THE REGULATION OF RESPIRATION. Part II. Normal Type.

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The generally accepted view is that, as insisted on by Haldane and his co-workers (1), CO_2 and possibly other fatigue products, *e.g.* sarcolactic acid, are the normal stimulants of the respiratory centres. Thus a rise of 0·2 p.c. of CO_2 in the alveolar air, doubles the pulmonary ventilation, while O_2 lack does not increase the respiratory rate until the atmospheric O_2 falls below 13 p.c. With regard to the influence of the vagus, opinions vary somewhat, but most authorities favour Head's conclusions (2) that the vagi contain two sets of fibres, one increasing the activity of the inspiratory part and the other increasing the activity of the expiratory part of the respiratory centre. Head confirmed Hering and Breuer's view that dilation of the lungs, however produced, promoted expiration, while whatever caused contraction of the lungs inhibited expiration and produced inspiration. F. H. Scott (3) stated that after vagotomy excess of CO_2 or great diminution of O_2 increases the depth but not the rate of breathing. Probably all physiologists agree that vagotomy invariably causes the breathing to become deeper and slower. Everything I have noticed has confirmed the view supported by Haldane and others, that the amount of CO_2 in the blood is the normal respiratory stimulus.

In previous communications (4) I have put forward evidence to indicate that natural quiet breathing results from periodic inhibition of prolonged inspiratory tonus, through the rhythmical activity of the pneumotaxic centre in the upper half of the pons. My view is that the excitability of this centre is raised by the H-ions circulating through it, till it reaches a certain point at which discharge occurs, giving rise to an impulse which inhibits momentarily the inspiratory tonus (apneusis). The moment after discharge the excitability of the pneumotaxic centre may be supposed to be at its lowest level and it rises under normal conditions more or less quickly in accordance with the amount of CO_2 in the blood till the next discharge occurs. In accordance with this view the rate of respiration depends primarily on the pneumotaxic centre while the amplitude of the breathing, *i.e.* the amount of air taken in

and expelled at each breath, depends on the stimulation of the apneustic and expiratory centres which both respond as indicated in my previous paper to the percentage of CO_2 in the blood, while the apneustic centre alone is stimulated also to some extent by serious lack of O_2 (10 p.c. or less). It will be apparent that if these views are correct, then even after vagotomy, excess of CO_2 should be able by its effect on the pneumotaxic centre to increase the respiratory rate. The methods employed were those described in my previous papers. As a routine method of recording respiratory tracings I prefer the use of abdominal and thoracic tambours to the diaphragm slip method. A good deal of the effects seen when using Head's method are I think adventitious, and misleading.

Since I have shown(4) that apart from the vagi the rhythm of breathing depends chiefly upon the pneumotaxic centre, Scott's conclusion referred to above would point to that centre being, as far as acceleration is concerned, unresponsive to the amount of CO_2 which circulates through it. In a series of experiments I investigated this point before and after vagotomy, in intact anæsthetised animals (cats (cf. Fig. 1, Pt. I) and rabbits), and also in animals whose brain stem was divided at level 1; the results obtained appear in Tables I and II and are illustrated in Figs. 1, 2 and 3. In some cases continuous ventilation was used but generally the animal breathed the excess of CO_2 or lack of O_2 through valves.

The effect of breathing an excess of CO_2 shows itself in the intact animal (cat) by a sequence of events which is very characteristic and constant (Fig. 1). First for $\frac{1}{2}$–1 minute, the inspiratory tracing progressively increases in height (apneustic centre stimulated); at the end of this period the expiration deepens and becomes active (expiratory centre stimulated). The rate of breathing now begins to increase continuously (vagus and pneumotaxic centre stimulated), until the limit of maximal response is reached in 2 or 3 minutes. Provided that a sufficiency of O_2 is supplied, respiration continues at this level for a long time without apparent harm, even when large amounts (over 20 p.c.) of CO_2 are employed. Thus in a typical experiment, a rabbit (normal respiration 65 p.m.; pulse rate 260 p.m.; blood-pressure 140–150 mm.) breathed 30 p.c. CO_2 with 25 p.c. O_2 for two hours, at the end of which time there was hyperpnœa of normal type (resp. 48 p.m.) the heart-beat was slower (120 p.m.) but stronger, and the blood-pressure was steady and high (150 mm.). The excessive amount of CO_2 maintained a moderate anæsthesia without continued administration of ether. The CO_2 was now

increased to 60 p.c. and the O_2 to 40 p.c. Anæsthesia became very deep, the respiration very slow (12 p.m.) and the heart-beats, though regular

