A STUDY OF THE HERING-BREUER REFLEX.

By RICHMOND L. MOORE, M.D.

(From the Hospital of The Rockefeller Institute for Medical Research.)

INTRODUCTION.

The observation has been made by several investigators that a rapid respiratory rate depends on intact vagal conduction. In experiments on anesthetized rabbits, Scott (1908) showed that an increase of carbon dioxide (not above 6 to 7 per cent) in the inspired air after the vagi had been divided was followed by an increase in the depth of breathing, but that the rate remained practically unaltered. On the contrary, the response of animals with intact vagi was an increase in rate, as well as in depth of respiration. Porter and Newburgh (1917) found that the rapid respirations occurring in dogs in whom they had produced an experimental pneumonia became normal after cocainizing the vagus nerves. They had noted before this that if the vagal trunks were sectioned previous to infecting the animals the respirations did not become rapid (1916). Dunn (1920), and still later Binger and his coworkers (1924), demonstrated that the rapid and shallow breathing, produced experimentally in animals by the intravenous injection oɪ a suspension of potato starch granules, disappears immediately if the vagus nerves are divided or frozen. It was shown later that animals in whom the vagi had been sectioned several months previous to the injection of starch granules did not accelerate their rate (Binger and Moore, 1926). It would appear from the investigations of these latter authors (Dunn and Binger) that the Hering-Breuer reflex was enormously exaggerated under the conditions of their experiments. Presumably section of the vagi blocked the peripheral stimuli that were essential to the rapid rate.

In spite of the many studies that have been made of the vagal influence on breathing, the manner in which the vagal nerve endings are excited is not yet clear. Our interest in this subject developed from

an effort to explain the rapid and shallow breathing seen clinically in pneumonia, and produced experimentally in animals by the intravenous injection of potato starch granules. The experiments that will be presented were designed to study the nature of the Hering-Breuer stimulus.

Historical.

Early last century Legallois (1812) observed that section of the vagus nerves is followed by slowing and deepening of the respirations.

Hering and Breuer (1868), in a series of experiments performed on dogs and rabbits, both with and without anesthesia, showed that inflation of the lungs at once produces a movement of expiration and deflation a movement of inspiration. These observations were made both when the animals breathed naturally and when the lungs were expanded or collapsed artificially. The influence was not present when the vagi were divided. On the basis of their evidence Hering and Breuer formulated a theory for the self-regulation of respiration. They concluded that the respiratory center was continuously influenced through the vagi by the movements of the lungs, expansion checking inspiration and initiating expiration, and collapse checking expiration and initiating inspiration. Hering and Breuer also described a pause in respiratory movement following distention of the lungs. They explained this as an inspiratory inhibition due to vagal excitation following expansion.

The observations of Hering and Breuer were confirmed and elaborated by Head (1889), and later by Christiansen and Haldane (1914), and Haldane and Mavrogordato (1916). Head showed that inflation of the lungs produces an instant and complete relaxation of the diaphragm, and that if air be sucked out of the lungs the diaphragm will go into a state of tonic contraction. Both of these effects were absent if the vagi had been previously cut.

Christiansen and Haldane were the first to study the effect of distending the lungs on the human respiration. Distention was provided at the end of expiration by having the subjects breathe from a bag containing air, and so weighted that the air was under a pressure of 6 to 8 cm. of water. The respirations were recorded with a stethograph. When the lungs were distended in this manner, the respiratory movements invariably ceased, for usually about half a minute.[1] That the pause was not due merely to lowering of the alveolar CO_2 pressure was shown by the fact that it was still produced when the air in the bag contained 7.3 per cent of CO_2 and 8.2 per cent of O_2. At this time, Christiansen and Haldane explained the pause that they had observed in man as an Hering-Breuer "inhibitory" effect.

---

[1] The pause in respiratory movements referred to here is the primary pause and must be distinguished from a secondary pause that was also observed. This latter was clearly shown to be related to a lowered CO_2 percentage in the inspired air and was described as a true chemical apnea.

This interpretation, however, was subsequently changed by Haldane (1922), and the pause has since been described as simply a prolonged expiratory effort.

Haldane and Mavrogordato demonstrated in man that interruption of either respiratory phase interrupts the previous rhythm of the respiratory center. If expiration is interrupted, there follows a prolonged expiratory phase during which the intrapulmonary pressure gradually rises. This is finally terminated by an inspiratory effort. If inspiration is obstructed, a prolonged inspiratory effort follows, but under these conditions the intrapulmonary pressure falls and the negative phase is terminated by an expiratory effort. Commenting upon these and the foregoing experiments, Haldane (1922) says: "The respiratory center does not act independently of the lung movements, but inspiratory or expiratory discharge of the center goes hand in hand with actual inspiration or expiration, as if the center were one piece with the lungs."

