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By J. TREVAN and E. BOOCK.

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Rosenthal(1) was the first to point out that the effect of section of the vagi was modified by the transection of the brain at different levels. He showed that a section through the brain stem at the level of the posterior border of the posterior colliculi, followed by division of the vagi, resulted in such profound modifications of the respiratory response, that the animal dies of asphyxia in a short while, although before cutting the nerves the respiration is not very conspicuously different from the normal. These experiments were repeated and extended in 1916 (Trevan(2)). The respiratory centre is considerably modified in its response to other changes when the posterior colliculi are removed. It is, for example, less sensitive to the effect of change in the reaction of the plasma (Trevan(2)), and it is no longer stimulated by the injection of acetyl acetone and similar substances (Hurtley and Trevan(3)). The usual effect of section of the vagi in an anæsthetised animal is a much less profound change in the respiratory movements, whilst Schafer(4), on cats and rabbits, has shown that if an animal is allowed to recover from the anæsthetic, the effect on the normal rate and depth of the respiration on section of the vagi is very slight, provided laryngeal palsy is prevented. Schafer gives also a large number of experiments to show that anæsthetised animals do not constantly or often give the classical results.

The following experiments were made in an attempt to correlate in some degree these different actions.

Decerebrate cats. Cats, anæsthetised with ether and tracheotomised, were decerebrated with Sherrington's guillotine and the remainder of the cerebrum was removed with a scalpel. The carcase was then left

for periods of three to six hours, in order to recover from the shock. In our experience, the respiratory centre is working at its best between the sixth and the tenth hour after the operation; the carcase should be untouched for at least three hours for even gentle handling before this time may considerably modify the response of the centre. The respiration was recorded by a string stitched to the abdominal wall and run over a pulley to a lever; in the tracings down stroke is inspiration.

If the section of the brain stem is made at level I in Fig. 1, respiration

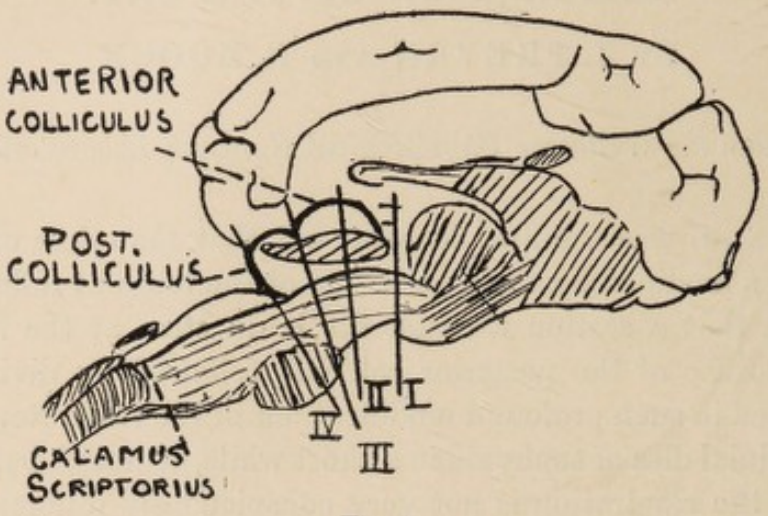


Fig. 1.