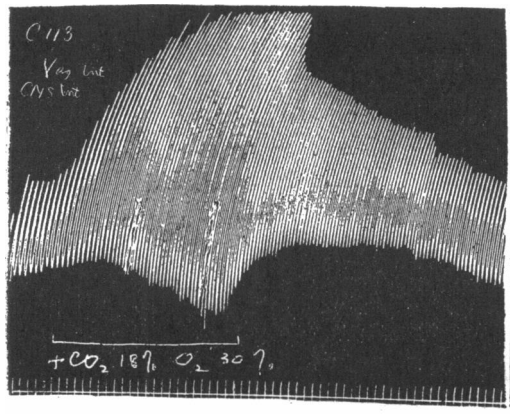

Fig. 1.

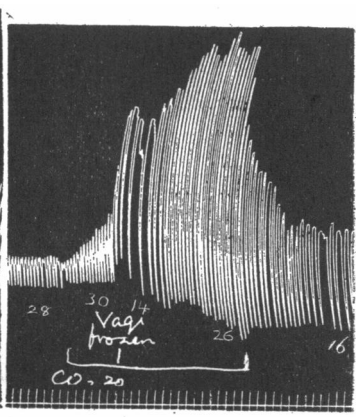

Fig. 2.

Figs. 1 and 2. Cat. Thoracic tracing. Fig. 1. Effect of breathing 18 p.c. CO_2. Vagi intact. Time tracing 5 secs. Insp. up. Fig. 2. Vagi frozen during inhalation of 20 p.c. CO_2.

and very powerful, were infrequent (61 p.m.). After ten minutes the blood-pressure fell progressively to 40 mm. The 30 p.c. CO_2 mixture was then re-administered and recovery was rapid and complete. The vagi were now frozen, causing slowing (15 p.m.) and deepening of breathing, but the heart-beat and blood-pressure (now 100 mm.) remained satisfactory for over an hour. Breathing the 60 p.c. CO_2 mixture now evoked short apneuses, with prolonged (20 sec.) expiratory phases between the apneuses. The blood-pressure fell gradually, but when after ten minutes the 30 p.c. CO_2 mixture was re-supplied, recovery again took place, the blood-pressure rising again to 100 mm.

Similar results were obtained in cats, so that we may conclude that respiration of CO_2 does not prove rapidly detrimental till its concentration is over 30 p.c. When yet higher percentages are inspired they probably prove harmful by paralysing the central nervous system from above downwards, like overdosage with any other anæsthetic. Death in asphyxia must therefore result solely from lack of oxygen. When after a short inhalation of CO_2 (2–15 minutes) air is re-admitted freely, the inspiratory and expiratory increases rapidly lessen concurrently, but for a minute or two the rate of breathing may continue to increase as it gets shallower (Fig. 1).

In ten cats breathing from 5 to 20 p.c. of CO_2 the rate of breathing

increased from an average of 24 to an average of 36 per min., *i.e.* a 50 p.c. increase. The rate soon after the re-admission of pure air was 25·6 p.m., the height of the tracing (by no means a reliable index of the amplitude of the breathing) increased to between two and three times its original amount.

In seven experiments the vagi were divided during CO_2 dyspnœa (Fig. 2). Table I shows the results.

TABLE I. Effects of vagotomy during respiration of excess of CO_2 (Cat). The figures give the respirations per min.

	Exp.	Rate on air	CO_2 %	O_2 %	Rate on CO_2 before vagotomy	Rate after vagotomy on CO_2 at first	Later	Rate after vagotomy on air
Brain stem divided at level 1	1	40	5½	22	50	16	28	18
	2	48	7	30	60	12	12	12*
	3	18	13	27	24	4	4	4†
	4	18	16	50	28	18	22	24
Brain stem intact	5	18	10	30	18	11	12	13
	6	33	10	30	42	21	27	15
	7	28	20	30	30	14	26	16

* Paraffin injection. † Pneumotaxic centre damaged.

The average rate before inhaling CO_2 was 29, at the moment before vagotomy the rate was 36, for half a minute, thereafter it was 13·7; this rate then increased again to 18·7; when air breathing had been resumed for some minutes the rate fell again to 14·6 per min.

In a series of ten cats breathing various percentages of CO_2 after vagotomy had been performed the average figures before, during and after CO_2 inhalation were 13·8, 19·7, 15·1 respectively, the proportionate increase during the experiment was 42·8 p.c., so that the respiratory rate increased nearly in the same ratio after vagotomy as before, though the actual rates were all much slower. The individual figures in this series are shown in Table II and Fig. 3.

