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RESPIRATORY REFLEXES FROM THE TRACHEA AND BRONCHI OF THE CAT

By J. G. WIDDICOMBE

From the Nuffield Institute for Medical Research, University of Oxford

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Although considerable work has been carried out on respiratory reflexes from the lungs, less attention has been paid to the trachea and bronchi. Having completed an analysis of afferent nerve fibres from the tracheobronchial tree of the cat (Widdicombe, 1954*a*), it was desirable to identify the reflexes from this area, so that the functions of each afferent fibre group could be distinguished. This paper describes the experiments on tracheobronchial reflexes. The best known of these is the cough reflex which, although of obvious physiological and pathological importance, has been little investigated experimentally.

As well as the cough reflex another tracheobronchial reflex has been described. Hammouda & Wilson (1936) showed that changes in the tracheal diameter of the dog caused a slowing of respiration. This reflex has been investigated in cats.

METHODS

Cats have been used, anaesthetized with intraperitoneal sodium pentobarbitone (32 mg/kg) or with intravenous chloralose (60 mg/kg), the latter after induction with ethyl chloride and ethyl ether. Decerebrate cats were used for one series of experiments; these were prepared under ether anaesthesia and, as with chloralose, no experimental observations were made until sufficient time had elapsed for the volatile anaesthetics to be blown off (30–60 min). A tracheal cannula was inserted.

Respiration was usually recorded with the body plethysmograph described by Dawes, Mott & Widdicombe (1951); the volume changes of the animal's body from the neck downwards were registered by a float spirometer which wrote upon a smoked drum. In some experiments a spirometer was used in which the float was attached by its centre of rotation to the moving arm of a potentiometer; the latter was connected to a potential source and the voltage changes from the moving arm were amplified and recorded on a direct-coupled cathode-ray oscilloscope; the response was very nearly linear.

In cats which had had a thoracic operation it was often inconvenient to enclose the animal in the plethysmograph, and the respiration was recorded using a modification of the method of Donald & Christie (1949) for man (Fig. 1). The cat breathed through inspiratory and expiratory valves (V_I and V_E) of small dead space and resistance; inspired and expired airs were separated by a thin-walled rubber bag and the volume changes of the system recorded by a float spirometer.

The rubber bag collapsed at a rate corresponding to the minute volume of the animal's respiration, so that the length of time for which the apparatus could be used was limited by the capacity of the bag. If a large rubber bag was used the frequency response of the apparatus was low, and it did not record accurately the rapid volume changes of coughing and gasping. To overcome this difficulty a bag of about 200 ml. was used, and the inspiratory and expiratory sides of the circuit were connected by small bore tubing to 10 l. bottles, with water draining from the expiratory to the inspiratory bottle. As long as the flow of water was greater than the minute volume of the cat the rubber bag did not collapse, and the result was equivalent to using a bag of over 10 l. The records obtained reproduced accurately those from a body plethysmograph when the animal gasped and coughed. With most cats a continuous record could be obtained for 20 min; at the end of this period the water had to be returned to the upper bottle.

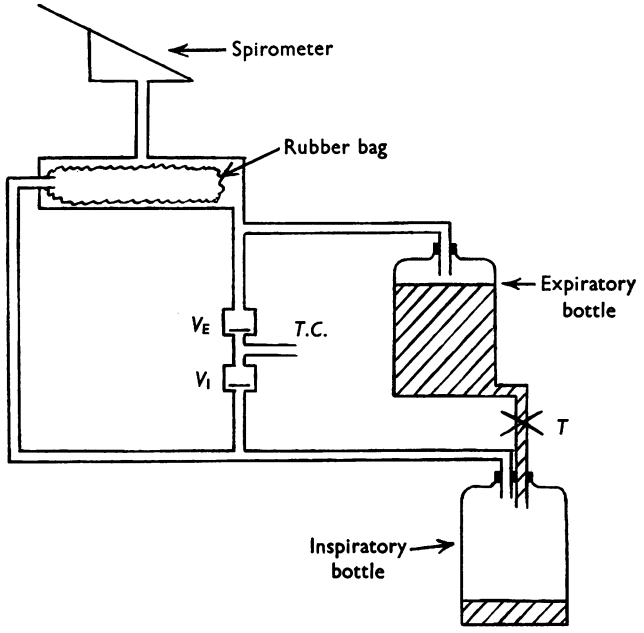

Fig. 1. Diagram of apparatus for recording respiration. *T.C.*, tracheal cannula. V_E and V_I, expiratory and inspiratory valves. *T*, adjustable tap controlling the flow of water from the expiratory to the inspiratory bottle. For description see text.

Intratracheal pressure was recorded by an electrical condenser manometer on a cathode-ray oscilloscope; occasionally a mercury manometer was used.

Phrenic nerve action potentials were recorded from the upper root of the left phrenic nerve in the neck. Strands containing single active fibres were placed on electrodes and their action potentials amplified and displayed on a cathode-ray oscilloscope. Fuller details of the electrical apparatus are given elsewhere (Widdicombe, 1954*a*).

