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WILLIAM F. ALLEN

From the Department of Anatomy of the University of Oregon Medical School, Portland, Oregon

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II. VAGUS AND VAGOTOMY EXPERIMENTS

WILLIAM F. ALLEN

From the Department of Anatomy of the University of Oregon Medical School, Portland, Oregon

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The purpose of this investigation is threefold: first, to determine the effect of inhaling strong and weak irritating vapors on respiration and circulation in a *vagal* animal, by which is meant an animal deprived of all effective sensory nerves supplying its upper respiratory passages (olfactory and trigeminal); second, to ascertain if there is any alteration of respiration and circulation during the inhalation of irritants in a *vagal* rabbit after double vagotomy; third, to repeat the experiments of several previous investigators on insufflation of irritating vapors into the trachea of vagotomized animals in which both positive and negative results have been obtained.

In attempting to solve the first problem suggested above, there is apparently no available technique (unless it be some complicated modification of the isolated head technique) for completely eliminating the possibility of humoral and secondary mechanical stimulation of the periphery or of humoral stimulation of the medulla centers. If negative results are obtained in the experiments of the second and third problems suggested, it may be inferred that humoral medulla-spinal stimulation is not a factor in the first problem. A previous paper and especially one to follow indicate that humoral and secondary mechanical factors take but little part in the alteration of respiration and circulation where these vapors were inhaled for relatively short periods of time.

The vagus changes in respiration following the blowing of an irritant into the trachea, as demonstrated by Zagari, consists of a considerable depression and acceleration. As reported by Roger, Mayer Magne and Plantefol, Craigie, Larsell and Burget, it includes a period of violent coughing or spasm followed by apnea or shallow respiration. Brodie and Russell's and Roger's blood pressure tracings show a distinct drop and a

strengthening of the pulse, and Craigie's tracings disclose a fall at the time of stimulation.

Effect of various inhalants on respiration, blood pressure and carotid pulse in vagal rabbits. Several days before these tests were made the olfactory tracts, the naso-ciliary and maxillary nerves were sectioned in the manner described in a previous report; severance of these nerves was previously found to be as effective in blocking trigeminal impulses from inhalations as division of the trigeminal roots intracranially. Thoracic respiratory and blood pressure tracings were taken as described previously with the animal under veronal-sodium hypnosis.

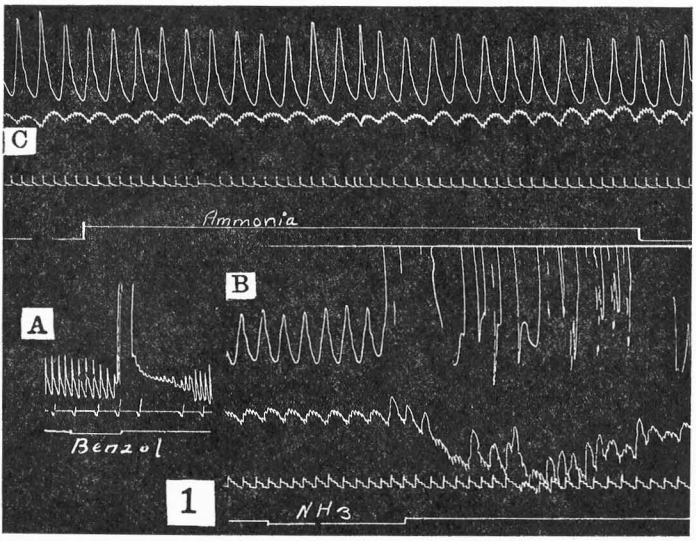

Fig. 1 A. *Vagal* rabbit, stimulation by inhalation, thoracic-respiratory graph, inspiration upstroke, time in 5 seconds; B and C, *vagal* rabbit, inhalation stimulation, thoracic-respiratory and blood pressure tracings, time in seconds; in C, depressors, vagi, and cervical sympathetics were cut.

In the first rabbit (563) the graphs were confined to respiratory tracings taken during the inhalation of ammonia, benzol and xylol from cones saturated with these substances. The ammonia cone was held about 7 cm. from the nostrils, the benzol about 4 cm., and the xylol about 3 cm. The benzol graph (fig. 1, A) reveals three distinct changes taking place in respiration. First, there is a short interval of depression. This gives way to a sudden expansion of the chest, starting during an expiration, it continues as a series of coughs or spasm. The extreme height of these forced movements of the lever was purposely stopped by a bar. This important phase is abruptly followed by a period of shallow and somewhat acceler-

ated excursions and a gradual return to normal. The graphs obtained during the inhalation of ammonia and xylol were somewhat similar. The chief difference is in the time of appearance of the altered respiration and the duration time of the coughing spell. The change appears within 9 seconds in the ammonia tracing, within 10 secones in the benzol record, and not until 20 seconds in the xylol graph. The coughing spell is longest in the ammonia record and shortest in the xylol. In the ammonia record there is some inhibition as well as depression in the first period, and only a moderate depression of the excursions following the coughing period.