TABLE II. After vagotomy effects of breathing excess of CO_2 (Cat).

Exp.	Brain stem	CO_2 %	O_2 %	Resp. per min. on air	Resp. on CO_2	Resp. after on air
8	Intact	5	16	10	24	15
1	Level 1	5½	22	18	26	20
9	—	10	30	12	14	14
5	Intact	10	35	12	14	12
6	Level 1	10	30	18	24	20
10	Intact	12½	27	17	28	22
11	Level 1	12½	30	8	10	9
12	—	16	50	12	13	8
13	Intact	18	30	15	20	15
7	Intact	20	30	16	24	16

Exps. 1, 5, 6, 9, were on cats referred to in Table I.

From these experiments it is plain that using percentages of from 5 to 20 p.c. of CO_2 every animal showed a distinct power to increase the

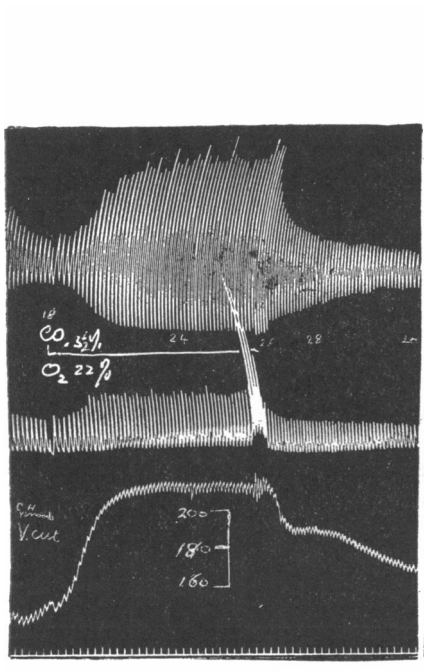

Fig. 3.

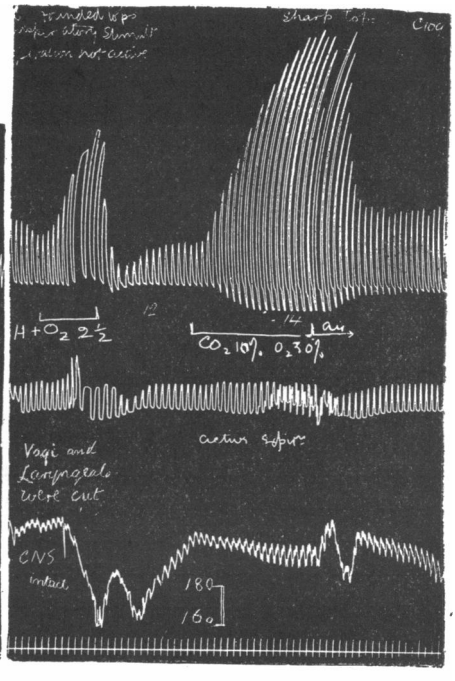

Fig. 4.

Figs. 3 and 4. Cat. Thoracic, abdominal and blood-pressure tracings. Vagi cut. Fig. 3. Decerebrate inhalation of 5·5 p.c. CO_2. Fig. 4. Inhalation of 2·5 p.c. O_2 and later of 10 p.c. CO_2.

rate of breathing as well as the depth, except Exps. 2 and 3 in Table I, and in each of these the pneumotaxic centre was known to be seriously damaged. There seems then no doubt that the pneumotaxic centre when healthy can, without the aid of the vagus, increase the rate of respiration. As explained above (while treating of the effect of vagal influences during apneustic respiration) the vagus constantly diminishes both the height of inspiration and the depth of expiration and thus tonically quickens the breathing and renders it shallower, so that vagotomy slows and deepens respiration at its apneustic sources whether the chemical calls for hyperpnœa are great or small. The finer vagal adjustments are, however, probably effected through the pneumotaxic centre.

In almost all my experiments the increase of rate after vagotomy took over a minute to appear, and often two minutes to declare itself

fully. The same is not infrequently the case when the vagi are intact. Since in his article (p. 307) Scott states that "although the animals breathed these mixtures usually for less than a minute the rhythm is given in so many per minute," it is not surprising that he usually found no increase of rate after vagotomy. Scott's animals were all chloralised (p. 304); this is not nearly so satisfactory as decerebration since chloral depresses the excitability of the pneumotaxic centre. Thus any increase of rate was apt to be vagal, and to cease after vagotomy. He also omits to mention the rate of respiration after the experiment. The above points explain the difference between Scott's negative results and my positive results.