Boothby and Berry (1915) also studied the effects of distention of the lungs on the respiratory rhythm in man, and extended their observations to normal and vagotomized dogs. The lungs were distended by having the subjects breathe from a spirometer so weighted that the air was under a pressure of 8 to 16 cm. of water. The dogs did not require anesthesia. The respiratory movements were recorded qualitatively by means of a pneumograph, and quantitative curves of the "coordinated total respiratory movements" were written by the spirometer. None of the curves that they obtained showed a primary inspiratory inhibition. In regard to the experiments of Hering and Breuer, they say: "The pause noted by Hering and Breuer is not at the top of inspiration but at the bottom of expiration, that is, the next expiratory phase is prolonged and inspiration is delayed, or, as they say, 'inhibited,' by vagal stimulation." In experiments on dogs, in which the pulmonary branches of both vagi had been divided, Boothby and Berry obtained several instances of a short apnea on distention of the lungs. They concluded that the vagi do not transmit impulses which, according to Hering and Breuer, arise from distention of the lungs and inhibit inspiration.

Einthoven (1908) studied the action currents in the peripheral end of the divided vagus by means of a string galvanometer. Anesthetized dogs were used and the vagus was divided high up in the neck. Records of the electrical changes in the nerve were made by photographing the image of the galvanometer string. When the animals breathed naturally curves were obtained that showed undulations synchronous with the respiratory movements. Additional experiments were carried out on the effects of insufflating and deflating the lungs. These showed that the excitatory state of the vagus nerve endings was related to lung volume and not to intrapulmonary pressure. In other experiments of this type Einthoven found that electrical changes occurred in the peripheral end of the cut nerve that were synchronous with artificial deflation of the lungs. He accepted his findings as evidence of the presence of two kinds of pulmonary vagus fibres, and concluded that his experiments gave support to the theory on the self-regulation of respiratory movements that had been advanced by Hering and Breuer.

Schafer (1919) admits that respirations are affected by influences coming from the lungs, but calls attention to the fact that double vagotomy is not always followed by constant effects. He believes that the results of vagotomy may be influenced considerably by obstruction at the glottis from paralysis of the laryngeal muscles and a falling together of the thyroarytenoid ligaments. When this is avoided Schafer states that the slowing of breathing is often absent or transitory, and that animals may survive section of the vagi indefinitely.

Pi Suñer and Bellido (1921) claim to have produced evidence to show that the vagal nerve endings in the lungs are susceptible of being stimulated by high concentrations of carbon dioxide in the alveolar air. This idea was not a new one, for Traube (1871) had supposed that carbon dioxide could act by directly stimulating the pulmonary terminations of the vagi.

More recently Lumsden (1923) advanced the theory that in easy breathing the vagal endings are stimulated by the air currents passing in and out over the ciliated tracheal mucous membrane. Lumsden, however, admits that extreme distention and collapse of the lungs give rise to vagal impulses of a different kind.

It is obvious from this brief review of the literature that our knowledge of the true character of the Hering-Breuer stimulus is incomplete.

Method.

The method used is similar to the one described by Churchill and Agassiz (1926). It permits separate recording of the respiratory movements of each lung. Two brass tubes serve to divide the trachea into two separate compartments. The tubes are 14 and 22 cm. long and both have an internal diameter of 6 mm. The longer one is ligated in the bronchus on one side. The shorter extends downward to the opposite bronchus, but does not necessarily enter it. Each cannula connects with a separate respiration system including inspiratory and expiratory valves, soda lime for removing CO_2, and a small spirometer for recording the changes in respiratory movements. Tracings of the respiratory curves were made by equipping the spirometers with writing pens. Dogs anesthetized with barbital-sodium were used, as previously described (Moore and Binger (1927)).

The operative procedure was the same in all experiments. When satisfactory anesthesia had been obtained the trachea was exposed in the neck and the right and left vagus trunks were isolated. The trachea was then opened and the metal tubes introduced and temporarily anchored in place by a ligature. After this mechanical respiration was provided separately for each lung by forcing air intermittently under slight presure into the two tubes. The air escaped through one branch of a Y-shaped tube connected with the system. The dog was placed on the side with the forelegs extended and the thorax was opened through the 5th intercostal space, right or left as the occasion demanded. During the operative procedures within the thorax the ribs were held apart by a mechanical retractor and the lungs retracted from the field by cotton packs soaked in warm, physiological sodium chloride solution. In isolating the bronchus blunt dissection was used

as much as possible in order to lessen the danger of nerve injury. After placing a ligature beneath the bronchus the long cannula was manipulated into position, and tied firmly in place. Expansion of all lobes subsequent to this indicated that the correct position had been obtained. The further procedure depended on the nature of the experiment and will be mentioned in the descriptions of the individual experiments. Before completely closing the thorax the lungs were expanded to expel the air from the chest. Closure was accomplished by suturing the intercostal muscles. Placing of ligatures about the ribs was purposely avoided for fear of limiting the free motion of the thoracic wall. When closure was complete the opening in the trachea was made tight after the manner described by Churchill and Agassiz, and the animal connected with the two respiration systems. All animals breathed 90 to 95 per cent oxygen throughout the period of observation. During operation the animals were kept warm by an electric pad and the rectal temperature was recorded at repeated intervals. During the period of observation the animals were surrounded by warm air.