In the second part of this experiment the depressors, vagi, and cervical sympathetics were sectioned at the level of the larynx, and respiratory tracings obtained during the inhalation of ammonia, benzol and acetic acid for periods of fifty seconds, as shown by the benzol graph (fig. 2, A), reveal respiration unchanged.

Both parts of this experiment were repeated in two other *vagal* rabbits with like results.

In *vagal* rabbits (571 and 572) this experiment was repeated and its scope was enlarged to include blood pressure tracings. The respiratory responses obtained during the inhalation of ammonia, aromatic spirits of ammonia, acetic acid, chloroform, oil of mustard, wintergreen, benzol and xylol are very similar to those obtained in the previous animals. Every record shows a considerable drop in blood pressure accompanied, usually, by some slowing and strengthening of the pulse.

In one graph (fig. 1, B) an ammonia cone was purposely held close to the nostrils to elicit a maximum stimulation. It is apparent that the reaction is concerned almost entirely with the interval of coughing, which appears in 9 seconds and lasts for 20 seconds. There is no depression or inhibition of the excursions preceding the period of coughing and only an acceleration of a few excursions immediately following. Meanwhile the blood pressure tracing discloses a drop of 20 mm. and there appears to be some slowing and strengthening of the pulse.

As in the previous animals the xylol reaction is the weakest and slowest in appearing.

After sectioning the depressors, vagi and cervical sympathetics, the same vapors inhaled for periods of 50 seconds evoke no change in respiration or pulse or any drop in blood pressure (see ammonia graph fig. 1, C). The apparent inhibition of respiration during the last part of this tracing is shown to be due to a speeding up of the drum. It is obvious from the blood pressure tracing (fig. 1, C) that there is no change for 32 seconds, the slight rise which occurs a little later may come from humoral stimulation of the medulla.

Effect from inhalation of weak and very weak irritants in vagal animals. It was stated in the previous experiment that xylol was one of the weakest

stimulants of the vagus, so that a weak xylol stimulation should yield a very weak vagal reaction, if it produces any at all. Figure 2, B was obtained while a cone, saturated with xylol, was held at some distance from the nostrils for 40 seconds. After 32 seconds of inhalation (allowance being made for the omitted portion of the record) there is a slight inhibition of respiration and a small drop in blood pressure without any change in the pulse. These changes are not thought to be of humoral medulla-spinal cord origin for the reason that none of the writer's graphs taken from vagotomized *vagal* rabbits show any alteration of respiration and blood pressure from inhalations of much stronger xylol vapor for a con-

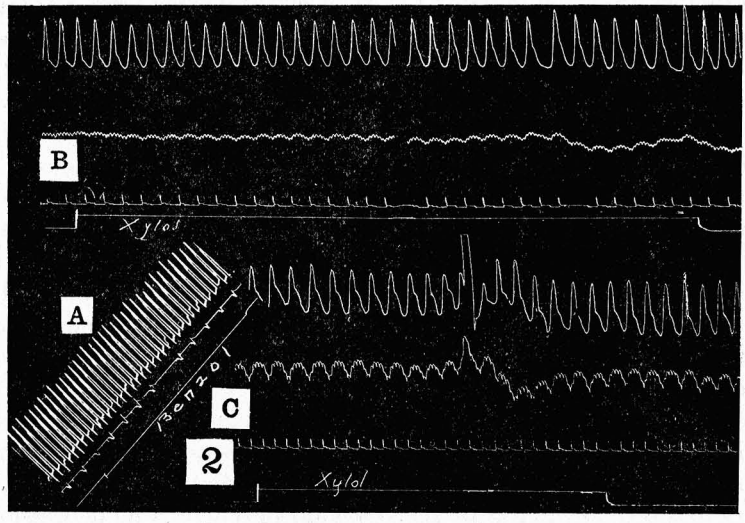

Fig. 2 A. Same as 1 A, except that depressors, vagi, and cervical sympathetics were severed; B and C, *vagal* rabbit, stimulations by low and very low concentrations of xylol inhaled, thoracic-respiration and blood pressure tracings (omitted portion in B represents 7 seconds), time in seconds.

siderably longer time. Also the drop in blood pressure speaks for a vagal stimulation.