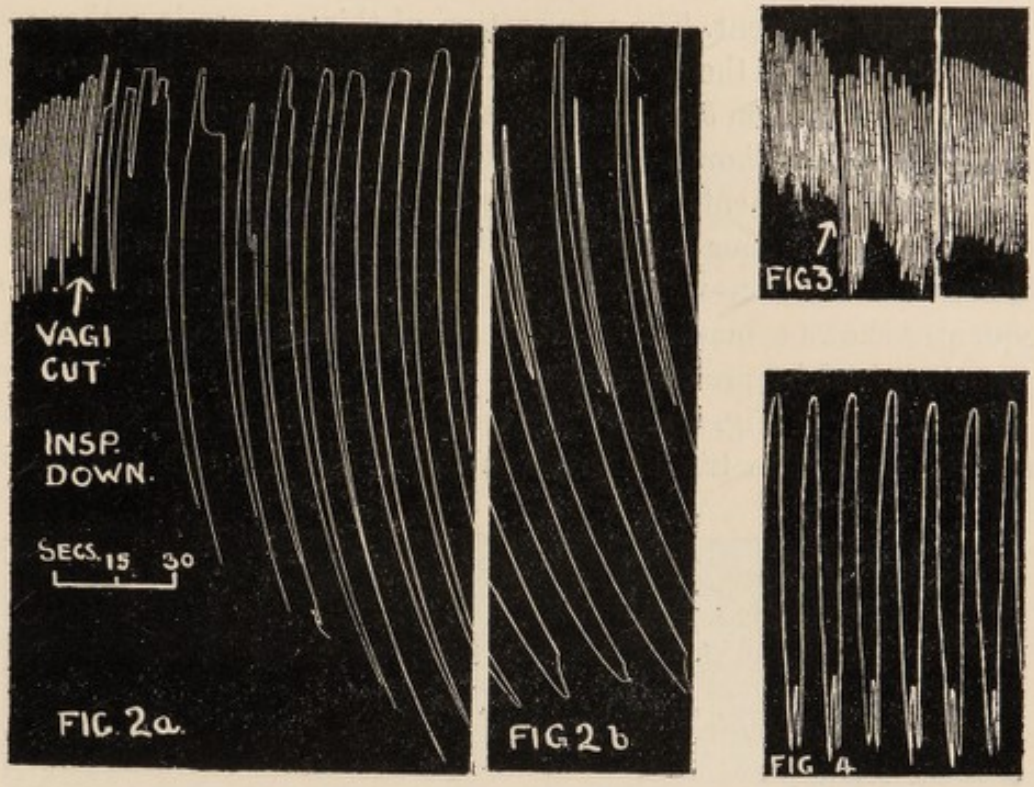
may be slightly deeper and slower than normal, but it is not seriously altered. If the section is behind this point, deepening becomes more marked and corresponding slowing appears, the depth usually continually increasing, the further the medulla is encroached upon.

The response of the centre to section of the vagi depends on the level of the section through the brain stem.

Section of the vagi in a cat decerebrated at level IV causes profound alteration, similar to that recorded by Rosenthal. The respiratory movements consist of a series of inspiratory gasps with pauses in the inspiratory position—a sort of vagal ataxia. A record is shown in Fig. 2. About 20 minutes after the termination of the tracing, the animal died of asphyxia, the rate having become much slower, the inspiratory standstill much longer. Death may be delayed for half an hour, but rarely longer. The differences are further illustrated by the following measurements:

	Depth	Rate	Minute volume
Before division of vagi	17	27	459
After ,, ,,	48	6	288
After (maximum)	70	6	420

If the section passes through the anterior colliculi (level II) the effect of the division of the vagi is much less marked. There is slight slowing



Figs. 2, 3, 4. Effect on respiration of section of the vagi after decerebration. Fig. 2. Decerebration at level IV of Fig. 1. The interval between *a* and *b* was 20 mins. Fig. 3. Decerebration at level II. Both vagi divided at the arrow. Gap in the tracing about 3 mins. Fig. 4. Decerebration at level III. The abdominal movement precedes the thoracic.

and compensatory deepening, shown in the tracing given in Fig. 3. Measurements of the tracing give the following results:

	Depth	Rate	Minute volume
Before section ...	21	28	588
After „	24	23	552

If the section passes between the colliculi (level III), division of the vagi gives a greater deepening of the respiration, and a curious incoordination of the respiratory movements usually shows itself at this stage, especially, and sometimes only, on increasing the dead space of the tracheal cannula. It consists of a time dissociation of the abdominal and thoracic respiratory movements. It is illustrated in Fig. 4. The inspiratory movement is downwards, and the first wave on the curve at *A* was found by inspection at the time of the experiment to be

synchronous with the abdominal movement, the second with the thoracic movement.