EXPERIMENTAL.

I. The Effect of Cutting One Vagus Nerve on the Respiratory Movements of Each Lung.

Schafer (1919) calls attention to the possibility of vagal section leading to a collapse of the smaller bronchial tubes from paralysis of their muscular layer. If such were the case, cutting the vagus nerve on one side might seriously interfere with the passage of air into and out of the respiratory bronchioles of the lung on the side of vagal section. Under these conditions one would expect less air to enter the lung, the vagus of which has been divided. The following experiment (No. 1) was made to test this point.

Experiment 1.—An animal, anesthetized with barbital-sodium, breathed during the control period at the rate of 28 per minute. The tidal air of the right lung was 44 cc. and the tidal air of the left lung was 56 cc. Immediately following section of the right vagus nerve the respiratory rate dropped to 14, the tidal air of the right lung rose to 55 cc., and the tidal air of the left lung to 72 cc. These figures show that unilateral vagotomy was accompanied by an increase in the tidal air of both lungs. A similar, but exaggerated response was noted after cutting the left vagus. When the left vagus was cut the right and left lungs showed an increase in tidal air to 100 and 138 cc., respectively. The experimental data are brought out in Table I and the respiratory curves are reproduced in Fig. 1.
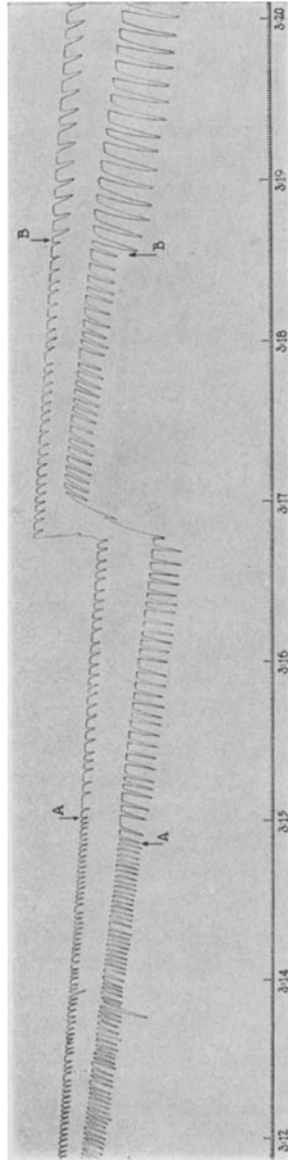
Fig. 1. Experiment 1. Effect of cutting one vagus nerve on the respiratory movements of each lung. The curve passes from left to right. Upper tracing made by the right lung. Lower tracing made by the left lung. Inspiration down and expiration up in both tracings. In the upper tracing an excursion of 0.9 cm. represents a 100 cc. change in the volume of the recording spirometer. In the lower tracing, written by a smaller spirometer, a volume change of 100 cc. causes an excursion of 1.88 cm. At A the right vagus nerve was cut. The effect was a slowing and deepening of the respirations of both lungs. At B the left vagus nerve was cut. The effect was the same, but more pronounced. Time in seconds.

This experiment was repeated, and similar results were obtained.

As a corollary to these experiments, the effect of partial obstruction of the bronchus of one lung on the tidal air of each lung has been studied. The right bronchus was gradually occluded by means of a specially constructed metal tap, previously described by us (Moore and Binger, 1927) which was introduced into the system between the bronchial cannula and the respiration valves. Blalock, Harrison, and Wilson (1926) found, in their studies on morphinized dogs, that partial obstruction of the trachea in both phases of respiration causes slow, shallow breathing. In the light of these findings it was anticipated

TABLE I.

Experiment 1. The Effect of Cutting One Vagus Nerve on the Respiratory Movements of Each Lung.

Weight of dog, 17.5 kilos. Total barbital-sodium, 0.33 gm. per kilo body weight.

Time	Procedure	Respiratory rate per minute	Tidal air	
			Right lung	Left lung
			cc.	cc.
3.12	Dog breathing 90–95 per cent O$_2$ throughout experiment	28	44	56
3.14		28	44	56
3.15	Cut right vagus			
3.15+		14	55	72
3.17		15	51	64
3.18+	Cut left vagus			
3.19		9	100	138

that resistance to the passage of air into and out of one lung would decrease the depth of respiration of the lung on the side of the resistance and probably increase the depth of breathing of the opposite lung. In Experiment 2, Fig. 2, during the period of resistance on the right side the tidal air of the right lung dropped from 61 to 20 cc., whereas the tidal air of the left lung increased from 79 to 116 cc. Similar results were obtained on two other occasions.