The effect of breathing low percentages of O_2 was investigated. It was found that, as stated by Haldane and others, very little change was seen in the respiration till the O_2 became less than 12 or even 10 p.c. When an animal breathed 8 p.c. O_2 before vagotomy the rate increased from 20 to 23 per min. After vagotomy the figures were 16 and 19 respectively. There is a much greater increase in the amplitude of the breathing after vagotomy, which corresponds with the slower rate. The increase is entirely inspiratory and as shown in my preceding paper is due to stimulation of the apneustic centre.

Vagotomy performed during respiration of H_2 pure or of $2\frac{1}{2}$ p.c. of O_2, increases the height of the inspiratory tracing enormously; the rate remains almost unaffected. Active expiration does not occur. The purely inspiratory effect of O_2 lack after vagotomy is particularly well seen in Fig. 4, and the difference of the dyspnœa due to O_2 lack and that resulting from excess of CO_2 is apparent.

After vagotomy O_2 lack is as one would expect even more rapidly fatal than usual. In a cat in which after vagotomy, CO_2 excess did not increase the rate of breathing there was marked quickening of the respiration when O_2 was concurrently lacking, and in this experiment it appeared that the increase of rate coincided with diminution in depth of breathing, an evidence of apneustic failure with a still effective pneumotaxic centre.

The Source of Vagal Respiratory Impulses.

A large number of experiments (over 100) were made on cats and rabbits with a view to determining the origin of the vagal impulses affecting the respiratory centres. The methods of investigation employed were chiefly closure of the trachea at every phase between full inspiration and full expiration, both before and after vagotomy, and during powerful positive and negative ventilation.

Closure of the trachea.

Vagi intact (Fig. 5). (*a*) If the closure is effected at the height of inspiration (INSP. V.I.) attempts to empty the chest so as to regain the zero position of pressure and distention (*i.e.* expiratory efforts) predominate. Since the chest was full when closed, lack of oxygen does not play much part in the immediate effects observed.

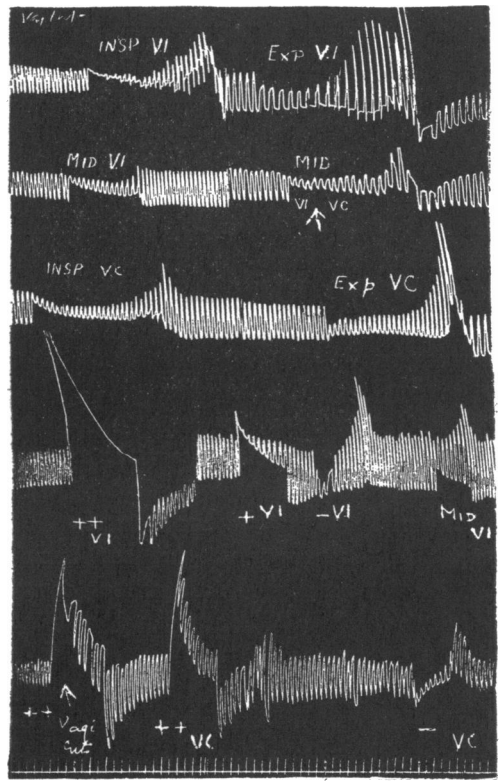

Fig. 5. Cats. Closure of the trachea in different conditions of the lungs (see text). V.I., vagi intact; V.C., vagi cut; +, positive pressure; −, negative pressure.

(*b*) Closure at the moment when the chest has been emptied by expiration (EXP. V.I.) produces more complicated effects. First the respiration becomes slow and the inspiratory rises on the tracing have rounded apices. After half a minute or so, each inspiration ends in a gasp. Soon the apneustic part of the inspiration lessens, the superimposed gasp increasing *pari passu*. After a minute only gasps interspersed with expiratory spasms occur. These effects are obviously in part due to lack of oxygen causing, as usual, failure of the respiratory centres in order from above downwards; the primary inspiratory phase being the only one attributable to vagal impulses of pressure and position.

(*c*) Closure midway between inspiration and expiration (MID. V.I.) gives effects very much the same whether the vagi are cut or not; since neither deflation nor distention was present to arouse any continuous vagal impulses of position or pressure and O_2 lack is not at once serious, respiratory movements simply continue slowly and deeply as if the vagi had been cut.