Bronchial tone was measured in cats with widely opened chests by the method of Konzett & Rössler (1940). A constant volume of air was injected at each pump stroke into the tracheal cannula, a side arm of which led to a constant pressure overflow valve. Any change in the resistance to inflation was detected by the change in overflow volume. In the results to be described pulmonary cardiovascular changes have been virtually eliminated as a factor in the variations in

respiratory resistance; alterations in resistance to distension of the pulmonary parenchyma and in bronchial secretion would last longer than the changes observed. Eserine sulphate (0·1 mg/kg) was sometimes administered to increase the resting bronchial tone.

The vagus nerves were cooled by placing them on hollow silver thermodes through which cold alcohol was circulated; the temperatures were recorded by thermocouples. A fuller description of this technique has already been given (Dawes *et al.* 1951).

Stimulation of coughing

Coughing was produced in several ways. For a *mechanical* stimulus a length of polythene tubing was passed down the cannulated trachea to the carina, or a probe passed up the cephalic end of the trachea to the larynx. To stimulate the inside of the main bronchi without first touching the tracheal walls or the carina, cats with open chests were used, artificially ventilated on the right lung only (see below), and the lower trachea was slit along its right side. A catheter could then be inserted into the left main bronchi, care being taken not to touch the carina. Alternatively, a catheter was passed retrogradely into one of the bronchi of the left upper lobe.

As a *chemical* stimulus to coughing sulphur dioxide was used. Of readily available gases sulphur dioxide causes coughing in far lower concentrations than those which exert toxic effects. According to Henderson & Haggard (1943) a concentration of 1 in 50,000 will elicit the cough reflex, while 1 in 10,000 to 20,000 administered for 30–60 min is required to cause toxic symptoms. Other noxious gases (ammonia, phosgene, etc.) may be harmful in concentrations too low to cause coughing. Sulphur dioxide was generated by adding dilute hydrochloric acid to some crystals of sodium thiosulphate in a conical flask. In order to make the cat cough a few ml. of air were bubbled through the liquid into the trachea during an inspiration. Such a method is entirely qualitative, but in any cat it was possible to cause a cough of reproducible magnitude by controlling the amount of air blown through the mixture. Powdered talc and starch were also used; these were blown into the trachea during an inspiration. Ethyl ether vapour was administered from an Oxford vaporizer, calibrated for use with a Palmer pump. Procaine solution spray was obtained from a clinical 'atomizer'. Gases could be passed into the lungs without being in contact with the trachea by means of an endobronchial catheter (Widdicombe, 1954*a*).

Operative procedures

To determine the reflex effect of stimuli limited to the tracheobronchial tree, the cat was artificially ventilated and the chest opened by a right intercostal incision. The azygos vein was tied and cut and a cannula inserted into the right main bronchus at its origin; this cannula had an internal bore of 3–4 mm. The proximal stump of the right main bronchus was ligatured and the right lung was artificially ventilated through the cannula. Both lobes of the left lung were tied off through the same incision, so that the trachea was left in continuity with the left main bronchi as a closed channel. The chest was then closed, the right bronchial cannula being connected to the exterior by a short length of rubber tubing. The animals invariably breathed again spontaneously, and remained in good condition for 1–3 hr; the tidal and minute volumes were within the normal range, and there was no obvious cyanosis. The operation usually involved collapse of the right upper lobe, which arises high from the right main bronchus, but the right lower and subcardiac lobes seemed sufficient to maintain the cats. The right vagus was undamaged, apart from its atrial branches.

A modification of this method was used to observe the effects of distension and collapse of the trachea and main bronchi on bronchial tone. The right lung was artificially ventilated as described, and the left *upper* lobe tied off. An endobronchial catheter was passed through the trachea to the left main bronchi, and the left *lower* lobe ventilated through the catheter; the resistance to inflation of this lobe was measured by the method of Konzett & Rössler (1940). The trachea and left bronchi proximal to the balloon on the catheter tip could be inflated and deflated, and the response of the bronchial muscle of the left lower lobe observed.

RESULTS

Respiratory reflexes

Mechanical stimuli. In spontaneously breathing cats the insertion of polythene tubing into the trachea caused coughing. Animals under chloralose usually gave an initial expiratory effort (Fig. 2), which was sometimes followed by gasps alternating with strong expirations if the catheter was allowed to remain *in situ*; since the trachea was cannulated it was impossible to say to what extent laryngeal closure might have influenced this course of events. A few cats showed a short pause in the course of an inspiration followed at

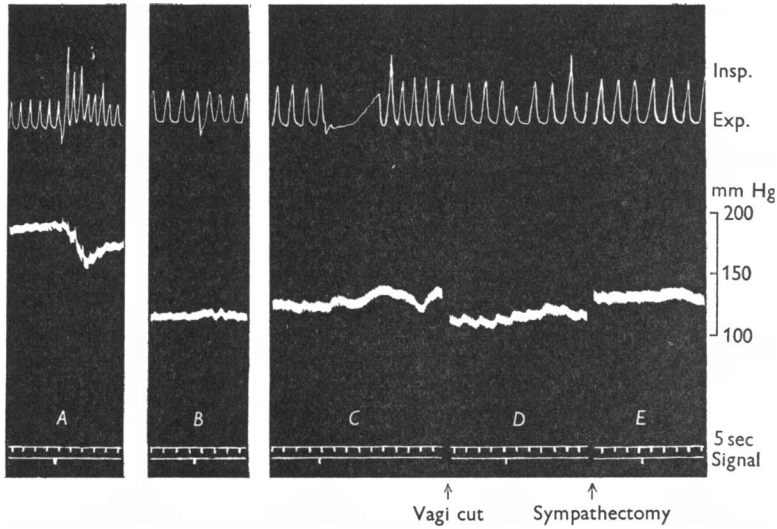

Fig. 2. Coughing in response to tracheal irritation by a cannula. Upper record: respiration. Lower record: systemic blood pressure. *A*, *B* and *C* show different types of response from three cats (chloralose anaesthesia). *C*, *D* and *E* are from the same cat; the vagi were cut between *C* and *D*, a bilateral thoracic sympathectomy was performed between *D* and *E*. This and subsequent kymograph records have been retouched.

