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VENTILATION VOLUME AS A STIMULUS TO SPONTANEOUS VENTILATION AFTER PROLONGED ARTIFICIAL VENTILATION

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The observations reported in this paper are intended to determine whether the ventilation *volume* imposed during artificial ventilation has an effect on subsequent spontaneous ventilation. It reports investigations on paretic patients in which the tidal volume imposed during artificial ventilation was varied, but the end-tidal pCO_2 and the ventilatory frequency were kept constant. A variable volume of external dead space was introduced during artificial ventilation. Periods of spontaneous ventilation were subsequently permitted, and during these periods the external dead space was small. The effect has been observed of these changes in imposed tidal volume on the ventilation subsequently chosen by the patient when breathing spontaneously, and on his response to CO_2 added to the inspired air.

METHODS

Material. Two patients with respiratory weakness were investigated. Both had tracheotomies, and their lungs were clinically and radiologically normal.

Patient V. H., a female aged 41 years, weighing 49·5 kg, suffered from myasthenia gravis, and had received artificial respiration for about 8 months. She received injections of neostigmine and atropine every 2 hr. At the time of these investigations her maximum ventilatory capacity, measured over 1 min at the conclusion of the periods of spontaneous respiration, lay between 31 and 43 l./min.

Patient S. W., a male aged 12 years, weighing 40 kg, suffered from acute polyneuritis and had received artificial respiration for about 4 weeks. At the time of these investigations his maximum ventilatory capacity lay between 42 and 50 l./min.

Ventilation. The patients received artificial ventilation by intermittent positive pressure from a Radcliffe Respiration Pump (Russell, Schuster, Smith & Spalding, 1956) through a cuffed tracheotomy tube (Spalding & Smith, 1956) which provided an airtight seal in the trachea. The frequency imposed during artificial ventilation was constant for each patient, and the patients were artificially ventilated for at least 18 hr daily. Throughout the period of artificial ventilation a variable volume of external dead space was inserted between the tracheotomy tube and the inspiratory and expiratory leads from the respiration pump. Tidal volume was adjusted to keep the end-tidal pCO_2 at the tracheotomy tube constant. The total external dead space was between 25 and 500 ml. and it consisted of plastic tubing

of 1·0 or 2·0 cm internal diameter. In spite of the external dead space gaseous exchange was adequate, for end-tidal pCO_2 was below normal (31·5–33·5 mm Hg in patient V.H., 30–32 mm in patient S.W.), and end-tidal pO_2 was never below 100 mm.

Spontaneous ventilation was permitted at intervals during normal waking hours, for periods lasting between 30 min and 5 hr, and together totalling not more than 6 hr in 24 hr. Spontaneous ventilation was not continued if the patient was tired and on no occasion did it exceed 50 % of the patient's maximum ventilatory capacity measured over 1 min. During spontaneous ventilation the patients breathed through the apparatus shown in Fig. 1. The Siebe Gorman valve had an opening pressure of 0·2 cm H_2O and a resistance of 0·4 cm H_2O at an air flow of 60 l./min. The dead space of the apparatus (Fig. 1, shaded area) was 47 ml. for patient V.H. and 35 ml. for patient S.W. Tracheotomy reduces the natural dead space by at least this amount.

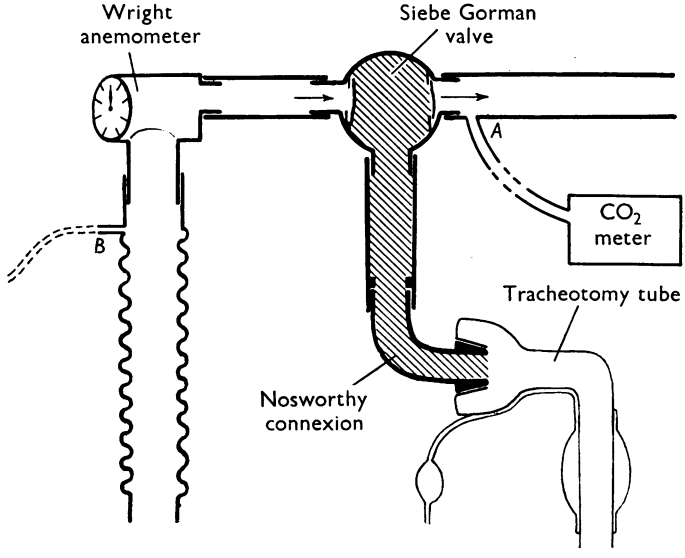

Fig. 1. Apparatus through which patients breathed during spontaneous ventilation.