Vagi cut (Fig. 5, INSP. V.C. and EXP. V.C.). Closure in any of the above positions after vagotomy gives in all cases very much the same result. The reason of this appears to be that the centres (vagal impulses having been eliminated by tracheal closure) had already accommodated themselves to breathing without vagal assistance. Closure therefore acts like making an animal, whose vagi had previously been cut, breathe an atmosphere lacking in O_2 and overladen with CO_2. As pointed out above vagotomy performed during CO_2 dyspnœa causes for a short time much disorganisation of the breathing but after a minute or so the centres accommodate themselves and make a very fair effort to deal with the excessive CO_2 by increasing both the height and rate of respiration. If vagotomy had been performed some time before inhalation of CO_2 is begun there is no disorganisation, compensatory hyperpnœa of central origin appears at once in an ordered and regular manner. Similarly, closure of the trachea some time after vagotomy, merely evokes a centrally controlled hyperpnœa with no special bias towards either inspiration or expiration, since the brain stem is no longer informed of any abnormality of either position or pressure.

Excessive distention and deflation (Fig. 5). Distention being associated with positive pressure is much more effective than deflation and negative pressure. Closure of the trachea during distention at a pressure of 30 to 50 mm. Hg (++ V.I.) causes complete inhibition of the normal inspiratory tonus with expiratory apnœa. Sooner or later this is broken by typical gasps released by the inhibition of the higher centres and by the asphyxial state of the blood. If less pressure is employed (+ V.I.) the inhibition lasts only momentarily and inspirations of normal type are then resumed. If during the apnœa which results from excessive distention of the lungs the vagi are cut (++ vagi cut), rounded apneustic inspirations immediately occur (the inhibition which must have been vagal having been removed); these are quite distinct from the gasps just mentioned. It is therefore clear that intense distention is during its continuance an adequate vagal stimulus but it must be borne in mind that here we are dealing with pressures such as can never occur during natural inspiration and which are distinctly nocuous, for emphysematous changes can be seen post mortem.

Closure of the trachea during suction (− V.I.) gives rise during the first few seconds to inspiratory effects of apneustic type and then attempts at respiration are resumed with a gasp superimposed on each inspiration, the effects noted under closure in expiration being reproduced with some exaggeration. After vagotomy closure in deflation and also

closure in distention show no special effects of nervous origin, the results differing only mechanically from closure after vagotomy in any other position.

The immediate effects of vagotomy during closure of the trachea.

Vagotomy in this condition never slows the respiration which as above explained had already assumed the centrally determined rhythm. This indicates that the accelerating effects of the vagal impulses depend not on the amount of distention or deflation but upon the passage of air outwards and inwards; the effects which are observed are all in the direction of a diminution of efforts which would, but for the closure, result in resumption of the zero point of position and pressure, or rather in and out play of inspiration and expiration round that point. Vagotomy during closure in full inspiration thus diminishes the expiratory efforts, which were occurring. Vagotomy during closure with the chest in the expiratory position has little effect except that it increases the gasps which were superimposed on the attempted inspirations. Vagotomy during closure midway has no appreciable effect (Fig. 5, MID. V.I. V.C.). Vagotomy during great distention has been referred to above.

Rhythmic ventilation.

As stated by Hering and Breuer and confirmed by Head, rhythmically repeated ventilations dictate the rhythm of breathing as long as the vagi are intact. After vagotomy this does not happen. This I consider to be due to vagal impulses aroused by the currents of air as they pass in and out through the trachea and bronchi. It is of interest here to note Jappelli's(5) observation that in man, dogs, and rabbits, rhythmical stimulation of various other nerves, *e.g.* sciatic, could in like manner prescribe the rate at which respiration occurred.

That such air currents are sufficient to stimulate the vagus can be proved, after low vagotomy, by blowing air inwards through the larynx and upper part of the trachea, while continuous ventilation is performed through a tracheotomy opening below the portion of trachea blown into (Fig. 6). The downward current of air inhibits inspiration or apneusis quite as efficiently as electrical stimulation of the vagus. Similarly by blowing air upwards expiration may be inhibited, but this effect is less striking and less easily demonstrated.

Again, during continuous ventilation of the lungs performed so that only midway distention is caused we find that active expiration tends

to occur even when no CO_2 is included in the ventilating gas. Vagotomy stops this effect.