A stronger xylol stimulus obtained from holding the cone closer to the nostrils (fig. 2, C) demonstrates the changes in respiration and blood pressure appearing within 16 seconds. The respiratory response, in the upper tracing, shows a cough reflex or spasm preceded and followed by short periods of depression. There is considerable drop in blood pressure and some slowing and strengthening of the pulse.

A typical vagal respiratory and circulatory response was obtained in a tracheotomized *vagal* rabbit with the laryngeal branch of the vagus intact by blowing large quantities of ammonia into both nostrils. Later when

the pharynx was slit above the larynx so that little or no ammonia reached the larynx, no vagus reaction was obtained from insufflation into the nostrils. This is apparently confirmatory of Kratschmer's results obtained by blowing an irritant directly into an isolated larynx.

Effect of insufflation of ammonia and other vapors into the trachea of vagotomized rabbits. Of the investigators who have stimulated the lower respiratory passages of vagotomized animals by blowing irritants into the trachea, Zagari, Mayer, Magne and Plantefol, and Larsell and Burget report no respiratory reaction; while Roger and Craigie obtained definite respiratory and blood pressure changes. Roger's figure 10 portrays considerable depression and inhibition in respiration and a drop in blood pressure during chloroform insufflation, and Craigie's graphs disclose the normal vagus changes slightly weakened. After a study of these publications it appeared likely that the difference in results might be largely attributed to variations in technique.

This experiment or problem passed through three different stages as unforeseen factors were encountered.

First,—a number of thoracic respiratory and blood pressure tracings were made from several vagotomized rabbits during the time that ammonia vapor was blown into the tracheal cannula through which the animal was breathing. These records demonstrate a varying amount of expansion of the thorax, a depression of respiration, and a fall in blood pressure. It was evident that these changes might be explained by local pulmonary changes offering a greater resistance to the respiratory movements of the thorax, due possibly to an increased expansion of the lungs from the insufflations or to a spasm of the constrictor muscles of the trachea and bronchi. With these possibilities in mind it became necessary to pay more attention to air controls and to the amount of pressure used during insufflation.

Second,—the previous procedure of taking thoracic and blood pressure records during insufflations into the trachea of rabbits deprived of their depressors, vagi, and cervical sympathetics was repeated and expanded to include a respiratory tracing taken from the trachea. The apparatus for obtaining the tracheal record consisted of a Y-shaped tracheal cannula, one external arm of which was connected to a previously described blowing bottle by a rubber tube with a pinch clamp, and the other external arm was in direct communication with a large air bottle and recording tambour. The bottle in addition to supplying some air for ventilation served as a sort of buffer. The wounds in the neck, the mouth, and the nostrils were covered with cotton.

The procedure of insufflation was as follows: the animal breathed from the air chamber for a short interval, then air and insufflated vapor for periods of from 3 to 17 seconds, and finally from the air chamber. In a

few tests this technique was varied by the attachment of two blowing bottles to one arm of the cannula, so that air blown from the first bottle into the trachea could be followed immediately by an irritating vapor from the second. A large number of simultaneous thoracic-respiratory, tracheal-respiratory, and blood pressure tracings were obtained from five rabbits during the insufflation of ammonia, acetic acid, ether, and especially air, under great variations of pressure.

These records reveal that there is a direct relationship between any given tracheal respiratory excursion and the corresponding thoracic ex-

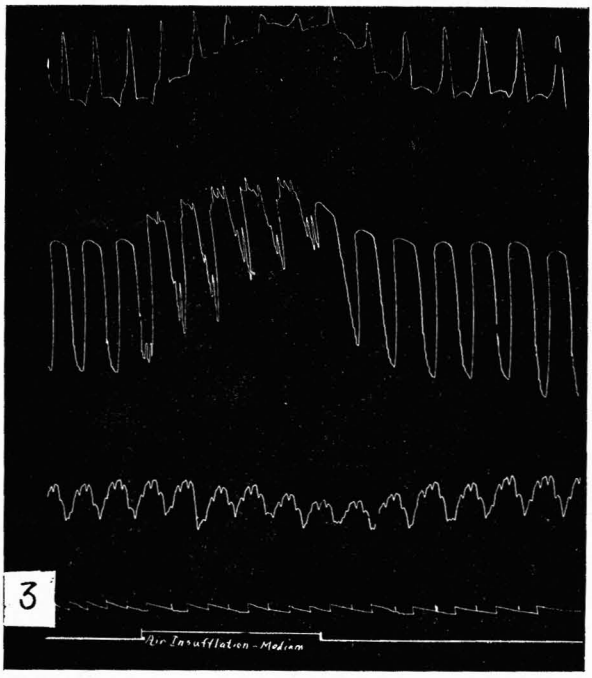

Fig. 3. Vagotomized rabbit, tracheal insufflation, thoracic-respiratory, tracheal-respiratory, and blood pressure tracings, time in seconds.