Respiratory minute volume was measured over consecutive periods of 1 min at ambient temperature and pressure. During artificial ventilation the expired minute volume was measured with a dry gas meter (Parkinson & Cowan, type CD). During spontaneous ventilation the inspired minute volume was measured with a Wright anemometer (Wright, 1955) (Fig. 1). The anemometer readings had previously been compared with those of a dry gas meter with tidal volumes of 150 ml.–2 l., and throughout the range agreement was within 2 % of the recorded volume. All gas volumes are expressed at ambient temperature and pressure.

End-tidal pCO_2 was derived from the records of a direct-writing infra-red CO_2 analyser ('Irdometer', Infra-Red Development Co., Welwyn Garden City, Herts). The analyser was calibrated before and during each investigation with gas from a cylinder containing about 5 % CO_2 in air, the precise composition of which was measured with a development of the Haldane apparatus (Lloyd, 1958). The analyser was also calibrated with air-CO_2 mixtures containing smaller proportions of CO_2 measured by the Haldane method, and the calibration curve conformed to that supplied by the manufacturers.

During artificial ventilation inspired and expired gas was continuously sampled at 100–150 ml./min from the external end of the tracheotomy tube, and was led to the infra-red

CO_2 analyser. The end-tidal pCO_2 obtained in this way agreed with the results obtained at the same time with a mechanical end-tidal sampler (Smith, Schuster & Spalding, 1959) and volumetric gas analysis.

During spontaneous ventilation expired gas was continuously sampled from the proximal end of the expiratory tube (*A*, Fig. 1). There was no systematic difference between end-tidal pCO_2 obtained in this way and from samples taken at the same time from the external end of the tracheotomy tube. Agreement was within 1 mm in 37 out of 38 comparisons.

The response to CO_2 was assessed by adding CO_2 to the inspired air through orifice *B* (Fig. 1). The inspired CO_2 concentration was raised and lowered in steps of about 0·5 % and kept at each level for three to 5 min. The effect on respiratory minute volume was observed as the CO_2 rose and as it fell. Each of these tests took not more than 30 min.

RESULTS

In Fig. 2*a* and *b* spontaneous respiratory minute volumes and spontaneous tidal volumes are plotted against the preceding artificial minute volumes and tidal volumes respectively. In Figs. 3 and 4 minute volume is plotted against end-tidal pCO_2 before (large closed circles) and after (small closed circles) artificial ventilation was discontinued, for five of the same experiments. The minute volume imposed during artificial ventilation varied from 7·8 to 16 l./min in patient V.H. and from 7·8 to 14·2 l./min in patient S.W. If the external dead space during artificial respiration was 100 ml. or more, minute volume during spontaneous ventilation was 67–83 % of that previously imposed during artificial ventilation (Fig. 2*a*). The tidal volume during spontaneous ventilation was about 65 % in patient V.H. and 80 % in patient S.W. of that imposed during artificial ventilation (Fig. 2*b*).

End-tidal pCO_2 during artificial ventilation did not vary by more than 2 mm. During spontaneous ventilation, however, the end-tidal pCO_2 was lower than during artificial ventilation by amounts up to 11 mm (Figs. 3 and 4).

Respiratory frequency showed little change when spontaneous breathing replaced artificial respiration.

When CO_2 was added to the inspired air during spontaneous ventilation in patient V.H., there was only a slight increase in minute volume until the pCO_2 had risen from its initial level to about 32 mm (Fig. 3, crosses), close to the value at which it had been maintained during artificial ventilation. This rise might be as much as 11 mm (Fig. 3*d*). When this level was reached there was a marked increase in minute volume. In patient S.W. the effects of CO_2 inhalation were substantially the same (Fig. 4). Figure 4 also illustrates that the minute volume/pCO_2 curve obtained as the pCO_2 rose was similar to that as pCO_2 fell.

Minute volume during spontaneous ventilation was proportional to that during artificial ventilation only if artificial ventilation with a large

external dead space and large tidal volume had been maintained for more than 5–10 hr, usually about 6 hr.