When the section is above the anterior colliculi (level I), the results are strikingly different. The preparation of this carcase is rather more difficult than that of the two previous. There is a tendency for convulsive seizures to develop on slight sensory stimulation, which are followed by profound shock, although the carcase remains quite passive if undisturbed. The movements which make up the convulsion are rhythmic movements of all four limbs, accompanied by opisthotonus and protraction of the claws—a "fighting reflex." The preparation thus made frequently shows a marked auditory reflex, proving that such sections are not followed by prolonged shock.

The tracing in Fig. 5 shows the result of section of the vagi in such an experiment. The tracing given is continuous through the time of

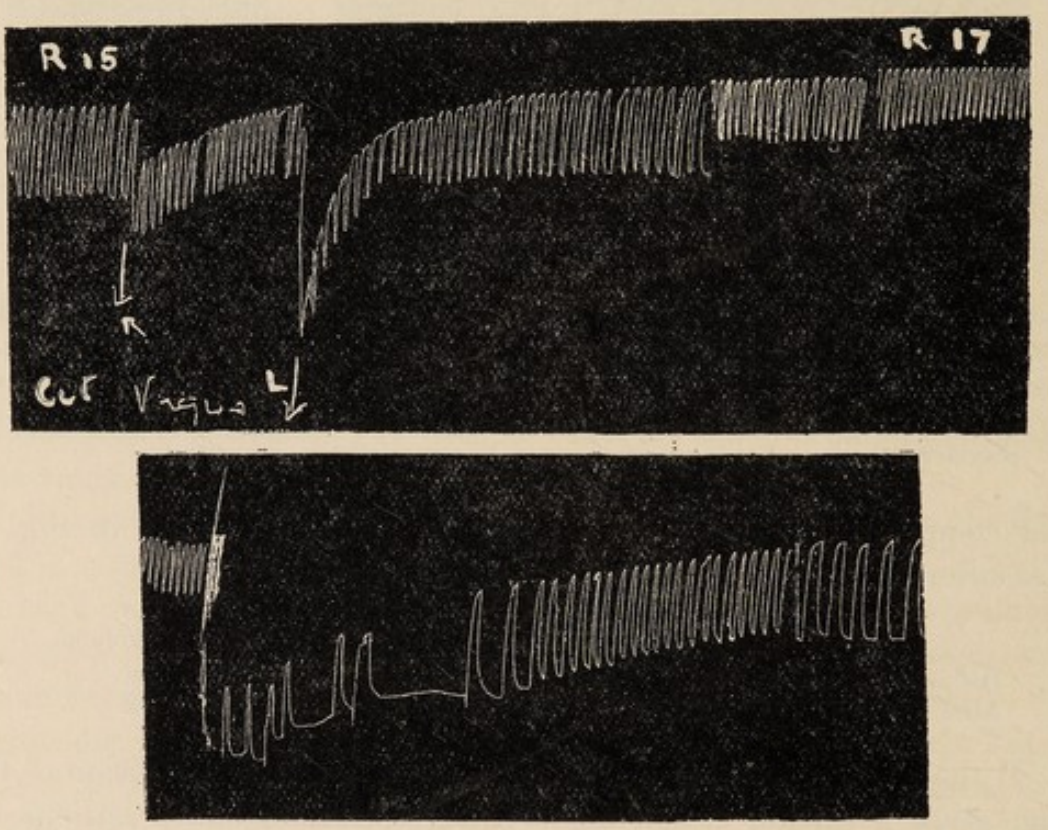


Fig. 5. Decerebration at level I. Intervals between the tracings, 6 mins. Duration of short tracings, 1 min. Fig. 6. Subsequent section in the same cat at level II. 1st tracing, 4½ mins. Interval, 8 mins. 2nd tracing, 1 min.

cutting the vagi, and it will be seen that after the preliminary stimulation of the section is over, the respiration is actually faster and shallower than before the vagi were cut. This effect has been obtained in three cats:

in others a slight increase in the depth of the respiration sometimes follows. The differences are probably to be explained by the small margin of nervous tissue through which the section must be made: for if too little is removed, the animal has too much reflex excitability for the experiment to be carried on, and if too much is removed, the essential part of the respiratory mechanism is destroyed. In the cat giving the tracing Fig. 5, the mid-brain was further removed as far as level II, when the typical vagal effect was brought on (Fig. 6).