once by a gasp. The stimulus caused an immediate inspiratory effort in two cats out of twenty. The reflex effects were completely abolished by cutting the vagi in three of five cats; the other two showed a slight inhibition of inspiratory activity after vagotomy (Fig. 2). This was abolished by bilateral thoracic sympathectomy. This effect was not due to mechanical obstruction of the bronchi; the catheter was inserted swiftly and removed at once, so that it was free of the trachea before the respiratory inhibition appeared.

The mechanical cough reflex was also elicited in cats which had been anaesthetized with intraperitoneal pentobarbitone (32 mg/kg). These animals almost invariably gave strong expiratory and inspiratory gasps rather than an isolated expiratory effort. In three cats under pentobarbitone an initial

intraperitoneal dose of 20 mg/kg was followed by repeated intravenous doses of 5 mg/kg while the cough reflex was induced after each injection. Similar results were observed in all three cats (Fig. 3). In a lightly anaesthetized cat the cough reflex was of the gasping type, but as anaesthesia deepened the respiratory response became a simple expiratory effort. Control experiments established that the reflex did not become refractory when repeated without deepening the anaesthesia. A strong impression was obtained that at comparable levels of anaesthesia the inspiratory component of coughing was depressed by chloralose much more than by pentobarbitone. Four decerebrate cats were also tested, and each gave a cough reflex of the gasping type.

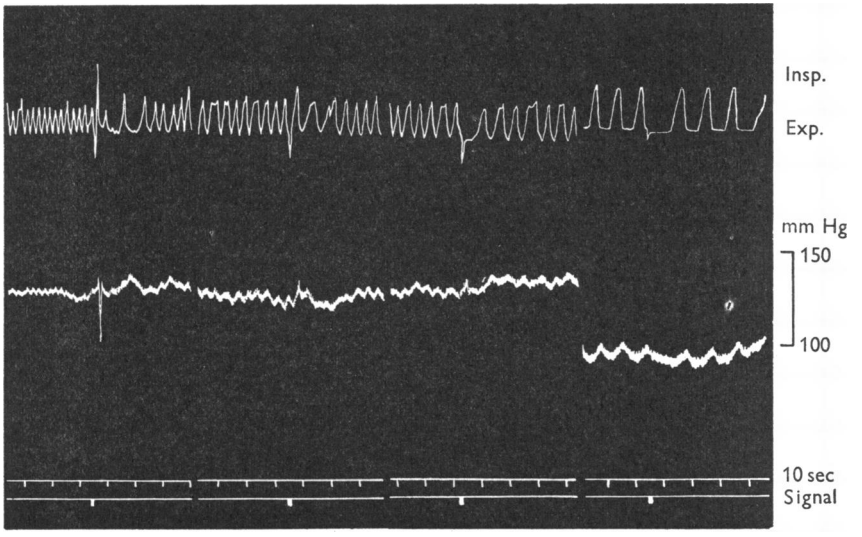

Fig. 3. Cat, 2·5 kg. Intraperitoneal pentobarbitone, 25 mg/kg. At each signal the carina was briefly irritated with an endotracheal catheter. Between each run 5 mg/kg pentobarbitone was administered intravenously.

The most sensitive site for eliciting the cough reflex by a mechanical stimulus was the larynx. The next most sensitive area was the tracheal bifurcation, followed by the lower half of the trachea. Mechanical stimulation of the main bronchi caused only very weak expiratory efforts in two of five cats, and no effect in the other three, although the tracheal cough reflex was active. These findings, for the cat, are similar to those of Larsell & Burget (1924) in rabbits.

In an attempt to delimit the range of afferent nerve fibres which might be mediating the reflex, in nine cats the vagi were cooled and the trachea stimulated. The cough reflex was blocked by vagal temperatures between 7 and 14° C, which suggests that the afferent fibres were rather large in diameter. Torrance (1947) found that cooling the vagi abolished the cough reflex at 'temperatures

at which Head's paradoxical response remains'. Since the latter is blocked over a range of 5–11° C (Widdicombe, 1954*b*), his finding would be in general agreement with the observations reported here.