Spontaneous ventilation which was proportional to the ventilation volume previously imposed during artificial ventilation was observed to continue for periods up to 5 hr at a time. If the patient, however, fell

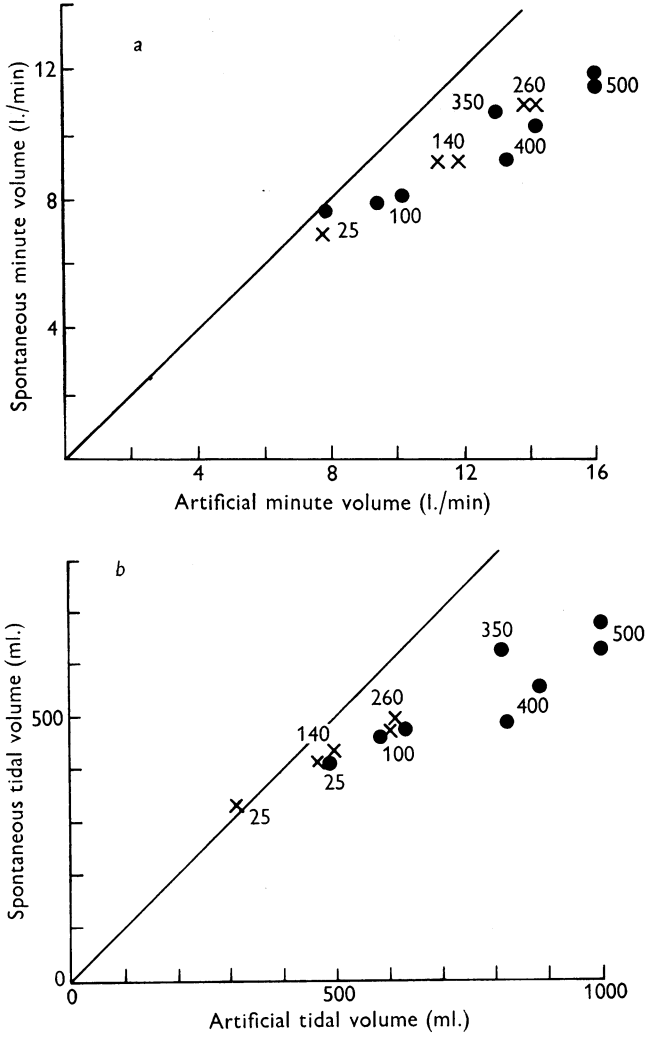

Fig. 2*a* and *b*. Relation of respiratory minute volume and tidal volume during spontaneous ventilation, to minute volume and tidal volume during the preceding artificial ventilation. The figures beside the points are the external dead spaces (ml.) required to keep the end-tidal pCO_2 constant during artificial ventilation. The external dead spaces during spontaneous ventilation were 47 ml. (V.H., ●) and 35 ml. (S.W., ×). The full line is the line of equality.

