hypothermia (27-28° C.)		Rewarmed to Normothermia (37° C.)	
	Vagi Warm	Vagi Cold	Vagi Warm	Vagi Cold	Vagi Warm	Vagi Cold
Respiratory rate per minute	32.1	22.0	9.9	6.4	34.3	20.3
Pulmonary ventilation (l./minute, BTPS)	4.3	3.4	1.2	1.0	4.7	4.0
Respiratory work (Gm.-cm.)						
Insp. viscous	96.5	156.5	53.5	92.0	83	136
Insp. elastic	205	369	137	226	241	400
Expir. viscous	140	208	48	58	165	166
Work/breath	301	526	190	319	324	536
Work/minute	9,676	11,570	1,884	2,038	11,016	10,877
Work/l./minute	2,271	3,364	1,583	2,080	2,344	2,712

and placed in the special cooling devices. Rectal temperature was maintained between 37-38° C. Simultaneous recordings of respired gas volume and intrapleural pressure were made for one minute with vagi at 37° C. The vagi were then blocked (1.2° C.) for six minutes and volume and pressure recorded during the last minute. Warm water was circulated through the blocks and vagi rewarmed to body temperature for six minutes. Recordings were made during the last minute. The animal respired from the tank only during the time of recording. Following the observation at normal temperature the animal was lowered on the trough into the tank containing an ice water mixture to a depth which was just below the tracheal cannula. Water was continuously poured over the thoracic and abdominal area. At a rectal temperature of 29° C. the ice water was drained from the tank and rectal temperature fell slowly usually stabilizing at 27-28° C. Recordings of volume exchange and intrapleural pressures with the vagi warm, cooled and rewarmed were made as before with the animal in a stable hypothermic state. Warm water (42-45° C.) was then added to the tank to the same depth as the ice water and poured over the thoracic and abdominal areas. Rewarming to the normal rectal temperature was accomplished in 60-75 minutes. Recordings were made in the same manner as during the prehypothermic state.

Average pressure-volume respiratory loops

were constructed from at least three consecutive respiratory cycles. Each breath was divided into five equal time intervals and the pressure and volume at each interval was measured. Viscous and elastic work were calculated by planimetric integration of the loops according to the method of Otis, Fenn and Rahn.<sup>7</sup> The interaction of elastic forces between the lungs and chest as described by Otis<sup>8</sup> was not taken into account in these analyses. Respiratory rate and pulmonary ventilation were calculated from the volume exchange records.

#### RESULTS AND DISCUSSION

The effects of cooling the vagi on the work of breathing during normothermia, hypothermia and rewarming to normothermia are presented in table 1. Previous reports from our laboratory have shown that blockade of vagal afferents during inspiration of room air at normal body temperature produced an increase in respiratory work per minute. Qualitatively the same results are again reported. Elastic work was increased 80 per cent mainly as a result of an increase in tidal volume. Respiratory frequency was decreased 31 per cent. Energy expended to move the lungs and air expressed as respiratory work per minute was 9,676 Gm.-cm. with the vagi warm and 11,570 Gm.-cm. when the vagi were blocked (cooled), table 1. In order to compare the change in respiratory work with vagi blocked during normothermia with previous

reports and with the change during hypothermia respiratory work per unit volume of ventilation was calculated. During normothermia the respiratory work per liter of total ventilation per minute was 2,271 Gm.-cm. with the vagi warm and 3,364 Gm.-cm. with the vagi blocked. This represents an increase of 48 per cent in the respiratory work per liter of total ventilation per minute. This value compares favorably with previous values of 37 per cent by Zechman, Salzano and Hall,<sup>3</sup> 39 per cent by Salzano and Hall<sup>4</sup> and 45 per cent by Lim, Luft and Grodins.<sup>5</sup>

The hypothermic animals exhibited a marked decrease in frequency of respiratory activity from an average of 32 cycles per minute in the normothermic state to 9.9 at rectal temperature of 27–28° C. Pulmonary ventilation decreased from 4.26 l./minute to 1.19 l./minute. However, the influence of vagal activity is as prominent during hypothermia as during normal body temperature. During normothermia vagal cooling produced a decrease of 31 per cent in respiratory frequency (32.1 to 22.0) and a fall of 19 per cent in pulmonary ventilation per minute. At a rectal temperature of 27–28° C. cooling the vagi to 1.2° C. resulted in a fall of 35 per cent in respiratory frequency and an 18 per cent decrease in pulmonary ventilation.

A further indication that vagal afferents influence respiratory activity in the hypothermic animal was shown by a comparison of the effects of vagal blockade on respiratory work per liter of total ventilation. This was found to increase 32 per cent (1,583 to 2,080) which is within the range of the increases reported for the normothermic animal.