Anæsthetised cats. Schafer, apparently, favours the view that, if the anæsthetised animal is tracheotomised, no lasting vagal effect is produced: that the paralysis of the larynx is responsible for many of the early results: and that the transitory nature of the effect which he sometimes got indicated that it was due to the stimulation of the section. We think the experiment described above and shown in Fig. 6, disposes of this last assumption, for there the vagi had been cut sometime previously, and the typical effect was brought about by a section through the mid-brain which does not produce the effect when the vagi are intact. All our cats were tracheotomised, which disposes of the other objections.

In view of the striking regularity of the appearance of the effects described above for the unanæsthetised decerebrated carcase, we have cut the vagi in a number of anæsthetised cats. We find that deepening and slowing of the respiration can be obtained in practically every animal, and that it is usually accompanied by the typical inspiratory pause. But this result is only obtained if the anæsthesia is of a certain depth. If it is too light, the effect is not obtained, nor if it is too deep. There are several factors which may interfere with the development of the classical effect.

(1) Alteration of the depth of anæsthesia produces alteration in the response to vagal section similar to the alterations produced by removal of various parts of the brain stem; so that a lightly anæsthetised animal corresponds to one in which decerebration is far forward, and a more deeply anæsthetised animal to one in which the section is farther back. Consequently, to obtain a deepening of the respiration on section of the vagi, the animal must be sufficiently deeply anæsthetised.

(2) As the depth of anæsthesia in animals with either intact or cut vagi increases, the respiration generally tends to become shallower and finally to disappear. This shallowing sets in at different levels in the anæsthesia of different cats and tends to mask the vagal effect. It is accompanied by a rise in the alveolar CO_2, as was pointed out in a previous communication (5).

Fig. 7 shows the effect of ether on the respiratory rate of the cat. The depth of anæsthesia was varied by increasing the amount of ether inhaled. As the corneal reflex disappeared it will be seen that the respiration became shallower and quicker. If the ether administration is continued, the shallowing becomes very marked, and the respiratory movements stop. If the anæsthesia is not allowed to go so far as to stop the respiratory movements, the respiration deepens with diminution in the anæsthesia, and the original depth and rhythm were restored. If the very deep anæsthesia is maintained for any length of time, the lightening of the anæsthesia sometimes results in the establishment of a vagal type of respiration, although the vagi are intact.

Fig. 8, top tracing, shows the effect of section of the vagi in a cat

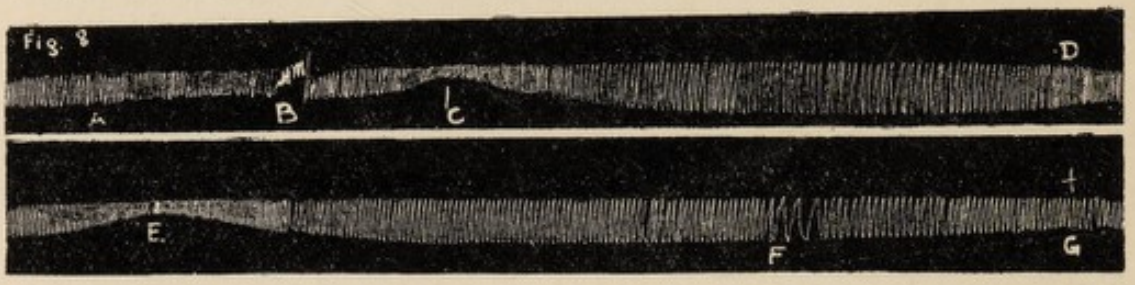


Fig. 7. Increase of ether with intact vagi. Corneal reflex present, $CR+$; absent, $CR-$. Ether increased, $E+$.

