THE RELATION BETWEEN RESPIRATION AND THE PULSE-RATE.

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It is well known that a close relationship usually (though not invariably) exists between the degree of activity of the respiratory centre and the rate of the pulse. In man, for example, the dyspnœa induced by breathing air containing a slight excess of carbonic acid is often associated with considerable acceleration of the pulse-rate. Several explanations of this relationship have been put forward. Traube suggested that, when the respiratory centre is unusually active, an overflow or irradiation of impulses from the respiratory to the cardio-inhibitory centre takes place and that these impulses lessen the tone of the cardio-inhibitory centre. This view was supported by the observation of Frédéricq that, when the chest was open and the lungs collapsed, the frequency of the pulse varied synchronously with the respiratory efforts made by the animal. On the other hand, Hering's observations led him to conclude that afferent impulses passing from the lungs to the cardio-inhibitory centre reflexly alter the pulse-rate, and that such impulses, set up by distension or collapse of the lungs, are responsible for the inspiratory quickening and expiratory slowing of the pulse often observed in animals. This conclusion was accepted by Brodie who found that stimulation of the central end of the pulmonary branches of the vagi caused inhibition of the heart. Another possibility is that increased respiratory movements influence the pulse-rate mainly or entirely by increasing the return of blood to the heart, thereby evoking reflex acceleration of the heart.

The experiments described in this paper were carried out in order to determine first how far each of these explanations holds good and, second, to what extent the respiratory system is concerned in the regulation of the pulse-rate.

Methods. Almost all the experiments were carried out on cats anæsthetised with ether; a few observations were made on dogs anæsthetised

with chloroform and ether after a preliminary dose of morphia. The chest was widely opened and the phrenic nerves cut in order to exclude as far as possible the mechanical influence of the respiratory movements on the circulation. Artificial respiration was maintained by means of a pump, and the degree of ventilation of the lungs was usually recorded by connecting a side tube on the tracheal cannula with a recording tambour. The composition of the air blown into the lungs could be varied by attaching a bag containing the desired mixture of gases to the inlet tube of the respiration pump. The respiratory movements made by the animals were recorded by attaching a thread to the chest wall; the other end of the thread was attached to a recording lever or tambour. As a rule, either the stellate ganglia were removed or the cardiac accelerated nerves were divided.

Except where otherwise stated the upper tracing in each figure represents the respiratory movements of the chest wall, the middle tracing indicates the blast of the respiration pump, and the lower tracing records the arterial pressure. The time marker records periods of ten seconds. The numbers placed either below the blood-pressure tracing or just beneath the record of the respiratory pump indicate the pulse-rate at that moment.

Results.

The observations to be described fall into two main groups. The first consists of experiments relating to the possibility of irradiation of impulses from the respiratory to the vagus centre; the second includes experiments carried out to determine whether distension and collapse of the lungs gives rise to afferent impulses travelling up the vagi to the vagus centre, and reflexly modifying its tone.

Irradiation from the respiratory centre. The activity of the respiratory centre was excited, or increased, by raising the tension of carbonic acid in the blood, and several methods were adopted for this purpose. In some experiments the blast of the respiration pump was kept constant, and a small amount of carbonic acid was added to the air blown into the lungs (Fig. 1). In others, in confirmation of experiments previously described (2), the blast of the pump was reduced so as to cause very slight inflation of the lungs, oxygenation of the blood being maintained by blowing into the lungs air containing a very large percentage of oxygen. In other experiments again the artificial respiration was almost stopped for a short time (Fig. 2).