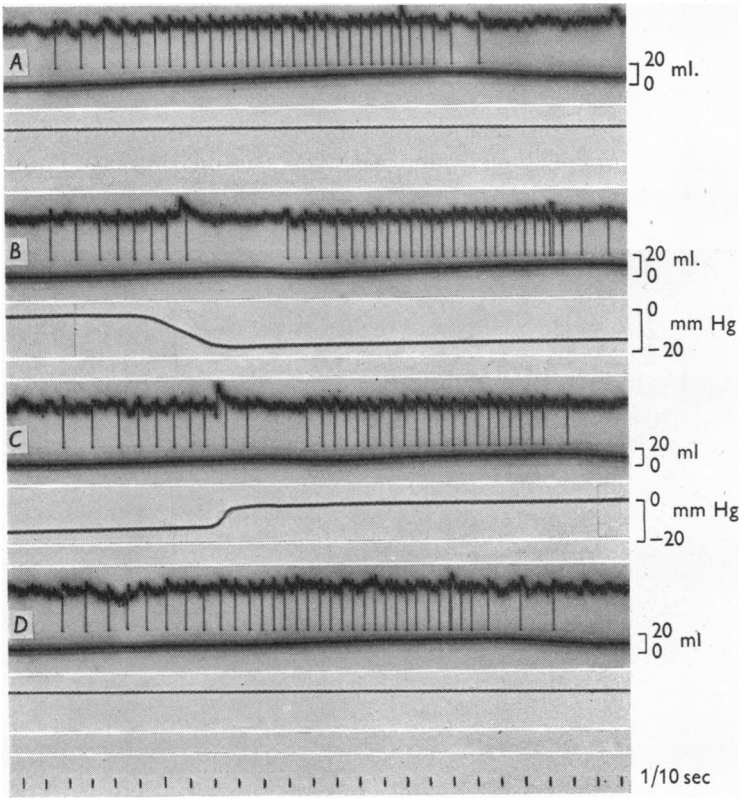

Fig. 4. Cat, 2·7 kg. Chloralose, 60 mg/kg. Effect of deflation of the trachea and left main bronchi on spontaneous respiration. Uppermost record: action potentials from a single motoneurone in the left phrenic nerve. Middle record: volume record of respiration. Lowest record: intratracheal pressure. *A* is a control eupnoeic inspiration; *B* is the subsequent inspiration during which the trachea and bronchi were deflated. *C*, is an inspiration several breaths later, during which the intratracheal pressure was restored to atmospheric. *D* is the next inspiration (control).

The effect of a change in volume of the trachea and left bronchi was observed using the preparation described in Methods; action potentials from phrenic motoneurones were recorded, and respiratory volume changes. A result is shown in Fig. 4. When the intratracheal pressure was decreased during an inspiratory effort (*B*) the phrenic discharge was inhibited for a short period ($\frac{1}{4}$–$\frac{1}{2}$ sec) and the volume record of respiration showed an expiration. The phrenic discharge then began again and the total depth of the inspiration was approximately the same as that of the control (*A*). On opening the trachea to

atmospheric pressure there was again a short expiratory effort (*C*). Inflation of the trachea and bronchi had a similar effect; both distension of the air passages and the restoration of atmospheric pressure caused an expiratory effort, but it was always weaker than that after deflation and release of the deflation. The response was similar to the expiratory effort caused by an endotracheal catheter, and was therefore thought to be a short cough. The reflex was always abolished by vagotomy, and in two cats by cooling the vagi to 10 and 12° C respectively. It could also be blocked by intratracheal administration of ether vapour (15–20%) and by a procaine solution spray (5–10%). These drugs also abolished the coughing due to introduction of a catheter into the air passages.

Volume changes of the air passages caused coughing in cats under chloralose and under pentobarbitone anaesthesia, and in those decerebrated. The thresholds for the reflex expiratory efforts was from −20 to −40 mm Hg for negative pressures, and from 60 to 80 mm Hg for positive pressures. Application of a negative pressure was less effective than its removal.

Hammouda & Wilson (1936) found that tracheal distension and collapse caused a slowing of the respiratory cycle in the dog; they did not report any expiratory efforts, but the carina was not included in the area deformed. In our experiments with cats anaesthetized with pentobarbitone, collapse of the tracheobronchial tree caused a slowing of respiration with or without a decrease in tidal volume in four out of five animals (Fig. 5). The threshold for this reflex was from −10 to −30 mm Hg. Inflation of the air passages was less effective, causing respiratory slowing in only three cats (threshold 25–50 mm Hg). *Deflation* of the airways with large pressures did not produce slowing of the respiratory cycle but instead a large increase in respiratory rate (Fig. 5), sometimes with an increase in the expiratory volume of the lungs. The pressures at which the inhibitory reflex was converted to an excitatory one were sharply defined, at −50, −55, −70 and −90 mm Hg for the four cats. Negative pressures greater than the appropriate threshold invariably caused quickening of respiration, lower pressures caused slowing. *Inflation* of the airways with pressures up to 100 mg Hg never caused a quickening of the respiratory cycle.

Cutting both vagi in the neck abolished both the inhibitory and the excitatory reflexes, and also the cough reflex produced by tracheobronchial volume changes. In two cats, after cutting the left vagus the cough reflex remained intact but the other two reflexes were abolished (Fig. 5); the cough reflex was eliminated by subsequent section of the right vagus. Since the trachea and carina supply afferent nerve fibres to both vagi, while fibres from the left main bronchi are largely restricted to the left vagus, it seems likely that the excitatory and the inhibitory reflexes arise from the bronchi rather than the trachea.

In four of six decerebrate cats an inhibitory reflex very similar to that seen in animals under pentobarbitone was observed, but in only one did large

negative pressures in the tracheobronchial tree cause quickening of respiration. In six cats under chloralose anaesthesia pressure changes in the air passages caused no change in respiratory rate, although the animals had active cough reflexes.