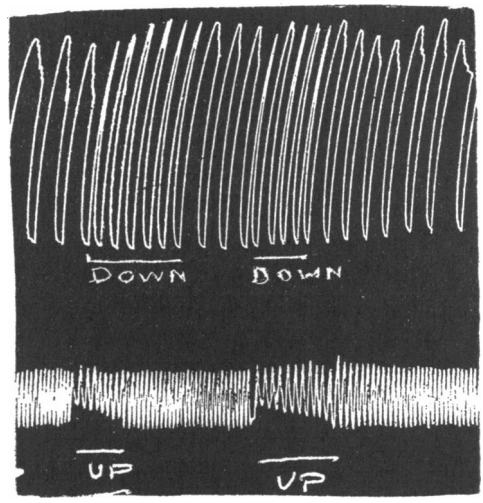

Fig. 6. Cat. Inhibition of inspiration by blowing intermittently downwards through larynx. Inhibition of expiration by blowing continuously upwards through the trachea.

Discussion.

From the results given above it emerges that closure of the trachea produces:

1. An effect which *invariably* ensues, whatever position the lungs were in at the moment of closure. This effect is immediate slowing of the breathing similar to that which results from vagotomy. If we assume that the accelerating influence of the vagus, results from stimulation of its nerve endings by the passage of air outwards and inwards, shutting off these air currents would account satisfactorily for the slowing effect which follows tracheal closure. Arguments will be brought forward presently to prove that this assumption is correct.

2. A group of effects which are not constant, but vary proportionately with the amount of distention or deflation of the lungs. These effects show themselves as efforts at expiration if the lungs were distended, or as inspiratory efforts if the lungs were deflated. In both cases attempts are made to resume the position of greatest ease and least exertion, which is midway between distention and deflation, and the position in which the intra-pulmonary equals the atmospheric pressure. If all these

effects of tracheal closure resulted from the same cause, viz. stimulation of the same vagal nerve endings by the same excitant, we should expect them to vary proportionately to each other. This is manifestly not the case; the assumption is, I think, justifiable, that two causes are at work: one of these giving rise to vagal impulses which constantly accelerate the breathing and the other evoking variable efforts in the direction of either expiration or inspiration.

It may be well here to recapitulate the points which favour the view that the vagal accelerating impulses (automatically regulating respiration), are aroused by the passage of air currents through the bronchi, and not by distention of the lungs or changes in the intra-pulmonary pressure.

1. Closure of the trachea in any state of the lungs slows respiration to the central rhythm, hence subsequent vagotomy slows it no further. This effect is immediate and constant, which suggests that it is probably due to a constant cause, *e.g.* cessation of air currents, and not to a variable cause such as the amount of distention or deflation which existed at the moment of closure (Fig. 5).

2. Blowing air downwards through the larynx and out at a low tracheotomy opening has an expiratory effect by inhibiting inspiratory tonus. Blowing air upwards through the larynx from the upper end of a tracheotomy opening promotes inspiration by inhibiting expiration (Fig. 6).

3. Einthoven, Flohil and Ballaerd(6), using the string galvanometer with every precaution found that whenever the lungs are expanded (air passing inwards) a current of action passes up the vagi, a separate distinguishable current occurs during expiration (air passing outwards). These electrical variations cannot be due to increase or decrease of pressure, because they occur in the same order as usual when (during cessation of normal breathing) artificial respiration is performed by positive and negative ventilation, in which case the normal order of increase and decrease of pressure would be reversed. These observations seem to rule out the theory of Stefani and Sighicelli(7) that changes of pressure are the normal vagal stimulus, and thus to favour the theory that the inrush and outflow of air normally excite the vagal endings.

It is, however, certain that when very high positive pressure is used in distending the lung the vagi *are* stimulated for if they are now cut, the expiratory apnœa which resulted from the noxious distention, ceases at once and attempts at respiration occur.

4. A great many of the arguments brought forward by Hering and

Breuer, Head and others to prove that distention and deflation of the lungs and not changes of pressure were the causes of the vagal impulses, favour with equal cogency, and none of them refute, the view that the in and out currents of air are the normal vagal stimuli.

5. Loewy's(8) experiment also supports the air current theory. He opened the right pleura of a rabbit after the animal had been breathing O_2 for some time. The O_2 was soon absorbed and the lung collapsed completely. Yet the respiration continued normally at 66 per min. Loewy now cut the left vagus. The respiration immediately assumed the complete vagotomy type at a rate of 34 per min. He then performed artificial respiration and the respiration assumed the pump rate, or a multiple thereof. This experiment, which I have repeated in rabbits and cats, strongly supports the air current view of vagal excitation, for on the distention and collapse theory the collapsed right lung should have produced, especially after cutting the left vagus, not the normal vagotomy effect but a marked inspiratory excitation. Loewy's experiment falls into line with my observation that closure of the trachea in any natural position between full inspiration and expiration acts like vagotomy and that very little effect results if the vagi are frozen during such closure.