A comparison of the respiratory work per liter of total ventilation per minute with the vagi at body temperature in the normothermic animal with that of the hypothermic animal showed a change from 2,271 to 1,583 Gm.-cm. per l./minute, *i.e.*, a decrease of 30 per cent. When the vagi are blocked the normothermic animals expended 3,364 Gm.-cm. per l./minute to move the lungs and air, whereas the hypothermic animals ventilated with 2,080 Gm.-cm. per l./minute with vagi blocked, a difference of 39 per cent. These observations suggest that respiratory activity is more economical in the hypothermic animal.

Data are also presented in table 1 for the rewarmed animal. Although the values are qualitatively similar to the values before hypothermia there is some divergence. Respiratory work per liter of total ventilation increased only 16 per cent as a result of vagal cooling, (48 per cent during normothermia). This may be an experimental variation due to inadequate return to prehypothermic conditions. It would seem to warrant further investigation.

### SUMMARY

The effects of vagal blockade on respiratory work during water immersion hypothermia were studied on 8 anesthetized dogs. Blocking the vagi resulted in an increase of 48 per cent in respiratory work per unit volume of ventilation during maintenance of normal body temperature. An increase of 32 per cent was found when the rectal temperature of the same group of animals was reduced to 27–28° C. and the vagi blocked (cooled to 1.2° C.). Respiratory frequency was reduced 31 per cent and pulmonary ventilation fell 19 per cent when the vagi were blocked during normothermia. In the hypothermic state vagal blockade resulted in a reduction of 35 per cent in respiratory rate and a fall of 18 per cent in pulmonary ventilation. These data indicate that vagal impulses play as prominent a role in respiratory regulation during hypothermia as they do at normal body temperature.

This study was aided by Grant No. G-59-4 from the Life Insurance Medical Research Fund.

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**NEWBORN CIRCULATION** A number of circulatory adjustments occur in the normal newborn infant during the initial 24 hours. An immediate hemoconcentration takes place in the general circulation, possibly due to a rise in blood pressure. Immediately following delivery there is stasis in the peripheral vascular circulation of the order of 10 per cent. This persists to a limited extent after 24 hours, although it may be entirely resolved in some infants by this time. There are no changes of hematological values in the first 24 hours; variations observed in peripheral blood represent only adjustments of the peripheral vascular circulation. (*Low, A., and Kapsos, J.: Circulatory Adjustments in the Initial Neonatal Period, Canad. M. A. J.* 82: 70 (Jan. 9) 1960.)

**HYALINE MEMBRANE** In every one of a series of 22 infants who died at 6 to 72 hours after delivery by cesarean section, microscopic examination of the lungs showed contamination of the bronchioles and alveoli with blood, epithelial cells, and amorphous debris. Despite the brief period from incision of the uterus to the breathing of air, these babies had breathed the contaminated fluid surrounding them before birth. With the expansion of the lungs and the entrance of air following birth, there was a displacement of the foreign matter along the walls of the bronchioles and alveoli in a layer of varying thickness in widespread areas. No suggestions are offered as to how this may be prevented. (*Snyder, F. F.: The Origin of Pulmonary Hyaline Membrane Disease in Premature Infants Delivered by Cesarean Section before Labor, Obst. & Gynec.* 14: 730 (Dec.) 1959.)

**PLACENTAL SEPARATION** Twelve cases of separation of the placenta following administration of spinal anesthesia are reported. While other causes of abruption are recognized spinal anesthesia and the ensuing supine position cause hypotension and occlusion of the vena cava which together produce placental separation in some patients. Use of left lateral recumbent position following the administration of spinal anesthesia for delivery is recommended. Preanesthetic determinations of blood pressure are advised in the sitting and dorsal recumbent positions which may delineate abruption-prone candidates for obstetric spinal anesthesia. (*Crawford, M. E., and Murray, J. T.: Spinal Abruptio, Obst. & Gynec.* 15: 97 (Jan.) 1960.)

**LEGAL RESPONSIBILITY** Anesthetists perhaps never were the legal servants of the surgeons and certainly are not at present. Each is a professional entity with his own professional responsibilities to the patient and under some circumstances with some responsibility for the work of the other. (*Editorial: Legal Responsibilities of Surgeons and Anaesthetists, Canad. M. A. J.* 82: 215 (Jan. 23) 1960.)

**UNIVERSITY INSTITUTE OF ANESTHESIOLOGY** The University of Innsbruck, Austria, is the first German-speaking university to establish a central institute of Anesthesiology. Its director holds the rank of Associate Professor. The first director is Dr. Haid, who received his training at Iowa University Hospital and who was certified in 1959 by the American Board of Anesthesiology. (*Anaesthesist* 8: 364 (Dec.) 1959.)