Fig. 8. Effect of ether with vagi cut. See text. *D*, corneal reflex returned. Lower tracing, 45 mins. later. Deeply etherised at left end of tracing, lightly at right end.

anæsthetised with ether. The animal with one vagus cut already being deeply anæsthetised, the ether was increased at *A*. Then the second vagus was cut at *B*, and there was a slight deepening of the respiratory movements. Almost immediately afterwards the rapid shallow breathing foreshadowing respiratory failure from the anæsthetic set in, and the ether was taken off at *C*. This was followed quickly by deepening and slowing of the respiration till the rate went down to half what it was before the vagi were cut; there was a marked pause in inspiration at this stage. Then, as the anæsthesia became still lighter, the original rhythm returned. The whole cycle was repeated five times, and Fig. 8, bottom tracing, gives such a cycle obtained 45 minutes after the first. In each cycle vagal breathing appeared just about the time that the corneal reflex

disappeared, and vanished when the anæsthesia became very deep. The variation in rate is plotted in Fig. 9, with an arbitrary representation

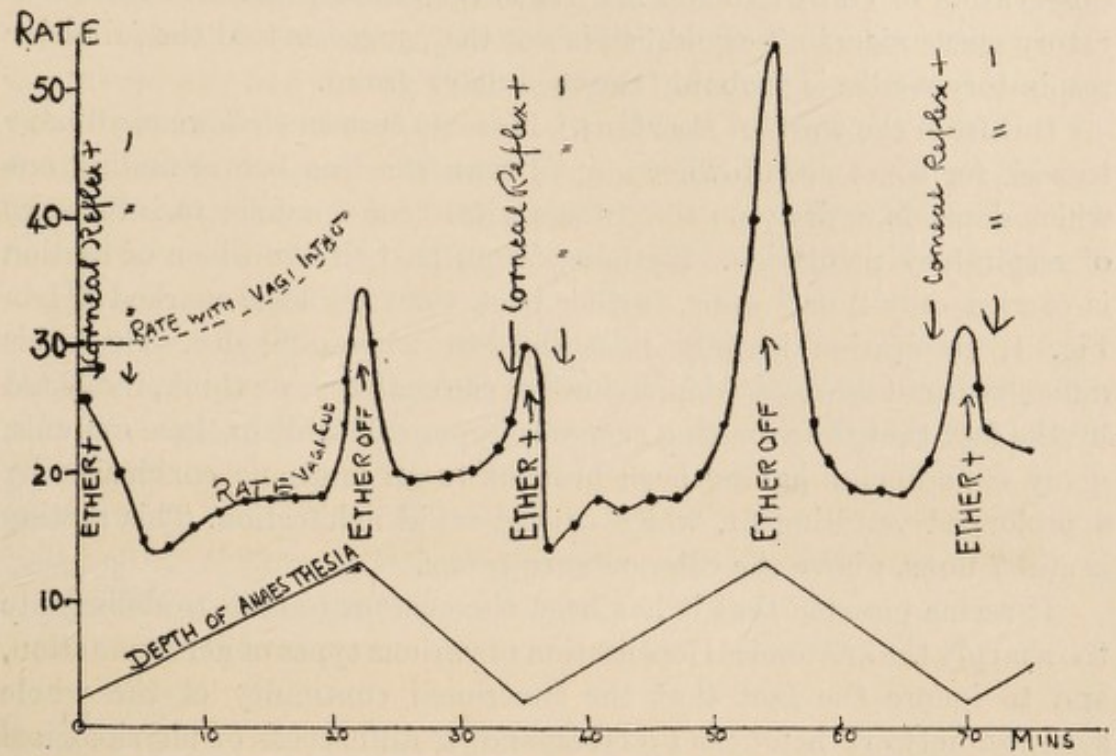


Fig. 9. Effect of varying depth of anæsthesia on rate of respiration after section of vagi. The top curve represents alteration of rate. The bottom one is an arbitrary representation of "depth of anæsthesia."

of the depth of anæsthesia. These results have been obtained in other cats, and, provided the animal is not kept very deeply anæsthetised too long, vary only in degree. The corneal reflex is not always a good index of the depth of anæsthesia, and the diminution in depth produced by the anæsthetic comes on more easily in some animals, and tends to mask the effect of vagotomy. This is practically always deepening of the respiration, although the inspiratory pause may not occur.