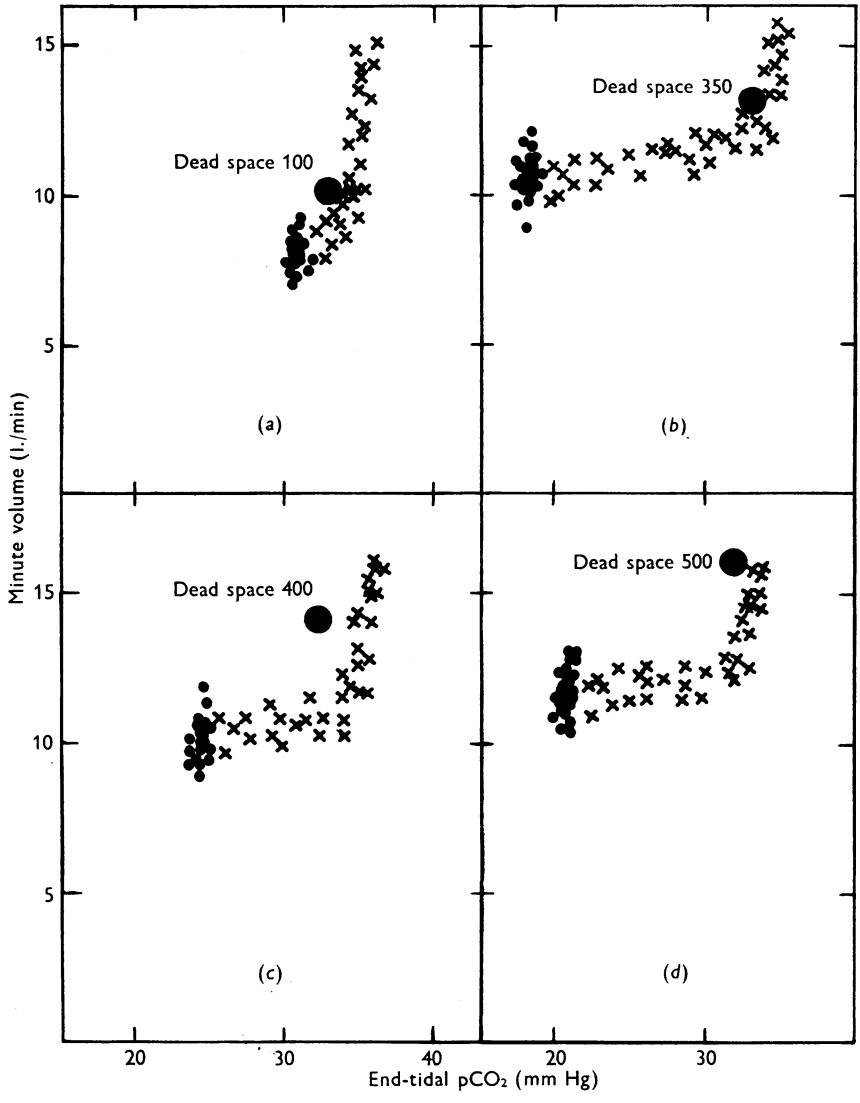

Fig. 3. Minute volume and end-tidal pCO_2 of patient V. H. during artificial ventilation (●) with various external dead spaces whose volumes (ml.) are shown beside the large symbol; during subsequent spontaneous ventilation with external dead space 47 ml. (●); and during spontaneous ventilation when CO_2 was added to the inspired air (×). Each point during spontaneous ventilation represents measurements made over 1 min.

asleep at any time when breathing spontaneously, minute volume fell and end-tidal pCO_2 rose (Figs. 5 and 6). If he remained asleep, end-tidal pCO_2 reached a new point of stability (Fig. 6*a*) and at this point the addition of CO_2 to the inspired air produced a marked and immediate increase in minute volume (Fig. 6*b*). When the patient awoke, minute volume rose slightly and the end-tidal pCO_2 fell by 4–6 mm. The pCO_2 then became

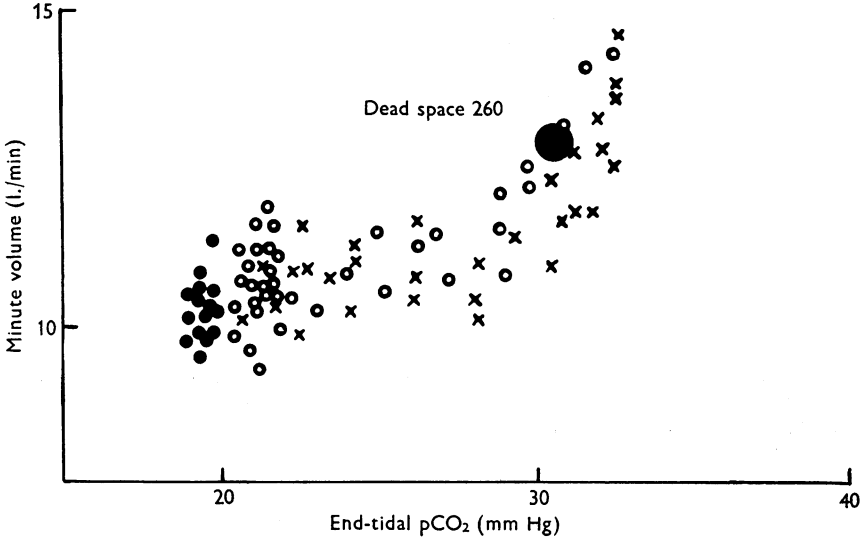

Fig. 4. Minute volume and end-tidal pCO_2 of patient S. W.; during artificial ventilation (●) with external dead space of 260 ml.; during subsequent spontaneous ventilation with external dead space of 35 ml. (●); and during spontaneous ventilation when CO_2 was added to the inspired air. Points are shown separately as pCO_2 was rising (×) and as it was falling (○), and each point represents measurements made over 1 min.

stable at the level at which the patient had been maintained during artificial ventilation, and addition of CO_2 to the inspired air produced a marked and immediate rise in minute volume (Fig. 6*b*).