The results of the experiments in this group, then, may be summarized as follows: The effect of unilateral vagotomy on the character of

breathing is the same in both lungs, namely: There occurs an equivalent slowing and deepening of respiratory movement. This would suggest that the variation in respiratory movement that follows vagal section is not due directly to local changes in the lungs. The evidence rather supports the view that is now generally held, namely, that cutting the vagus nerves blocks peripheral impluses that reflexly modify the character of breathing. The results that we obtained are in harmony with Einthoven's (1892) experiments. Einthoven measured the changes in intratracheal pressure in anesthetized dogs when artificial respiration was provided by blowing in and sucking out a constant volume of air at each respiration. In six experiments the changes in intratracheal pressure after cutting the vagus nerves were as follows: Three animals showed a drop that was less than 1 mm. H_2O, and the other three animals showed decreases of 7, 24, and 2 mm. H_2O, respectively. Einthoven accepted these findings as evidence that section of the vagus nerves does not cause any noticeable change in the cross-section area of the bronchioles. He concluded that, when the bronchial muscles are at rest, the vagi exert little or no tonic effect upon them.

II. The Effect of Blocking One Bronchus on the Respiratory Movements Recorded by the Opposite Lung.

In four experiments, using the technique described, the bronchus to one lung was completely obstructed while obtaining graphic tracings of the respiratory movements of the opposite lung. In each instance the right bronchus was the one blocked. The result of this manœuver was a slowing and deepening of the respirations in the functioning lung. On three occasions, after a brief interval, the animals became anoxemic and the respirations accelerated. This may be seen in Experiment 3, Fig. 3, and in Experiment 4, Fig. 4. Having established the type of response to obstruction of one bronchus we were then in a position to study the effects of this plus vagotomy on the corresponding side. This will be dealt with presently.

In the meanwhile, it should be incidentally mentioned that the response of the functioning lung was influenced by the position of the opposite lung at the time its bronchus was blocked. When the right bronchus was blocked at the end of expiration the next movement of

the left lung was a relatively deep inspiration (Fig. 4); when, on the other hand, the right bronchus was blocked at the end of inspiration, the next movement of the left lung was a relatively deep expiration (Fig. 3).
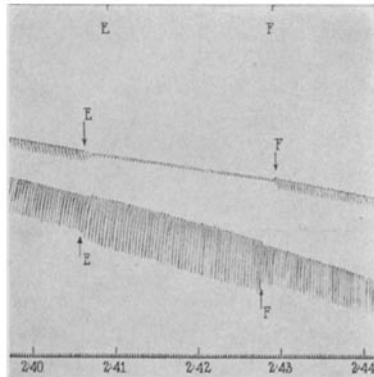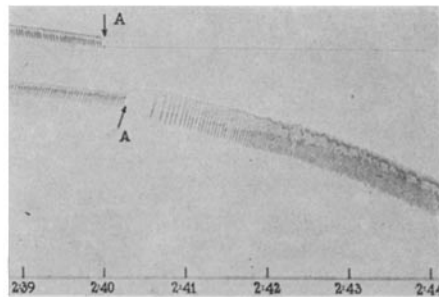

FIG. 2.

FIG. 3.

FIG. 2. Experiment 2. Effect of partial occlusion of the right bronchus on the respiratory movements of each lung. The curve passes from left to right. Upper tracing made by the right lung. Lower tracing made by the left lung. Inspiration down and expiration up in both tracings. In the upper tracing an excursion of 0.9 cm. represents a 100 cc. change in the volume of the recording spirometer. In the lower tracing, written by a smaller spirometer, a volume change of 100 cc. causes an excursion of 1.88 cm. At E the cross-section area of the top was finally reduced to 0.1 sq. cm. This caused the tidal air of the right lung to decrease from 56 to 20 cc. and the tidal air of the left lung to increase from 87 to 116 cc. At F the obstruction was removed and the tidal air of each lung returned immediately to the control level. Time interval 2 seconds.

