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# ELECTRICAL SLOW WAVES AND TONE OF GUINEA-PIG ISOLATED TRACHEALIS MUSCLE: EFFECTS OF DRUGS AND TEMPERATURE CHANGES

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**1** Simultaneous recordings of electrical and mechanical activity have been made from guinea-pig isolated trachealis muscle. Electrical activity was recorded both by extracellular and intracellular techniques.

**2** Extracellular studies showed that the spontaneous development of tone was accompanied by electrical slow waves which frequently exhibited pronounced waxing and waning. Intracellular recording confirmed the discharge of these slow waves in individual cells. Extracellularly-recorded slow waves were often of greatest amplitude while the tissue was developing rather than maintaining tension. Some tissues became electrically quiescent on reaching peak tone.

**3** Cooling to 27.5°C caused some relaxation. Slow wave amplitude and frequency fell, slow waves eventually being abolished. Subsequent rapid rewarming initially evoked a more profound relaxation. An intense discharge of slow waves then occurred as the tension rapidly rose again towards the pre-cooling value.

**4** Sodium nitrite, (−)-isoprenaline, adenosine and adenosine triphosphate (ATP) each evoked relaxation and reduced the frequency and amplitude of slow waves. High concentrations of these agents often abolished slow waves. The actions of these drugs were reversible.

**5** Treatment with methoxyverapamil (D600) 1 μmol/l for 15 min abolished slow wave activity but only evoked partial relaxation of the tissue.

**6** Acetylcholine, histamine and tetraethylammonium (TEA) each evoked contraction, but TEA was unique in consistently promoting slow waves and (in high concentration) spike activity. Spasm evoked by acetylcholine and histamine did not usually involve the initiation or promotion of slow waves. Indeed in appropriate concentration these two agents always suppressed slow wave activity. The actions of the spasmogens were reversible.

**7** It is concluded that the smooth muscle cells of the trachealis are electrically coupled. While co-ordinated slow wave activity is associated with the spontaneous development of tension in trachealis, it may not be necessary for the maintenance of the major part of the spontaneous tension exhibited by the tissue or for the spasm evoked by histamine or acetylcholine. Slow wave promotion by TEA suggests that the tissue may have a high resting potassium conductance which normally attenuates the slow waves. Slow waves may be suppressed by a variety of drugs acting by different mechanisms. Since D600 suppresses slow waves of the trachealis the mechanisms underlying the waves may be similar to those underlying spike activity in other smooth muscles.

## Introduction

Kirkpatrick (1981) has recently reviewed the present state of our knowledge regarding the electrophysiological properties of tracheobronchial smooth muscle. It seems clear that, compared with other smooth muscles, tracheobronchial tissue has received relatively little attention from electrophysiologists.

Studies have been made of the electrical properties of trachealis muscle of the cow (Kirkpatrick, 1975; Kirkpatrick & Tomita, 1978) and dog (Kroeger & Stephens, 1975; Suzuki, Morita & Kuriyama, 1976; Coburn & Yamaguchi, 1977). In both these species the isolated trachealis muscle is virtually devoid of spontaneous tone or electrical activity.

Guinea-pig trachealis muscle generates tone spontaneously. This property has made the tissue particularly useful in the screening of drugs for bronchodilator activity. A preliminary investigation (Clark & Small, 1979) of the electrical activity of guinea-pig trachealis was carried out using intracellular microelectrode recording. It was observed that many of the muscle cells exhibited spontaneous slow

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oscillations of membrane potential (slow waves) which often waxed and waned in a regular or irregular pattern. The slow waves were sometimes preceded by a small spike potential or were surmounted by a series of smaller rapid oscillations of potential. Preliminary experiments using (−)-noradrenaline revealed that relaxation induced by this agent was accompanied by abolition of slow wave activity, but little further information was gained about the relation between electrical and mechanical activity.

The present study describes a technique for the simultaneous extracellular recording of tone and slow wave activity from guinea-pig trachealis. The technique has been employed in studies of the effects of drugs and temperature changes. It usefully supplements the technically difficult intracellular recording method.

## Methods

### *Excision of the tissue*

Guinea-pigs (220–870 g) of either sex were killed by stunning and bleeding. Tracheae were excised from the animals, cleaned of adhering fat and connective tissue and opened by cutting longitudinally through the cartilaginous rings diametrically opposite the trachealis muscle.