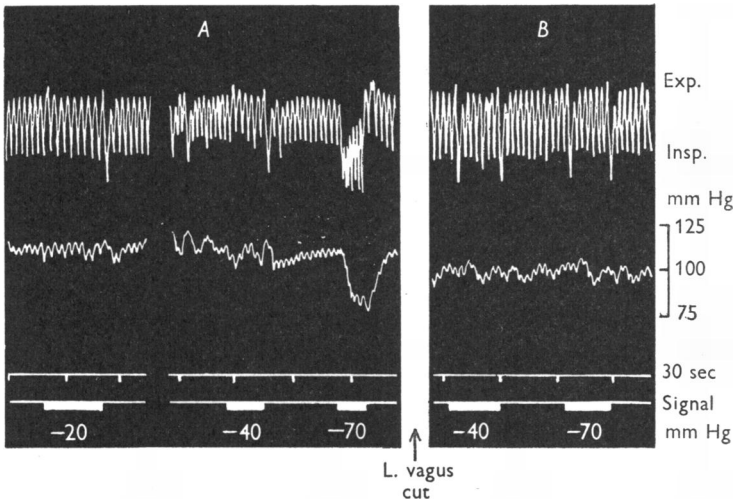

Fig. 5. Cat, 4·0 kg. Pentobarbitone, 32 mg/kg. Effect of deflation of the trachea and left main bronchi on spontaneous respiration. Upper record: respiration (inspiration downwards). Lower record: systemic blood pressure. During each signal indicated by the white bars the trachea and bronchi were deflated with a negative pressure. The left vagus was cut in the neck between *A* and *B*. Note the short coughs at onset and release of the stimuli.

Powders and sulphur dioxide. The inhalation of powdered talc or starch into the lungs caused coughing. Fig. 6 shows that the inspiration which drew in the powder was suddenly converted to a gasp, leading at once to a strong expiratory effort, and this sequence was repeated several times. Two cats out of four showed first an expiratory effort followed by gasps. The action of sulphur dioxide was very similar (Fig. 6), and in eight out of thirteen cats the initial change was an expiratory effort; these were not necessarily animals which gave an initial expiration in response to a mechanical stimulus or to talc. In three cats there was a large rise in expiratory volume, together with tachypnoea after the coughing.

During the experiments with sulphur dioxide it was noticed that bilateral vagotomy did not usually abolish all the reflex effects of the gas. There remained a depression of inspiration similar to, but larger than, that sometimes caused by a mechanical tracheal stimulus after cutting the vagi (Figs. 2, 6). In three cats bilateral sympathectomy was performed and this abolished the reflex. In these experiments the doses of sulphur dioxide were small in order to prevent the development of refractoriness. Sulphur dioxide differed from

a mechanical stimulus to coughing in that it was effective when given through an endobronchial catheter so that the gas did not come into contact with the trachea and extrapulmonary bronchi, but only the lungs and smaller bronchi. The cough reflex produced in this way was always stronger than when the gas was applied to the trachea and main bronchi alone.

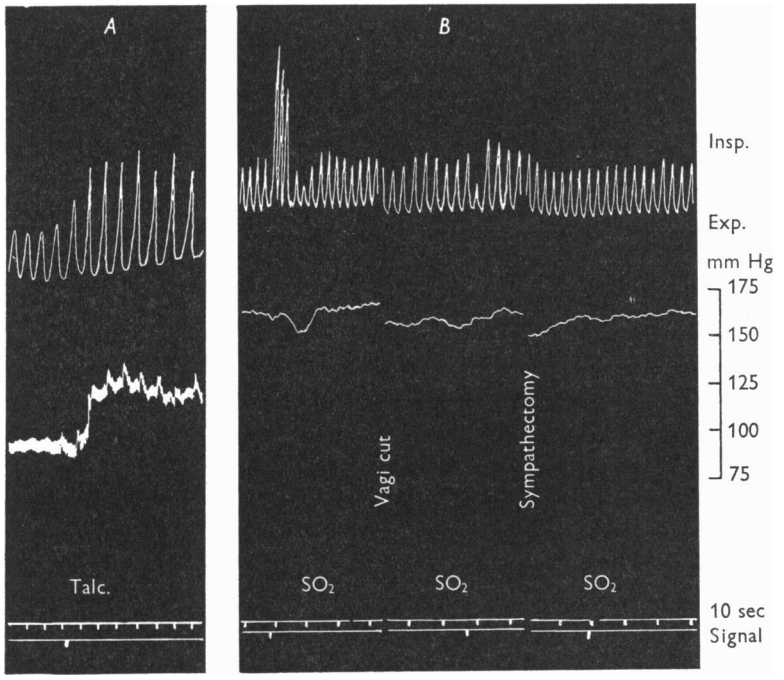

Fig. 6. *A*: cat, 1·9 kg. Chloralose, 60 mg/kg. Coughing induced by inhalation of powdered talc. *B*: cat, 2·8 kg. Pentobarbitone, 32 mg/kg. Coughing induced by inhalation of sulphur dioxide before and after cutting the vagi and performing a bilateral thoracic sympathectomy.