FIG. 3. Experiment 3. Effect of blocking the right bronchus on the respiratory movements recorded by the left lung. The curve passes from left to right. Upper tracing made by the right lung. Lower tracing made by the left lung. Inspiration down and expiration up in both tracings. In the upper tracing an excursion of 0.9 cm. represents a 100 cc. change in the volume of the recording spirometer. In the lower tracing, written by a smaller spirometer, a volume change of 100 cc. causes an excursion of 1.88 cm. At A the right bronchus was completely occluded at the end of inspiration. The next movement of the left lung was a deep expiration. The respiratory rate immediately slowed, but within 3 minutes accelerated to 38, 11 breaths above the control level. Time in seconds.
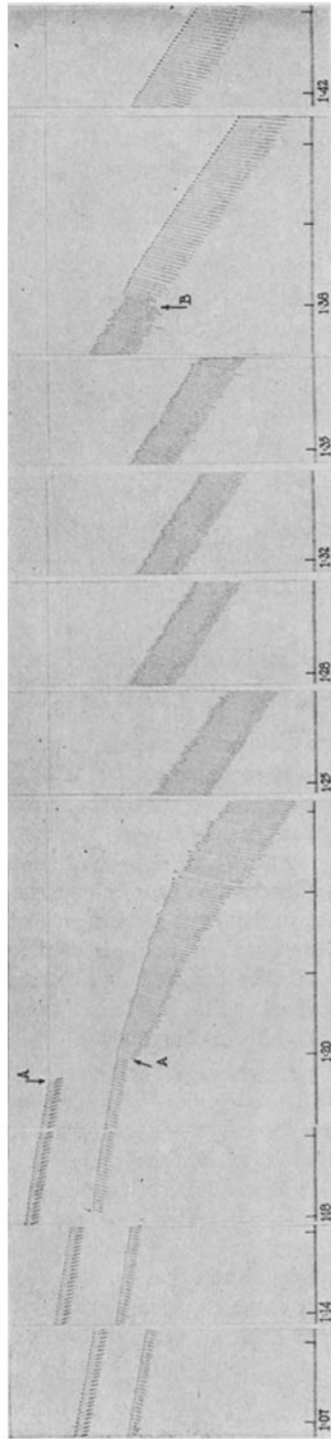
Fig. 4. Experiment 4. Effect of occlusion of the right bronchus plus right sided vagotomy on the ventilation of the left lung. The curve passes from left to right. Upper tracing made by the right lung. Lower tracing made by the left lung. Inspiration down and expiration up in both tracings. In the upper tracing an excursion of 0.9 cm. represents a 100 cc. change in the volume of the recording spirometer. In the lower tracing, written by a smaller spirometer, a volume change of 100 cc. causes an excursion of 1.88 cm. At A the right bronchus was blocked at the end of expiration. The next movement of the left lung was a deep inspiration. The respiratory rate immediately slowed, but after 5 minutes had accelerated to 34, 13 breaths above the control level. At B the right vagus nerve was cut. The respirations immediately became slower and deeper. Time in seconds.

828

III. The Effect of Occlusion of the Right Bronchus Plus Right Sided Vagotomy on the Ventilation of the Left Lung.

The object of this procedure was to learn whether or not the characteristic response of unilateral vagotomy, which we have just described, is influenced by the motions of the lung, the vagus of which has been sectioned. It has previously been assumed that the Hering-Breuer reflex is set off by the alternate expansion and collapse of the lungs.

TABLE II.

Experiment 4. The Effect of Occlusion of the Right Bronchus Plus Right Sided Vagotomy on the Ventilation of the Left Lung.

Weight of dog, 20 kilos. Total barbital-sodium, 0.32 gm. per kilo body weight.

Time	Procedure	Respiratory rate per minute	Tidal air	
			Right lung	Left lung
			cc.	*cc.*
1.07	Dog breathing 90–95 per cent O₂ throughout experiment	21	86	27
1.14		22	86	30
1.18		21	86	30
1.19+	Right bronchus blocked			
1.20			0	56
1.22		26	0	159
1.25		34	0	127
1.28		35	0	114
1.32		35	0	109
1.35		32	0	109
1.38	Right vagus divided with scissors			
1.39		22	0	116
1.42		24	0	130

The experiments described under this heading were designed for the purpose of inquiring into this point. It is admitted that their somewhat complicated and unnatural character is objectionable, but, by them, we were able to observe the respiratory movements of one relatively normal lung while its fellow was rendered functionless by blocking its bronchus and cutting or freezing its vagus nerve. Four experiments of this type were performed, of which one is reported in

more or less detail. In two the vagus nerves were cut; in the other two frozen. Both methods gave similar results.

Experiment 4.—In this experiment, during the control period, the animal breathed at the rate of 21 per minute. The tidal air of the right lung was 86 cc. and the tidal air of the left lung was 30 cc. When the right bronchus was blocked the tidal air of the left lung increased to 56 cc. with the very next breath. 2 minutes later it had risen to 159 cc. The respiratory rate slowed immediately after the bronchus was blocked, but within 3 minutes increased to 26. 3 minutes after this the animal was cyanotic, the rate had accelerated to 34, and the tidal

TABLE III.