Although each of these procedures led to a striking increase in the activity of the respiratory centre, as measured by the respiratory movements of the chest-wall, the pulse-rate was unaffected for a time, as is seen in Figs. 1 and 2; as the respiratory efforts became increasingly violent, marked slowing of the pulse took place. It was necessary, when carbonic acid was being blown into the lungs, to keep its percentage very low; if a large percentage of carbonic acid was blown into the lungs, the

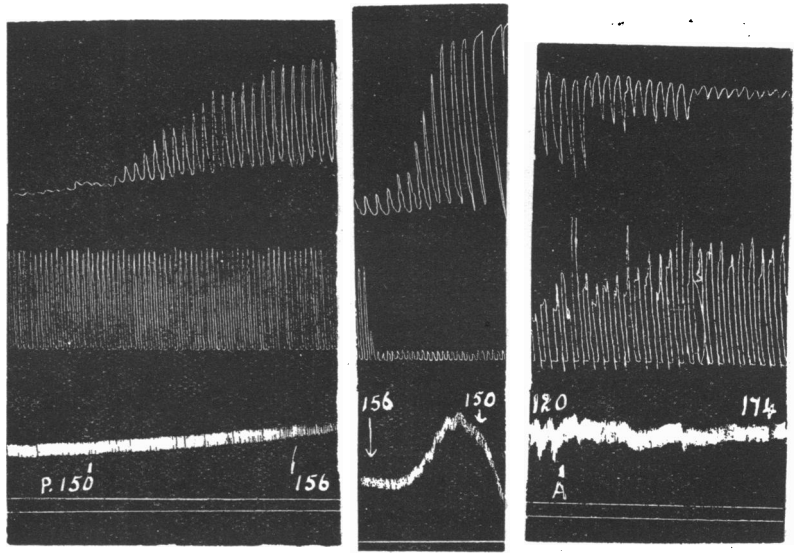

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Fig. 1. Effect of adding CO_2 to the air entering the lungs. Top tracing = resp. efforts, B.P. 90–95 mm. Hg.

Fig. 2. Effect of asphyxia. Top tracing = resp. efforts. B.P. at onset of asphyxia = 94 mm. Hg.

Fig. 3. At A the blast of the pump was gradually increased. B.P. = 110 to 115 mm Hg.

respiratory movements at once became very violent and the pulse-rate immediately became very slow. In all the experiments just described the presence of vagus tone, and therefore the possibility of acceleration of the pulse-rate, was demonstrated either by subsequent section of the vagi or by other means. Apart from the experiments in which asphyxia was produced, the arterial pressure and the pulse-pressure remained almost steady, and no evidence was obtained that the respiratory

efforts made by the animal appreciably affected the return of blood to the heart unless these efforts became almost convulsive in character.

These experiments show that, when the influence of the respiratory movements on the circulation is excluded, even marked and exaggerated activity of the respiratory centre, such as would normally manifest itself as severe dyspnœa, does not give rise to an overflow or irradiation of impulses to the cardio-inhibitory centre of such a kind as to lessen the tone of this centre. The cause of the slowing of the pulse-rate associated with very violent respiratory efforts will be discussed subsequently.

Afferent impulses from the lungs. In confirmation of Yandell Henderson's observation it was found that vigorous artificial ventilation of the lungs invariably brought about considerable acceleration of the pulse-rate and abolished the activity of the respiratory centre (Fig. 3).

The suggestion that the over-ventilation of the lungs mechanically interferes with the flow of blood through the lungs, and that the acceleration of the pulse is secondary to the changes in the circulation naturally presents itself in the first instance. Although excessive pulmonary ventilation undoubtedly obstructs the flow of blood through the lungs, it is possible, when the chest is opened and the lungs can expand freely, to carry out fairly vigorous artificial respiration and yet to avoid any material disturbance of the circulation. If the blast of the pump is carefully regulated the lungs can be considerably over-ventilated without producing any appreciable change in the arterial pressure and the pulse pressure, and with a comparatively small rise in the venous pressure. In a few experiments the pressure in the superior vena cava was noted, and it was found that even fairly vigorous artificial respiration raised the pressure by only a few mm. of water. It is probable, therefore, that mechanical interference with the circulation in these experiments plays a comparatively subsidiary part in bringing about the acceleration of the pulse, though its influence cannot always be entirely excluded.