If, however, the animal is kept for any length of time in the deeply anæsthetised state with the vagi cut, the return of the respiration to normal does not take place for a considerable time after the corneal reflex has reappeared.

Remarks. The importance of the part of the respiratory centre above the medulla pointed out by Rosenthal is emphasised by these experiments. We have not completely worked out the position of the nervous arcs involved. They are not actually in the colliculi, for in removing the anterior part of the brain stem, after the first stage of decerebration, interference with respiration only takes place when the ventral part of

the mid-brain is cut. The fact that the centre increases in sensitivity to the H-ion, from the medulla forwards, taken in conjunction with the observation of Osborne and Muntz(6) that the regulator of the respiratory mechanism in the gold-fish is not CO_2, suggests that the primitive respiratory centre is probably the medullary group.

But from the work of Martin(7), it seems certain that we shall have to seek for some even lowlier animal than the frog before finding one which depends entirely on the "nœud vital" for the delicate intricacies of respiratory regulation. We have found that, if the plane of section is carried only 2 or 3 mms. further back than the level marked III in Fig. 1, respiration is only re-established with difficulty. That this difficulty is not due to a "depression" of the centre is, we think, indicated by the fact that the vomiting centre is hyper-excitable in these animals, many experiments having been brought to an untimely conclusion by a prolonged vomiting fit, which caused rapid exhaustion. This section is still 7 mms. above the calamus scriptorius.

It seems possible that it has been the custom to seek to deliminate too sharply the anatomical localisation of various types of nervous action, and to ignore the fact that the functional continuity of the whole synaptic network betokens a corresponding diffuseness of physiological activity in the medulla and mid-brain.

As Scott(8) pointed out, section of the vagi leads to a condition in which the animal tolerates higher percentages of CO_2 without hyperpnœa; this he attributes to a lowering of the sensitivity of the centre. There was an increase in the alveolar CO_2 in the experiment described above, in which the uppermost section of the mid-brain was made, suggesting that the diminution of the respiration depended on the alteration in the sensitivity of the centre to H-ion, but in other cases no appreciable alteration of the alveolar CO_2 was found. This part of the mechanism is being further investigated.

Conclusions.

1. Cats with the brain removed in front of the anterior colliculi and at right angles to the neural axis, resemble normal animals in their response to section of the vagi, alteration of the reaction of the blood, injection of acetyl acetone, etc. Very lightly anæsthetised animals may show little or no change in the respiratory movements on section of the vagi.

2. With a section passing between the colliculi, the response of the animal to section of the vagi consists of slowing and slight deepening of

the respiratory movements, such as given usually by the moderately anæsthetised animal. The response to acid and acetyl acetone is not markedly different from the previous case.

3. When the section passes posterior to the posterior colliculi, the stimulation by acetyl acetone gives place to a depression, the sensitivity to acid is much depressed (Trevan(2)). The effect of division of the vagi is to produce the previously described incoordinated inspiratory gasps. The effect is that of deeper anæsthesia, except that in the latter case, the division of the vagi does not produce quite such drastic change, for the reasons given in the text.

4. The suggestion is tentatively put forward that the part of the respiratory centre remaining in an animal decerebrated just behind the anterior edge of the pons is a representative of a more primitive type of centre, in which the adaptation of the respiratory movements to the needs of the body depended more on vagal stimuli and less on the composition of the blood, than is the case in the more highly developed centre of the normal cat.

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