Experiment 5. The Effect of Occlusion of the Right Bronchus Plus Right Sided Vagotomy on the Ventilation of the Left Lung after Division of the Right Phrenic Nerve.

Weight of dog, 11 kilos.   Total barbital-sodium, 0.35 gm. per kilo body weight.

Time	Procedure	Respiratory rate per minute	Tidal air	
			Right lung	Left lung
			cc.	*cc.*
12.35	Dog breathing 90–95 per cent O₂ throughout experiment	32	20	30
12.38		32	20	35
12.39	Right bronchus blocked			
12.41		38	0	41
12.44		38	0	36
12.46	Section of right vagus			
12.47		29	0	38
12.53		27	0	38
12.59		24	0	40
1.03		23	0	40

air of the left lung had decreased to 127 cc. 10 minutes later the respiratory rate was 32 and the tidal air of the left lung was 109 cc. At this point the right vagus was cut. The rate immediately dropped to 22 and the tidal air of the left lung increased to 116 cc. During the next 3 minutes the tidal air of the left lung increased to 130 cc. These changes are brought out in Table II and Fig. 4. *They show that the response to one sided vagotomy is not altered by previously preventing respiratory motions in the vagotomized lung.* This is opposed to the view which is generally held as to the nature of the Hering-Breuer reflex.

Before drawing conclusions from our own observations we must consider two possibilities which may be of importance. First, does

blocking the bronchus actually prevent lung motion?   Second, could
the slowing of respirations be explained on the basis of crossed inner-
vation of the vagus fibres?

That lung motion is prevented by blocking the bronchus is probably
true, since all access of air to the lung has been excluded, and since
at autopsy the occluded lung presents a picture of complete collapse.
It is unlikely that an atelectatic lung could follow the movements of
the diaphragm and chest wall.   In this connection an experiment
(No. 5) was performed in which the expansion of the right lung was
severely limited from the start by cutting the right phrenic nerve in
the chest.   Presumably the limited expansion was due to partial or
complete paralysis of the right half of the diaphragm.   Under these
conditions the tidal air of the right lung was only 20 cc.   The tidal air
of the left lung was 35 cc.   The respiratory rate was 32.   The dog
was anoxemic as indicated by the dark color of its tongue.   5 minutes
after blocking the right bronchus the respiratory rate was 38 and the
tidal air of the left lung was 36 cc.   The right vagus nerve was cut at
this point.   The rate immediately slowed, but the amplitude of the
respirations of the opposite lung was practically unaltered.   The
results of this experment are presented in Table III.   With air unable
to enter the lung, and with the right half of the diaphragm paralyzed,
it is difficult to conceive that there could have been any lung motion.
Nevertheless, the respiratory rate slowed when the right vagus was
cut.   The experiment is of additional interest because it shows that
slowing of respirations which follows after occlusion of the right bron-
chus and section of the right vagus nerve still occurs even though the
phrenic nerve on the same side has been divided.   This indicates that
the slowing of respirations following unilateral vagotomy does not
depend upon the interruption of impulses arising from the contraction
and relaxation of the diaphragm.

Regarding the second possibility, the existence of crossed vagal
innervation has been recognized for some time.   This has recently
been demonstrated for the sensory fibres by Larsell (1921).

To control the influence of crossed innervation on our results, we
have devised a technique whereby the vagal fibres to the left lung were
divided at the hilum.   By this procedure we were able to observe
the effect of right sided bronchial occlusion and vagotomy on the

TABLE IV.

*Experiment 6. The Effect of Occlusion of the Right Bronchus Plus Right
Sided Vagotomy after Division of the Pulmonary Branches
of the Left Vagus Nerve.*

Weight of dog, 18.5 kilos.   Total barbital-sodium, 0.3 gm. per kilo body weight.

Time	Procedure	Respiratory rate per minute	Tidal air	
			Right lung	Left lung
			cc.	*cc.*
3.13	Dog breathing 90–95 per cent O₂ throughout experiment	22	64	64
3.17		22	66	67
3.18	Right bronchus blocked			
3.19		24	0	118
3.22		32	0	128
3.24		33	0	112
3.30	Section of right vagus			
3.33		16	0	160
3.35		19	0	155

TABLE V.

*Experiment 7. The Effect of Occlusion of the Right Bronchus Plus Right
Sided Vagotomy after Division of the Pulmonary Branches
of the Left Vagus Nerve.*

Weight of dog, 17.5 kilos.   Total barbital-sodium, 0.3 gm. per kilo body weight.