Apart from the mechanical factor, there are two possible explanations of the acceleration of the pulse brought about by over-ventilation of the lungs. The first is that the acceleration may be reflex in origin and dependent on the presence in the lungs of afferent fibres travelling up the vagus to the cardio-inhibitory centre, and that distension of the lungs sets up impulses which pass along these fibres and reflexly lessen the tone of the cardio-inhibitory centre. The second is that the alteration in the reaction of the blood, consequent on the over-ventilation of the lungs, directly affects the tone of the cardio-inhibitory centre.

For the purpose of deciding between these two possibilities, Brodie and Russell's experiments on the effect of stimulating the central end of the pulmonary branches of the vagi were repeated. These observers exposed the pulmonary vagi by resecting the sixth to the ninth ribs from the sternum to the vertebral column, usually on one side, in the dog. Stimulation of the different branches passing from the lungs to the vagus trunk led to slowing of the heart and inhibition of respiration; and comparatively weak stimuli were effective. In the present enquiry six experiments have been made on this point, four in cats and two in

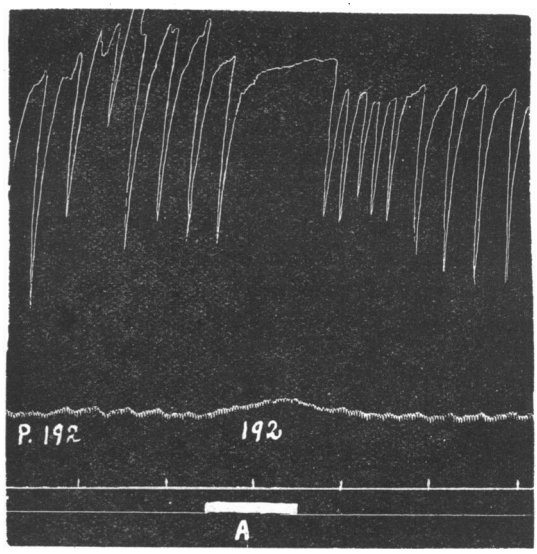

Fig. 4. Dog. Upper tracing = resp. efforts. B.P. 105 mm. Hg. At A the central end of the left pulmonary vagus was stimulated with a fairly strong current.

dogs; the chest was widely opened and the pulmonary nerves were exposed as they left the vagi to enter the lungs. On the left side the pulmonary branches leave the main vagus trunk just at or below the top of the aortic arch; on the right side they leave the vagus below the azygos vein. In the dog the nerves are sufficiently large to be dissected out and stimulated separately. The nerves in the cat are so slender that a different procedure was adopted. The vagus was divided below the lungs, and the central end of the vagus was stimulated just above the point at which the pulmonary fibres joined it and below the point at which the lowest cardiac fibres left the vagus trunk; for this purpose a

sufficient length of the vagus trunk is available, especially on the right side. In every experiment the pulmonary vagal branches were stimulated on both sides.

In the dog, stimulation of the central end of the pulmonary branches of the vagi caused absolutely no change in the pulse-rate, although the respiratory movements were completely inhibited (Fig. 4). The result