The patient's spontaneous ventilation was not altered by breathing pure oxygen instead of air. The lung compliance of each patient during spontaneous ventilation was approximately constant despite variations in the volume of the previous artificial ventilation.

DISCUSSION

Patients received artificial ventilation with various large tidal volumes, and their end-tidal pCO_2 was kept constant. We have demonstrated that when the patients were allowed to breathe spontaneously with only a

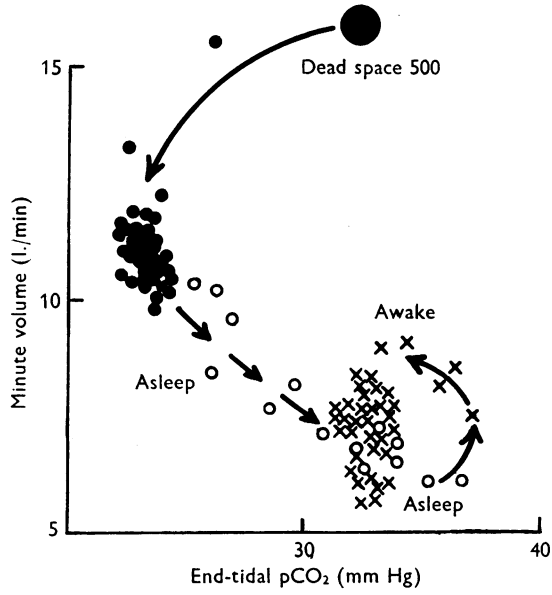

Fig. 5. Minute volume and end-tidal pCO_2 of patient V. H.: during artificial ventilation with external dead space of 500 ml. (●); during subsequent spontaneous ventilation with external dead space of 47 ml. when awake (●), when asleep (○), and after waking (×). Each point shown during spontaneous ventilation represents measurements made over 1 min.

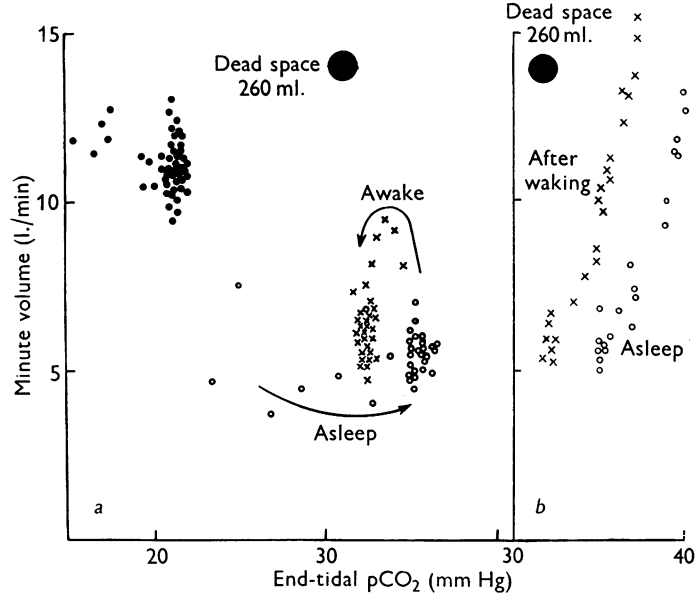

Fig. 6. (*a*) Minute volume and end-tidal pCO_2 of patient S. W.: during artificial ventilation (●) with external dead space of 260 ml.; during subsequent spontaneous ventilation with external dead space of 35 ml., awake (●), asleep (○) and after waking (×). Each point shown during spontaneous ventilation represents measurements made over 1 min. (*b*) Minute volume and end-tidal pCO_2 when CO_2 was added to the inspired air when the patient was asleep (○) and after waking (×).

small external dead space the minute volume and tidal volume were related to the minute volume and tidal volume during the preceding period of artificial ventilation with a large external dead space (Fig. 2). In this state the patient's end-tidal pCO_2 fell by amounts up to 11 mm Hg (Fig. 3*d*), and minute volume was almost unaffected by CO_2 added to the inspired air, until the end-tidal pCO_2 had risen to the level which had prevailed during artificial ventilation. The response to CO_2 was then brisk (Figs. 3 and 4). This ventilatory response to CO_2 is similar to that seen during hypocapnia produced in other ways, such as by hypoxia (Nielsen & Smith, 1951; Hall, 1953) and raised body temperature (Cunningham & O'Riordan, 1957).