Time	Procedure	Respiratory rate per minute	Tidal air	
			Right lung	Left lung
			cc.	*cc.*
2.49	Dog breathing 90–95 per cent O₂ throughout experiment	47	40	14
2.51	Right bronchus blocked			
2.52		37	0	66
2.55		43	0	66
2.58		40	0	66
3.00	Section of right vagus			
3.01		27	0	105

motions of the left lung, which had been previously denervated with
respect to its vagal fibres. There could, therefore, be no question
of crossed innervation. This experiment was done twice with identi-

cal results, which are presented in Tabes IV and V. The upshot of these experiments was entirely analagous to that of our previous ones, showing that crossed innervation of vagal fibres was not responsible for the results obtained.

IV. Is the Response to Unilateral Vagotomy Dependent upon an Intact Pulmonary Circulation?

We have seen thus far that the slowing and deepening of the respiratory movements of one lung, when the vagal impulses from the other
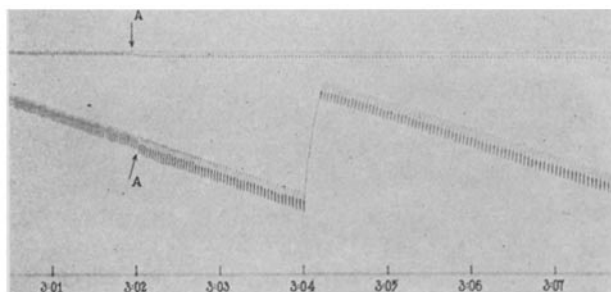

FIG. 5. Experiment 8. Effect of cutting the right vagus nerve on the respiratory movements of each lung after ligation of the right pulmonary artery. The artery was ligated within the pericardium. The curve passes from left to right. Upper tracing made by the right lung. Lower tracing made by the left lung. Inspiration down and expiration up in both tracings. In the upper tracing an excursion of 0.9 cm. represents a 100 cc. change in the volume of the recording spirometer. In the lower tracing, written by a smaller spirometer, a volume change of 100 cc. causes an excursion of 1.88 cm. During the control period the tidal air of the right lung was 30 cc. and the tidal air of the left lung was 36 cc. At A the right vagus nerve was divided. The respirations of each lung immediately became slower and deeper. Time in seconds.

lung are intercepted, does not depend upon the motions of the vagotomized lung nor upon the existence of crossed innervation of vagal fibres. It remained to discover whether blocking the circulation of blood through the pulmonary artery of the vagotomized lung would influence the response of the other lung to vagal section. The reason for regarding this as a possibility was thought to lie in the statement encountered from time to time in the literature, and pre-

viously alluded to, that the vagal endings in the lung are locally
sensitive to carbon dioxide.   Indeed, a mechanism has been suggested
wherein the fluctuation in tension of alveolar carbon dioxide has been
conceived as the excitatory stimulu for the Hering-Breuer reflex.
Adequate experimental evidence for the existence of such a mechanism
is, however, not at hand.   By obstructing the flow of blood through
the pulmonary artery of the lung whose vagus was subsequently
divided, we rendered this lung functionless in respect to its gas
exchange.   No normal fluctuations in the alveolar carbon dioxide
tension of such a lung could occur and in time the alveolar carbon
dioxide tension would be much reduced.   In Experiment 8 (Fig. 5)
samples of alveolar air were withdrawn from each lung a few minutes
after the vagus nerve had been cut.   This was accomplished by pass-
ing a small catheter deep into the bronchus and collecting the gas in
sampling tubes.   The air from the left lung contained 7.18 per cent of
carbon dioxide, whereas that from the right, whose pulmonary artery
had been ligated, contained only 1.16 per cent of carbon dioxide.   It
was found that vagotomy under these circumstances resulted in the
same slowing and deepening of respirations recorded by the other lung,
as occurred when the pulmonary circulation to the vagotomized lung
was intact.   This is shown in Fig. 5.   It may be concluded, therefore,
that the characteristic results of unilateral vagotomy do not depend
upon an intact pulmonary circulation.

DISCUSSION.

In the introduction of this paper we described the experiments of
several investigators to illustrate the point that a rapid respiratory
rate, experimentally produced in animals, disappears immediately if
the vagus nerves are divided.   Our own experiences in this field had
led us for some time to attach more and more importance to the local
excitation of vagal nerve endings in the lungs as the most likely expla-
nation of the rapid rates.   The literature on this subject was convinc-
ing in only one respect, namely, that excitation of the pulmonary
terminations of the vagus nerves is related to the alternate expansion
and collapse of the lungs.   The experiments that we have described
are unique in having shown that the vagal influence is still present
after lung motion has been prevented.   In this respect they modify

our knowledge of the nervous control of breathing. The experiments are incomplete in that they do not explain the origin of the reflex that we have studied.

The inferences drawn from our experiments are sound in so far as one is willing to admit that the slowing and deepening of respirations that follow unilateral vagotomy indicate an interruption of afferent impulses that normally travel this path. One will avoid confusion in following the argument by constantly bearing in mind that the slowing and deepening of breathing after vagotomy means, we believe, that a normal reflex has been interrupted.