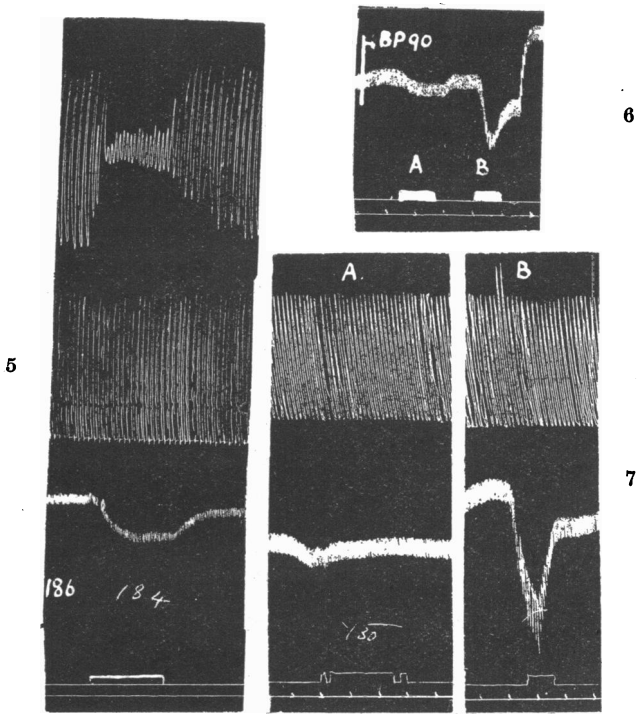

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Fig. 5. Cat. B.P. = 100 mm. Hg. Stimulation of right pulmonary vagus (central end). Upper tracing represents respiratory movements of the chest-wall.

Fig. 6. Cat. A, stimulation of right pulmonary vagus low down. B, electrodes moved up nearer the cardiac branches of the vagus.

Fig. 7. A, stimulation of left pulmonary vagus (central end). B, stimulation of left vagus (central end) in the neck.

was negative whatever the strength of current used. In the cat also, stimulation of the vagus just above the point at which the pulmonary fibres joined it, while inhibiting respiration, had no effect on the pulse-rate (Fig. 5), provided that care was taken not to use a very strong current and not to apply the electrodes too near the point at which the cardiac nerves leave the main vagus trunk; in the latter case some

slowing of the heart took place and was presumably due to escape of current. For example, in the experiment illustrated in Fig. 6 stimulation of the right pulmonary vagus as low down as possible (A) had no effect on the pulse-rate; when the electrodes were moved up nearer to the cardiac fibres inhibition of the heart took place (B). That the reflex path for cardiac inhibition had not been disturbed during the operative procedure involved in the experiments was always demonstrated either by subsequently cutting one vagus in the neck and stimulating its central end (Fig. 7 B) or by applying the electrodes to the central end of the cardiac branches of one vagus.

Some experiments were also made to determine the effect on the pulse-rate of over-ventilation of the lungs after section of the pulmonary branches of the vagi. It is obvious that, if the acceleration of the pulse is brought about by afferent impulses passing from the distended lungs to the cardio-inhibitory centre and lessening its tone, the effect should be abolished by cutting the pulmonary branches of the vagi. The experiments showed, however, that vigorous artificial respiration produced acceleration of the pulse equally well whether the pulmonary branches of the vagi were intact or had been divided. The result of a typical experiment is shown in the following protocol:

Cat; ether anæsthesia. Chest widely open and phrenic nerves divided; artificial respiration.

			Blast of pump	
			moderate	vigorous
(1) Vagi intact	Pulse-rate	(*a*)	144	192
		(*b*)	128	180
(2) Pulmonary branches of vagi divided	Pulse-rate	(*a*)	120	160
		(*b*)	120	180

The evidence just detailed definitely points to the conclusion that no afferent fibres pass (in the vagi) from the lungs to the cardio-inhibitory centre, and that, consequently, distension or deflation of the lungs does not give rise to impulses capable of reflexly bringing about an alteration in the pulse-rate.

The observation that vigorous artificial respiration leads to acceleration of the pulse-rate even after section of the pulmonary vagi suggests that the altered reaction of the blood, consequent on the washing out of carbonic acid from the blood, is responsible for the increased pulse-rate. Direct evidence in favour of this view was furnished by experiments in which vigorous artificial respiration was carried out, a small amount of carbonic acid being added to the air blown into the lungs. The amount of carbonic acid sent into the lungs was so adjusted as to compensate approximately for the over-ventilation and thus to prevent the washing

out of carbonic acid from the blood. Under these conditions, the activity of the respiratory centre and presumably the reaction of the blood were unaffected by the over-ventilation of the lungs. After a short time the blast of the pump was reduced and atmospheric air was once more blown into the lungs. The pulse-rate remained the same before, during, and after, the period of over-ventilation. This is shown in Fig. 8 which represents the transition from vigorous artificial respiration, carbonic acid being added to the air, to moderate artificial respiration with atmospheric air. The respiratory movements of the chest wall gave a poor graphic record, but direct observation of these movements showed that they were practically the same whether the blast of the pump was moderate or strong.