cursion, and it is immaterial whether this record is from insufflation of an irritant or air. An air control graph (fig. 3) demonstrates that a slight increase in air pressure is followed by some increase in the depth of the first thoracic respiratory excursion. After a certain point has been reached in the expansion of the lungs and thorax, a gradual increase in pressure elicits a gradual expansion of the thorax and a gradual reduction in the depth of thoracic respiration. In some records this has been increased to the extent of bringing pulmonary and thoracic respiration to a standstill. By varying the pressure in an air control graph, it is possible to duplicate any graph obtained from any irritant.

With the technique employed there is some indication of greater expansion in the lungs by some vapors (ether) than there is with some others under the same pressure.

Practically all of these records show some drop in blood pressure and no pulse change. In general, there is a considerably greater drop in the graphs obtained during the insufflation of an irritant than there is for air. The contour of the blood pressure curve appears to conform very closely to the curve of the general expansion of the thorax as is shown in figure 3.

Third,—in two rabbits the above stimulation technique was considerably modified. In place of insufflating the vapors into the tracheal cannula, the bulb was removed from the blowing bottle and the animal was permitted to inhale through the cannula air saturated with ammonia, acetic acid, and ether for periods of from 12 to 18 seconds. After each inhalant, air was inhaled through water for the same length of time. There can be no question but that this mode of procedure flooded the lungs with large quantities of air well saturated with these vapors. A comparison of any irritant graph with its air control discloses no difference. Both respiratory tracings of all the records show some expansion during the time of inhalation. Ordinarily blood pressure shows no changes in either record, but sometimes there is a slight drop in both tracings.

Comment. Two deductions appear to be fairly well warranted by the results obtained from the foregoing experiments—a, that certain nerves, supposed by Barry, Pike and Coombs, and Möllgaard to carry impulses from the lungs to spinal cord by way of the upper thoracic and lower cervical spinal nerves, are not stimulated to produce respiratory changes by large quantities of air containing a high concentration of very irritating vapors; b, that relatively short inhalations or insufflations of very irritating vapors do not cause a humoral medulla-spinal stimulation affecting respiration.

SUMMARY AND CONCLUSIONS

Moderately strong inhalations of various irritating vapors by way of the nose in the so-called *vagal* rabbits, animals having no protection from the olfactory or trigeminal nerves, produce somewhat similar respiratory and vascular changes to those described by others from blowing these irritants into the trachea.

This alteration of thoracic respiration consists of 1, a short period of depression or depression and inhibition; 2, a spasm or period of coughing, depending in length and strength on the irritant used; 3, a period of more or less depression with a gradual return to normal. The important character is the period of coughing.

Blood pressure drops in proportion to the strength of the irritant used and to the general expansion of the thorax. There is generally some slowing and strengthening of the carotid pulse.

A very powerful thoracic respiratory reaction from inhalations in a *vagal* rabbit consists of the immediate appearance of the coughing spell; while a very weak reaction shows only a slight inhibition of respiration, a little drop in blood pressure and no pulse changes.

Changes in respiration and circulation are elicited from inhalations of ammonia, acetic acid, formalin, oil of mustard, wintergreen, chloroform, ether, benzol and xylol.

After sectioning the depressors, vagi, and cervical sympathetics at the level of the larynx, any of the above vapors could be inhaled through the nostrils by a *vagal* rabbit for fifty seconds without any alteration of respiration or drop in blood pressure.

Insufflation of irritating vapors into the trachea of vagotomized rabbits is followed by a response in respiration and circulation very similar to that described by Roger for chloroform, consisting of a general expansion of the thorax, a depression of respiration, and a drop in blood pressure. Evidence is produced which shows that these respiratory changes in the writer's animals are probably caused by an increase in the intrapulmonary pressure resulting from the insufflations.

Vagotomized rabbits, inhaling through the trachea large quantities of air containing a high concentration of irritating vapors, show no greater respiratory and circulatory changes than when inhaling unmixed air under the same conditions.

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