In three animals the vagal temperatures needed to block the chemically produced cough reflex were 10, $9\frac{1}{2}$ and 8° C respectively, which did not appreciably differ from those which blocked the mechanical cough reflex. The afferent nerve fibres for the two types of coughing could, however, be differentiated. After several inhalations of a high concentration of sulphur dioxide the cats became completely refractory to the gas, but they gave normal responses to mechanical stimulation of the trachea. This result, which was unequivocal in six cats, showed that the mechanical cough receptors were not rendered refractory by repeated exposure to sulphur dioxide, and suggested that sulphur dioxide was not stimulating them. In four cats 5–10% procaine solution was sprayed into the trachea until the mechanical cough reflex was blocked. Sulphur dioxide still produced its usual effect.

Bronchomotor reflexes

Since the reflexes being examined arose from the tracheal and bronchial walls we looked for possible alterations in bronchial tone; the results are summarized in Table 1.

TABLE 1. The effect of mechanical stimulation of the air passages on bronchial tone

Experimental conditions	Deflation of the air passages	Inflation of the air passages	Irritation of the carina	Irritation of the larynx
Nervous system intact	15/0/0	5/1/0	11/1/0	7/0/0
Thoracic spinal cord cut	4/1/0	2/1/0	2/1/3	3/2/1

Each group of three figures gives the number of cats that showed bronchoconstriction/no change/bronchodilatation respectively. The sum of each group of three gives the number of cats in which each stimulus was tried, under the appropriate experimental conditions. Cats in which the thoracic spinal cord was cut showed no change in systemic or pulmonary arterial blood pressure on coughing.

Mechanical stimulation of the inside of the trachea with a catheter caused an increase in pulmonary resistance to inflation in thirteen out of eighteen cats. In six of these the lower thoracic spinal cord had been cut to eliminate any changes in the pulmonary circulation caused by contraction of the abdominal muscles during coughing. In these cats condenser manometer records of pulmonary and systemic arterial blood pressures showed no appreciable change, although slight movements of the ribs indicated that the cats were attempting to cough; manual pressure on the abdomen raised the blood pressures but the effect on resistance to inflation was never as great as with coughing. Three of these cats whose spinal cords had been interrupted showed a bronchodilatation on tracheal irritation, which was never seen in the animals without cord transection; no cause for this reversal of effect was discovered. Fig. 7 illustrates a bronchoconstrictor response to stimulation of the trachea (*A*) and the larynx (*C*); pressure on the abdomen increased the resistance to inflation (*B*), but after thoracic spinal section both the tracheal (*D*) and the laryngeal (*E*) cough reflexes included bronchoconstriction. In these cats the trachea and bronchi were not distended by the catheter; there was also no doubt that the bronchomotor reflex was more easily elicited from the tracheal bifurcation than from the trachea itself. The larynx was an even more sensitive area, and gave a more consistent bronchoconstrictor response. In ten out of thirteen cats passage of a probe up to the larynx caused bronchoconstriction, dilatation was observed once, and there were no changes in bronchial tone in the other two cats (Table 1).

In five cats the bronchoconstrictor reflex from the trachea was abolished by vagotomy, which would not only interrupt afferent nerve fibres but also bronchial efferent nerves; in two cats some effect remained, which was abolished

by bilateral sympathectomy. One of these latter experiments is illustrated in Fig. 8, together with the response to sulphur dioxide blown through the trachea into the left pulmonary lobe. Both effects persisted after section of the vagi,

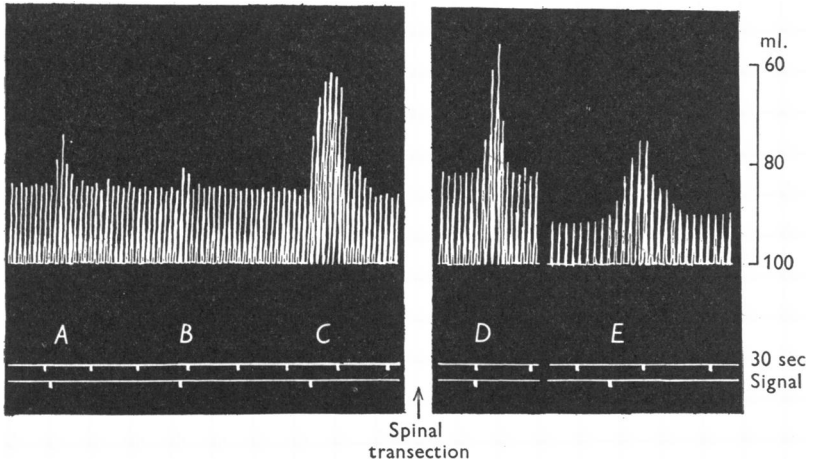

Fig. 7. Cat, 2·2 kg. Chloralose, 60 mg/kg. Eserine, 0·1 mg/kg. The effect of mechanical stimuli to the air passages on bronchial tone. The record is of tidal volume measured by the overflow method: an increase in the height of the tracing indicates an increase in the resistance to inflation of the lungs. *A*: mechanical irritation of the carina; *B*: firm pressure on the abdomen; C: mechanical irritation of the larynx. The spinal cord was then cut across low in the thoracic region. *D*: irritation of the carina. *E*: irritation of the larynx. The inflation pressure was adjusted between *D* and *E*.