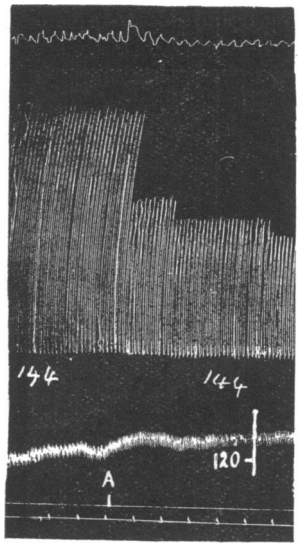

Fig. 8. Upper tracing = respiratory efforts. At A the blast of the pump was reduced, and air free from CO_2 was blown into the lungs. Previous to the point A the air entering the lungs contained carbonic acid.

This experiment makes it clear that neither distension of the lungs as such, nor mechanical disturbance of the circulation due to the distension, plays any significant part in bringing about the acceleration of the pulse usually associated with over-ventilation of the lungs, and that the important factor at work is the abolition of the activity of the respiratory centre consequent on a fall in the H ion concentration of the blood.

Hill and Flack have shown that the cardio-inhibitory centre is stimulated by a sudden rise in the tension of carbonic acid in the blood, and Langley has called attention to the readiness with which the centre responds to this stimulus. These observations have been repeatedly confirmed in the present enquiry. When the lungs are being artificially ventilated and the blast is constant, the addition of carbonic acid to the air entering the lungs must bring about a fall in the p_H of the blood, since there is no compensatory action on the part of the respiratory system. The intensity of the respiratory efforts made by the animal in these circumstances was taken as evidence of such a change, and no attempt was made to measure the p_H of the blood directly. Similarly the abolition of the activity of the respiratory centre as a result of over-ventilation of the lungs was assumed to be due to a rise of the p_H of the blood. There can be little doubt, therefore, that the tone

of the cardio-inhibitory centre is directly affected by the reaction of the blood, being intensified by a fall, and lessened or abolished by a rise, in the p_H of the blood. It does not seem very probable, however, that variations in the p_H of the blood can play any effective part in regulating the pulse-rate in the normal individual, since all the evidence goes to show that, except during muscular exercise, the reaction of the blood is practically constant; and during exercise other factors affecting the pulse-rate override the influence of the altered p_H of the blood.

The observations just described lead to the conclusion that neither the degree of activity of the respiratory centre nor the degree of distension of the lungs have in themselves any influence on the pulse-rate either by irradiation to the cardio-inhibitory centre, or by setting up a reflex alteration of the tone of this centre. The cause of the acceleration of the pulse usually observed in the normal animal or in man during hyperpnœa or dyspnœa must be sought, therefore, in the changes taking place in the circulation as a result of the respiratory movements. It appears necessary also to regard changes in the circulation as the most probable explanation of the inspiratory acceleration and expiratory slowing of the pulse-rate which, when it occurs in man, is known as sinus arrhythmia. Further, it seems clear that, since the respiratory system does not affect the pulse-rate either by irradiation or by afferent impulses from the lungs, the rate of the pulse must be controlled primarily by the heart itself. The work of Krogh and of Evans has made it evident that, generally speaking, the efficient and economical working of the heart necessitates a close correlation between the pulse-rate and the work done by the heart; and it is essential for this purpose that the heart should possess some means whereby it can regulate the frequency of the pulse. On this view, the variations in the pulse-rate during hyperpnœa or in sinus arrhythmia represent one aspect of a fundamental process concerned in regulating the pulse-rate under all conditions.

The means available are first the depressor nerve and, second, the reflex path whereby diastolic distension of the right side of the heart evokes acceleration of the pulse.

It appears highly probable that the acceleration of the pulse-rate associated with dyspnœa is due to the fact that the more vigorous respiratory movements lead to a larger return of blood to the heart; this, by bringing about some diastolic distension of the heart gives rise to reflex acceleration of the pulse. The presence of this reflex mechanism also furnishes a satisfactory explanation of rhythmic inspiratory acceleration and expiratory slowing of the pulse-rate (sinus arrhythmia).