6. During continuous ventilation, when gas is pouring downwards constantly through the air passages it evokes persistent expiratory efforts even if there is no marked distention of the lungs and though O_2 40 p.c. N_2 60 p.c. is used. Vagotomy abolishes this effect, and it ceases at once if the current is stopped and the lungs are allowed to collapse, in which case the air passes for a time outwards and inspiratory efforts occur.

Now, with regard to the variable effects which follow closure of the trachea, these show themselves most markedly when closure is effected after powerful distention or deflation, and that they do result from vagal influences is proved by the fact that they are not seen after vagotomy. Thus, as pointed out above, if during the expiratory apnœa which results from closure of the trachea after violent distention of the lungs, the vagi are cut, the apnœa ends at once and attempts at inspiration and expiration are resumed forthwith. This experiment alone is sufficient to indicate that the accelerating impulses are not the only ones carried by the vagi from the lungs. These nerves must also convey postural impulses relating to the position of the lungs in regard to distention and deflation and to the intra-pulmonary air pressure. We may suppose that at least one use of these impressions is to protect the lungs against either excessive distention or pressure; hence it seems natural that the response called

forth, say, by distention, is such as would resist further distention, *i.e.* an expiratory effort. In any case it is a fact that the response to any vagal message of pressure or position is always in the direction of safety and conservation of energy and muscular effort, viz. towards attaining the atmospheric pressure and the zero position midway between distention and deflation. In accordance with these views, we find that vagotomy performed during closure with the chest midway between inspiration and expiration (*i.e.* zero position) has no effect (Fig. 5). Respiration simply continues at the central rhythm already induced by the closure of the trachea. If, however, distention or deflation is present, efforts to attain the zero position are made as indicated above (Fig. 5).

On the whole I think it fair to conclude that in easy breathing the air currents as they pass over the ciliated bronchial mucous membrane form the natural vagal stimulus. But when distention or deflation assume abnormal degrees, they do give rise to postural vagal impulses which are not, however, concerned primarily with acceleration of breathing but with the tendency to attain the zero position of greatest ease and least exertion.

The vagi must also carry to the brain impulses aroused by painful and other nocuous stimuli, and these may have definite respiratory effects. Thus inhalation of an irritant gas gives rise (in both cats and rabbits) to active expiration, an effect which ceases after vagotomy.

I have observed a number of occurrences which suggest that deep sensations from the abdominal and thoracic parietes and viscera are of considerable respiratory importance. These impulses reach the cerebrum partly by the vagi and partly by the dorsal nerves, and among other facts they may explain the cessation of diaphragmatic respiration during acute abdominal inflammation or peritonitis. Another gastric vagal effect is hiccough.

Subjectively, we are aware of a number of these impulses, notably of the passage of air inwards and outwards, of pain, and of the position of the thoracic and abdominal walls and they probably therefore have important cortical respiratory effects. Since, however, the cerebrum and cerebellum can both be removed in their entirety without alteration in the rhythm of unconscious respiration, we must assume that the respiratory centres are independently capable of regulating the breathing in response to the pulmonary and bodily impulses just mentioned, and to the condition of the blood.

The trigemini have no tonic action on respiration for they can be cut without disordering it. If these nerves are irritated they have a protective

effect in one or other of two ways: they may, even after decerebration, aid in the expulsion of the noxious substance by giving rise to sneezing, while if an irritant gas is inspired through the nose temporary apnœa results; in the case of the tortoise this apnœa may last two hours or more. That after section of the 5th nerve this reflex ceases was, I believe, first pointed out by Kratschmer. The probable arrangement of the centres and their connections are diagrammatically represented in Fig. 7.

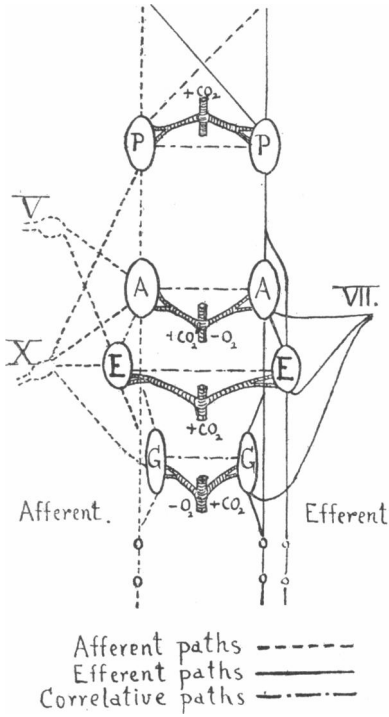

Fig. 7.