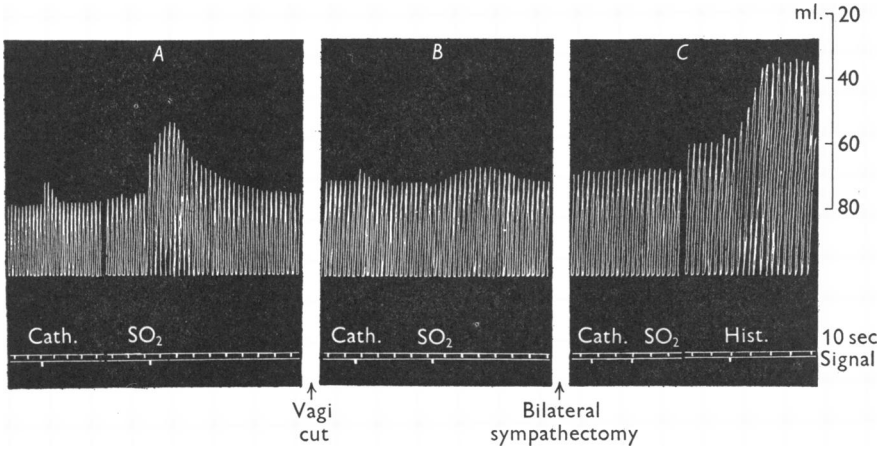

Fig. 8. Cat, 2·7 kg. Pentobarbitone, 32 mg/kg. Changes in the bronchomotor response to cough stimuli on nerve section. Cath: irritation of the carina with an endotracheal catheter. SO_2: administration of sulphur dioxide. Hist: intravenous injection of 250 μg histamine. The vagus nerves were cut in the neck between *A* and *B*, and a bilateral thoracic sympathectomy performed between *B* and *C*.

although they were considerably smaller. After sympathectomy neither stimulant caused any change in bronchial tone, although intravenous histamine caused a large constriction indicating that the bronchial muscles were capable of contracting (although they might have been refractory to other stimuli). Inhalation of sulphur dioxide caused bronchoconstriction in each of the four cats in which it was tried, but in view of the possibility that it might have a direct bronchomotor action as well as a reflex action (cf. Banister, Fegler & Hebb, 1949) only a few observations were made. In two of these cats sulphur dioxide restricted to the trachea did not cause any change in bronchial tone, although it was effective when blown into the lobes of the lung.

The results so far described are consistent with the view that bronchoconstriction is produced from the trachea and main bronchi by stimuli which elicit the cough reflex. Deflation and inflation of the trachea and large bronchi caused a bronchoconstrictor effect in nineteen of twenty cats (Table 1); the response was usually larger than that due to the irritation caused by an endotracheal catheter. In an attempt to discover whether this effect was due entirely to the cough reflex, the bronchoconstriction due to a *long* (10–20 sec) deflation of the trachea and bronchi was compared with that due to deflation and *immediate* release of the pressure; in the latter experiment there would be two stimuli to coughing (at the beginning and end of the deformation), while in the former experiment there would also be the effect of maintained stretch of the tracheobronchial walls. In one of three cats the results were equivocal. In the other two the prolonged deflation caused a considerably larger effect than the short deflation. In another cat the mechanical cough reflex was blocked by spraying the trachea with 5% procaine solution, but deflation of the trachea still caused a bronchoconstriction. In two other cats a constrictor response to distension and collapse of the air passages was observed, although mechanical stimulation of the carina was ineffective. These observations suggest that changes in volume of the air passages cause bronchoconstriction apart from that due to the cough reflex.

DISCUSSION

Evidence has been presented that the sensory receptors excited by a mechanical cough stimulus are different from those excited by sulphur dioxide. This evidence may be summarized as follows:

(1) In some cats the respiratory responses to the two stimuli were different; for example, an endotracheal catheter stimulated a short expiratory effort, but sulphur dioxide caused strong inspiratory and expiratory efforts.

(2) A mechanical stimulus was most effective at the carina, and relatively ineffective in the bronchi. Sulphur dioxide in the pulmonary lobes caused vigorous coughing, but only weak coughs when restricted to the trachea and large bronchi.

(3) Sulphur dioxide no longer caused coughing after inhalation of high concentrations, but the mechanical cough reflex was still active.

(4) Procaine solution sprayed into the trachea abolished the mechanically excited cough reflex but the chemical cough reflex was unaffected.

These observations suggest that the afferent pathway for the cough reflex is of greater complexity than had been thought. It would seem reasonable to suppose that other noxious gases act in the same way as sulphur dioxide, while chemically inert powders might be expected to stimulate receptors for the mechanical cough reflex.

TABLE 2. Species differences in coughing

Species	Stimulus	Nervous pathway	Primary response	Authors
Dog	Chemical	Vagus and sympathetic	Expiratory	Craigie (1921); Cromer, Young & Ivy (1933); Banister *et al.* (1949)
Rabbit	Chemical	Vagus	Expiratory	Larsell & Burget (1924); Banister *et al.* (1949)
	Mechanical	Vagus	Expiratory	Larsell & Burget (1924)
Cat	Chemical	Vagus	—	Banister *et al.* (1949)
	Soap powder	Vagus	Inspiratory	Bucher & Jacot (1951)
Man	Mechanical	Vagus	Inspiratory	Klassen, Morton & Curtis (1951)

The chemical stimuli were noxious gases such as ammonia, phosgene, acetic acid and ethyl ether vapour.