SUMMARY AND CONCLUSIONS.

1. Cutting one vagus nerve, while recording the pulmonary ventilation of each lung separately, has no unique effect on the ventilation of the denervated lung. Both lungs respond to unilateral vagotomy by an equivalent slowing and deepening of respiratory movement.

2. When the bronchus to one lung is blocked the first effect is a slowing and deepening of the respiratory movements recorded by the opposite lung. As oxygen want develops these movements become rapid and shallow.

3. With a combination of these two conditions, i.e., when the bronchus to one lung is blocked and its vagus nerve is severed, the pulmonary ventilation recorded by the opposite lung exhibits the same changes as may result from unilateral vagotomy alone, unaccompanied by occlusion of the bronchus.

4. From these facts it may be concluded that the slowing and deepening of breathing which follows unilateral vagotomy does not depend for its occurrence upon the passage of air in and out of the bronchus of the lung whose vagus nerve has been sectioned.

5. The slowing of respirations after occlusion of the bronchus to one lung and section of the corresponding vagus nerve still occurs even though the phrenic nerve on the same side has been divided. This indicates that the slowing of respirations following unilateral vagotomy does not depend on the movements of the diaphragm on the side of vagal section.

6. When the pulmonary artery to one lung has been ligated and the vagus nerve on the same side cut, the response of the other lung is the

same as has been described, namely, its respiratory movements become slower and deeper. This is taken as evidence that the results of unilateral vagotomy are not dependent upon an intact pulmonary circulation.

7. The general conclusions from these experiments are that the slowing and deepening of respirations following unilateral vagotomy do not depend upon: (a) Passage of air in and out of the trachea. (b) Expansion and collapse of the lung. (c) Existence of a normal pulmonary circulation in the vagotomized lung. (d) Normal fluctuations in alveolar carbon dioxide tension. (e) Contraction and relaxation of the diaphragm on the side of vagotomy.

8. The slowing and deepening of respirations, alluded to, may be presumed to indicate that a normal reflex (the Hering-Breuer reflex) has been interrupted. Since this interruption occurs in spite of all the conditions enumerated under Paragraph 7, we must conclude that none of these conditions is essential to the existence of this reflex.

I take great pleasure in expressing thanks to Dr. Carl A. L. Binger for valuable suggestions, and for his helpful interest in the course of this investigation.

BIBLIOGRAPHY.

Binger, C. A. L., Brow, G. R., and Branch, A., *J. Clin. Inv.*, 1924, i, 127.

Binger, C. A. L., and Moore, R. L., 1926, unpublished experiments.

Blalock, A., Harrison, T. R., and Wilson, C. P., *Arch. Surg.*, 1926, xiii, 81.

Boothby, W. M., and Berry, F. B., *Am. J. Physiol.*, 1915, xxxvii, 433.

Christiansen, J., and Haldane, J. S., *J. Physiol.*, 1914, xlviii, 272.

Churchill, E. D., and Agassiz, A., *Am. J. Physiol.*, 1926, lxxvi, 6.

Dunn, J. S., *Quart. J. Med.*, 1920, xiii, 129.

Einthoven, W., *Arch. ges. Physiol.*, 1892, li, 367.

Einthoven, W., *Arch. ges. Physiol.*, 1908, cxxiv, 246; *Quart. J. Exp. Physiol.*, 1908, i, 243.

Haldane, J. S., and Mavrogordato, A., *J. Physiol.*, 1916, l, p. xli.

Haldane, J. S., Respiration, New Haven, 1922, 46.

Head, H., *J. Physiol.*, 1889, x, 1.

Hering, E., and Breuer, J., *Sitzungsber. k. Akad. Wissench., Math.- naturw. Cl., Wien*, 1868, lvii, pt. 2, 672; lviii, pt. 2, 909.

Larsell, O., and Mason, M. L., *J. Comp. Neurol.*, 1921, xxxiii, 509.

Legallois, C. J. J., *Expériences sur la principe de la vie*, Paris, 1812.

Lumsden, T., *J. Physiol.*, 1923, lviii, 111.

Moore, R. L., and Binger, C. A. L., *J. Exp. Med.*, 1927, xlv, 1065.

Porter, W. T., and Newburgh, L. H., *Am. J. Physiol.*, 1916, xlii, 175.

Porter, W. T., and Newburgh, L. H., *Am. J. Physiol.*, 1917, xliii, 455.

Schafer, E. S., *Quart. J. Exp. Physiol.*, 1919, xii, 231.

Scott, F. W., *J. Physiol.*, 1908, xxxvii, 301.

Suñer, P. A., and Bellido, J. M., *J. phys. et path. gén.*, 1921, xix, 214.

Traube, L., *Ges. Beitr. Path. u. Physiol.*, 1871, ii, 882.