Two cases have recently been observed in which the apneustic type of respiration occurred in man. The first is recorded by Kirkwood and Myers(9). In this case I found hæmorrhages in the brain stem just above the striæ acousticæ, similar to those caused in cats by dragging on the auditory nerves during attempts to cut them. The brain stem of the second case is about to be examined.

Remarks and Conclusions.

During normal respiration neither inspiration nor expiration attains its full extent since the vagal impulses are constantly limiting alternately apneusis and expiration, especially the former. Since the vagus thus tonically accelerates the respiration in all cases, whatever its depth and rate may be, vagotomy always slows and deepens the breathing.

The H-ions in the blood continuously increase the excitability of the pneumotaxic centre so that it periodically discharges and inhibits the tonic apneusis and thus in conjunction with the vagus determines the rhythm of respiration of normal type.

Apart from vagal influences, *e.g.* after vagotomy, the height and depth of unconscious breathing is determined primarily by the stimulating effect which CO_2 excess exerts upon the apneustic, and when the excess is pronounced, upon the expiratory centres.

During waking life cerebral influences modify respiration to a variable degree, often profoundly. There is now no fixed base line (position of complete relaxation) to which each expiration returns, such as is seen during sleep and anæsthesia. The lower edge of a respiratory tracing taken during consciousness varies up and down continually.

When CO_2 is present in moderately increased amount the first effect is that the inspiration becomes deeper from stimulation of the apneustic centre, if the increase of CO_2 continues, expiration is also exaggerated, from stimulation of the expiratory centre. If these efforts do not succeed in diminishing the excess of CO_2 the pneumotaxic centre by becoming more excitable increases the rate of respiration and the larger currents of air passing through the bronchi stimulate the vagal endings more powerfully than usual, thus further adding to the acceleration of breathing by limiting more drastically than usual the continuance of both inspiratory and expiratory movements.

If during dyspnœa due to CO_2 excess the vagi are cut, the slowing and deepening of the breathing is much more marked and expiration becomes more intense and spastic than if vagotomy is performed during quiet respiration; an evidence that the vagi were carrying inhibitory messages more powerful than usual (Fig. 2).

Even after vagotomy the respiration may quicken very markedly during CO_2 dyspnœa, it is therefore clear that the vagus is not the only accelerating mechanism. It appears that the pneumotaxic, apneustic and expiratory centres are all rendered more excitable by excess of H-ions in the blood circulating through them and hence respond more actively than usual, thus quickening the breathing (Fig. 3).

When the pneumotaxic centre is damaged or is failing from any cause, the response to CO_2 excess is much less brisk than normal and if now the vagi are cut the respiration becomes enormously increased in height and slowed almost to the point of apneusis and thereafter no increase of rate occurs. This shows that it is largely through the pneumotaxic centre that the CO_2 central acceleration is effected.

The effects of oxygen lack on respiration vary with its intensity. A moderate lack of O_2 down to 12 p.c. produces hardly any dyspnœa at all, and the slight effect it ultimately shows is possibly due to increased sensitivity to CO_2. Greater lack of O_2 (2–8 p.c.) stimulates apneusis, thus heightening inspiration for a short time, but soon it paralyses first the pneumotaxic centre and thus apneuses appear. The centres at the striæ region next fail, gasping resulting, and soon this also stops and death ensues.

Asphyxial death is entirely due to O_2 lack. Very large amounts (20 to 30 p.c.) of CO_2 can be breathed for several hours on end without immediate danger to life.

It is probable that various nerves of deep sensibility supplying the thoracic and abdominal parietes and contents also aid in regulating respiration, and on occasion the trigemini certainly do, *e.g.* by inducing sneezing and by inhibiting respiration altogether when an irritant gas enters the nostrils.

The accelerating (inhibitory) vagal effects are normally evoked by the inrushing and outflowing currents of air; the former inhibits the inspiration which caused it and conversely the latter inhibits expiration.

Besides these accelerating impulses the vagi also convey to the brain stem postural impulses relating to the condition of the lungs as regards distention, deflation, positive and negative pressure, etc. The effect of these impulses is to evoke such muscular efforts as will make for quiescence at the zero point of pressure and the mid-way position of repose between inspiration and expiration. Within the pressures and limits of ordinary easy breathing these postural and pressure impulses are unimportant.

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