Table 2 summarizes previous work on coughing; as with other respiratory reflexes there are considerable differences between species (Dawes *et al.* 1951). Most workers have used chemical excitants, which produced a forced expiration as the primary response in dogs and rabbits. In the dog, there is good evidence for a sympathetic nervous component, first demonstrated by Craigie (1921). More recently, Banister *et al.* (1949) have administered phosgene and ammonia to dogs, cats and rabbits; in dogs there was an afferent component of the respiratory response running in the thoracic sympathetic nerves, whereas the response was completely abolished by vagotomy in cats and rabbits. This confirmed the work of Cromer *et al.* (1933) on the administration of ammonia to dogs. Neither group of workers was primarily interested in the cough reflex, and their records show that the animals (with the exception of the rabbit) did not usually cough. The results described above suggest that in both mechanical and chemical cough reflexes in the cat afferent nerve fibres in the sympathetic may be involved as well as in the vagus nerves.

The effect of inhalation of soap powder is difficult to interpret. Bucher & Jacot (1951) found that the inspiratory component of coughing was primary, and that if expansion of the lungs was prevented coughing did not take place. A possible explanation of their results was that each inspiration drew powdered soap (or froth?) deeper into the lungs and stimulated more cough receptors, so that the prevention of pulmonary distension would depress coughing; but

Weisser (1952) has tested this possibility and disproved it. There can be no doubt that in the experiments described above expiration was the initial and the main act of coughing in most instances, and no explanation has been found for the difference between these results and those of Bucher & Jacot.

The results with an endotracheal catheter agree well with those of Larsell & Burget (1924) using rabbits, the same patterns of sensitivity being found. In addition, inflation and deflation of the air passages also caused a cough, and when the trachea was opened to atmospheric pressure the cats coughed again. The threshold for this effect has been as low as −20 mm Hg, and this pressure across the tracheal walls is commonly exceeded in hyperpnoea and more violent respiratory movements (Kroepfli, 1950; Bucher & Jacot, 1951; Widdicombe, 1954*a*). It is clear that coughing and such movements as gasping and sneezing will themselves excite cough receptors. To what extent this mechanism modifies the respiratory pattern is not known.

Although coughing involves large changes in tracheal and bronchial diameter there has been some doubt whether these are active or passive in origin. The results described here confirm that there is a true active bronchoconstriction in response to cough stimuli. Whether this is large enough to account for a sevenfold change in airway volume (Franklin & Janker, 1938) is not certain, but it seems probable that both active constriction and passive mechanical effects are present. Both the effect described by Franklin & Janker and the wave of 'peristaltic' bronchial contraction which Di Rienzo (1949) observed accompanying the cough, follow the stimulus more quickly and pass off sooner than the bronchoconstriction described above. They occur only during the expiratory phases of the cough reflex, and have been ascribed to passive collapse of the bronchi by Peromet (1951).

The change in bronchial tone caused by noxious chemical stimuli has been shown to include both reflex and direct constrictor actions on the smooth muscle (Banister *et al.* 1949). In coughing there may also be large changes in blood pressure, and these may not only alter the pulmonary resistance to inflation by changes in the vascular bed of the lungs, but may exert a reflex effect via the baroreceptor zones (Daly & Schweitzer, 1951).

Two other respiratory reflexes arising from the respiratory tree have been described. The slowing of respiration produced by prolonged distension and collapse of the air passages is similar to the reflex observed by Hammouda & Wilson (1936) in the dog. The analogy between pulmonary and bronchial reflexes is striking. Whereas weak stimuli in the airways cause slowing and strong stimuli quickening of respiration, in the lungs small inflations elicit the Hering-Breuer *inhibitory* reflex, while large inflations also bring into play Head's paradoxical response, a reflex *excitatory* to the respiratory centre. However, no explanation can be offered for the facts that the excitatory bronchial reflex has never been elicited by distension of the tracheobronchial

tree, and that the inhibitory reflex is more feebly produced by distension than by collapse of the air passages.

The physiology of the tracheobronchial reflexes will be considered further in the paper dealing with afferent nerve fibres from the air passages (Widdicombe, 1954*a*).

SUMMARY

1. Reflexes arising from the tracheobronchial tree of the cat have been investigated; four have been identified.

2. Coughing can be produced by various mechanical stimuli; an endotracheal catheter is most effective at the carina, the main bronchi being insensitive. The primary effort of the cough is expiratory, and it is associated with active bronchoconstriction.

3. Volume changes of the air passages cause a short cough at the onset and at the release of the deformation.

4. The reflex response to the mechanical stimuli is blocked by intratracheal ether vapour or procaine spray. The pattern of the response varies with the type and depth of anaesthetic.

5. Sulphur dioxide in the lobes of the lung causes vigorous coughing, but the trachea and larger bronchi are rather insensitive. The response to sulphur dioxide becomes refractory on repetition but is not blocked by procaine.

6. In cats under pentobarbitone anaesthesia or decerebrated, volume changes of the air passages cause a slowing of the respiratory cycle, apart from the cough reflex at onset and release of the stimulus. An active bronchoconstriction is also produced.

7. Large negative pressures in the airways cause a great quickening of the respiratory cycle instead of the slowing seen with lower pressures.

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