Each inspiration increases the diastolic filling of the heart and gives rise to reflex acceleration of the pulse-rate; with the onset of expiration the stimulus to acceleration passes off and the pulse becomes less frequent. The conditions predisposing to sinus arrhythmia appear to be an infrequent pulse and slow deep breathing. In these circumstances, the diastolic filling of the heart will be greater than usual and the accelerator reflex will be more readily evoked.

On the other hand, it is possible that both the cardiac depressor reflex and the accelerator reflex are involved in the rhythmic variations of the pulse-rate during respiration, and that the occurrence of these rhythmic changes in pulse-rate is due to a balancing action on the part of these two opposing reflexes. On this view, the greater diastolic filling of the heart during inspiration leads to reflex quickening of the pulse-rate; at the same time the output of the heart increases and the arterial pressure rises. The rising arterial pressure brings the depressor reflex into action, and the pulse slows during expiration, partly for this reason and partly because the stimulus to acceleration passes off. If this explanation is correct, the normal steady rate of the pulse must be due either to a more perfect balancing of the depressor and accelerator reflexes or to their not being called into action.

An attempt was made to ascertain whether, under suitable conditions, both the accelerator and the inhibitory cardiac reflexes are simultaneously evoked. The abdomen was compressed before and after section of the left vagus. The heart was enclosed in a cardiometer and its volume and output were graphically recorded. It was found that the increased volume and output of the heart, and the raised arterial pressure, consequent on the abdominal compression, led to slowing of the pulse-rate when both vagi were intact, and in some experiments to acceleration of the pulse after section of the left vagus. The following protocol illustrates an experiment of this kind:

Cat anæsthetised with ether. Heart enclosed in cardiometer. Artificial respiration.

	Arterial pressure	Pulse-rate	Volume and output of heart
(*a*) Both vagi intact.			
(1) Before abd. compression	24	156	—
(2) During „ „	44	132	Vol. larger; output per beat almost doubled.
(*b*) Left vagus divided.			
(1) Before abd. compression	32	156	—
(2) During „ „	52	168	Vol. larger; output per beat increased.

The result just described was not invariably obtained and, as the outcome of a large number of experiments on this point, it seems probable that considerable variation exists in the relative proportion of afferent cardiac fibres running in the right and left vagus respectively. But it

appears that, at least in some cats, the cardiac depressor fibres which carry impulses bringing about reflex slowing of the pulse-rate run mainly, though not entirely, in the left vagus (including the depressor nerve). In such cases section of the left vagus makes it possible to bring about acceleration of the heart by abdominal compression. These experiments suggest, therefore, that, when the diastolic volume of the heart and the arterial pressure are simultaneously increased, both the accelerator and the inhibitory cardiac reflexes are set in action, although the inhibitory reflex is the more powerful.

In the present enquiry no definite evidence was obtained to show whether these reflexes are constantly in action or are only evoked when the arterial pressure or the diastolic distension of the right side of the heart rises above the normal level; but it is evident that, if they are not usually in action the cardio-inhibitory centre must possess an inherent tone susceptible of modification by these reflexes, whereas, if these reflexes are constantly at work, the tone of the cardio-inhibitory centre must be largely or even wholly reflex in origin. This point is being investigated.

Conclusions.

(1) No evidence was obtained either that impulses pass by irradiation from the respiratory centre to the cardio-inhibitory centre and alter the tone of the latter or that afferent impulses, capable of reflexly affecting the pulse-rate, pass from the lungs to the cardio-inhibitory centre.

(2) The tone of the cardio-inhibitory centre is modified by changes in the reaction of the blood, being increased by a fall, and diminished by a rise, in the p_H of the blood.

(3) The regulation of the pulse-rate is carried out primarily by the heart itself, and the respiratory movements influence the pulse-rate only in so far as, by bringing about changes in the circulation, they call into action the regulative mechanism possessed by the heart.

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