When a patient who was breathing spontaneously in this volume-dependent way fell asleep, his minute volume during sleep and after waking was quite different from that which prevailed before sleep (Figs. 5 and 6*a*). After sleep the patient ventilated at such a level that the end-tidal pCO_2 was at or slightly above that during the previous artificial ventilation. During sleep the patient's end-tidal pCO_2 was about 5 mm higher than when he subsequently woke, and this is similar to the change that occurs in normal subjects on waking (Reed & Kellogg, 1958). Both during sleep and after waking, addition of CO_2 to the patient's inspired air produced an immediate increase in minute volume (Fig. 6*b*). The minute volume/pCO_2 curve after waking was very similar to the steep part of the minute volume/pCO_2 curve observed before the patient fell asleep. The flat part of the minute volume/pCO_2 curve, however, was not present when the patient had fallen asleep and woken again. We conclude, therefore, that when the patient is asleep and later awakes, his minute volume is largely controlled by pCO_2, and that this mechanism is distinct from the volume-dependent mechanism which largely controlled minute volume before the patient fell asleep.

Some comments can be made about the mechanism by which the volume-dependent type of spontaneous ventilation observed in these patients may occur. The involuntary continuation of overventilation after less than 2 hr of voluntary active overventilation has been described by Boothby (1912) in himself, and by Mills (1946) in six normal subjects. Boothby's explanation was that the lowered arterial pCO_2 caused cerebral vasoconstriction, that this caused the pCO_2 of the 'respiratory centre' to rise from inadequate perfusion, and that the high intracellular pCO_2 provided the stimulus for continued overventilation. This hypothesis is only applicable when the original period of ventilation with a large volume is accompanied by hypocapnia, and this was not the case in our patients.

An alternative hypothesis, consistent with the present observations, is that ventilation volume influences the central mechanisms controlling

ventilation by means of an afferent pathway originating in receptors in the lungs and/or chest wall. If this hypothesis is correct, it may be that a change allied to habituation occurs in this afferent pathway or its central connexions during artificial ventilation with a large volume over a period exceeding about 6 hr. It is interesting that this suggested habituative change is abolished by sleep.

SUMMARY

1. Two paretic patients with tracheotomies received artificial ventilation at constant frequencies for at least 18 hr daily. External dead space of 25–500 ml. was added and tidal volume was adjusted between 312 and 1000 ml. to keep end-tidal pCO_2 unchanged at 31–32 mm Hg. The patients breathed spontaneously with minimum external dead space for periods up to 5 hr daily, and minute volume, frequency, end-tidal pCO_2, and response to inhalation of CO_2/air mixtures were observed.

2. If artificial ventilation was performed for more than about 6 hr with an external dead space of 100 ml or more, subsequent spontaneous minute volume and tidal volume were related to the minute volume and tidal volume previously imposed.

3. During volume-dependent ventilation of this type, end-tidal pCO_2 was lower than during artificial ventilation by amounts up to 11 mm Hg. Inspiration of CO_2/air mixtures produced only slight changes in minute volume until end-tidal pCO_2 reached the level which had prevailed during artificial ventilation. There was then a marked increase in minute volume.

4. If the patient fell asleep, minute volume fell and end-tidal pCO_2 rose. On waking, volume-dependent respiration was not resumed and end-tidal pCO_2 was maintained at the level which had prevailed during artificial ventilation.

5. It is concluded that spontaneous ventilation can be influenced by a factor other than pCO_2 and pO_2 and that in the circumstances described this factor is related to minute volume or tidal volume which has previously prevailed. The mechanism for this may be dependent on an afferent pathway originating in receptors in the lungs and/or chest wall.

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