### *Extracellular electrophysiological recording*

The opened trachea was pinned out mucosal surface uppermost on a block of paraffin wax under Krebs solution. A segment of tissue was removed by cutting transversely on each side of one of the cartilaginous rings. A Terylene thread was attached to each of the severed ends of cartilage in the preparation to facilitate its anchoring in the recording chamber and the isometric measurement of tension changes using a 2 oz Ether transducer.

The electrical activity of the trachealis was recorded by the perfused capillary method of Golenhofen & v. Loh (1970) in conjunction with a Grass polygraph (Jetley & Weston, 1980). The time constant of the a.c. preamplifier used to record the electrical activity was set at 100 ms so that both slow potential waves and fast spike activity could be recorded.

Bioelectric signals detected by the perfused capillary technique are necessarily of very low amplitude compared with the cellular transmembrane potentials which they reflect. For this reason several control experiments were performed to rule out the possibility that any signals recorded from the trachealis were artefactual. Firstly, a piece of thread was inserted into the capillary to simulate the presence of biological tissue. The flow of Krebs solution was then altered manually to simulate flow changes which might be caused by tissue contraction. The pattern of electrical activity characteristic of trachealis was not detected under these conditions. Secondly, pieces of guinea-pig taenia caeci or rat portal vein mounted in the apparatus exhibited spontaneous contractions associated with bursts of spike activity. These tissues did not generate the slower potential changes characteristic of the trachealis muscle. These control experiments clearly indicated that the slow potential changes recorded when trachealis muscle was in the capillary were not artefacts resulting either from outside electrical interference or tissue movement.

The capillary was routinely perfused with Krebs solution at 37.5°C with a flow rate of 7 ml/min. The effects of cooling were studied by switching off the pump which circulated warm water through outer jackets both of the recording chamber and the reservoir which supplied the perfusion fluid. This effected a temperature fall of 10°C within the recording chamber over a period of 30 min. The effects of rewarming were studied simply by switching the pump back on again. This raised the temperature of the recording chamber back to 37.5°C within 2 min.

The effects of drugs were studied by their addition to a calibrated reservoir containing the Krebs solution which superfused the tissue. With the exception of D600, all drugs were studied by constructing cumulative concentration-effect curves. An increment in drug concentration was made when it was judged that the previous concentration had equilibrated with the tissue.

### *Intracellular electrophysiological recording*

Intracellular microelectrodes were used to record the membrane potential changes of individual trachealis muscle cells. The methodology has been described previously (Clark & Small, 1979; Small & Weston, 1979).

### *Drugs and solutions*

The following drugs were used: acetylcholine chloride (BDH), adenosine (Sigma), the disodium salt of ATP (Sigma), methoxyverapamil (D600, Knoll), histamine acid phosphate (BDH), (−)-isoprenaline hydrochloride (Sigma), sodium nitrite (Sigma) and tetraethylammonium bromide (TEA, Sigma).

Stock solutions of D600 and TEA were prepared with double distilled water. A stock solution of (−)-isoprenaline was prepared in 0.1N HCl. All other drugs were weighed out and diluted in double distilled water immediately before use.

The Krebs solution was gassed with 5% $CO_2$ in $O_2$ and had the following composition (mmol/l): $Na^+$ 143.5, $K^+$ 5.9, $Ca^{2+}$ 2.6, $Mg^{2+}$ 1.2, $Cl^-$ 125, $HCO_3^-$ 25, $SO_4^{2-}$ 1.2, $H_2PO_4^-$ 1.2 and glucose 11.1.

## Results

### *Spontaneous activity of trachealis*

The tissue was initially mounted in the extracellular recording apparatus under imposed tension in the range 0.5–1 g, but it invariably then relaxed to assume a stable low level of tone. At this time the tissue seemed electrically quiescent. The spontaneous development of tension and the discharge of slow waves started only after a period in excess of 15 min.

The pattern of slow wave discharge seen while the tissue was developing tension was somewhat variable. When the discharge was continuous the frequency and amplitude of slow waves were relatively low initially, increasing as the tension rose. Often the amplitude of slow waves waxed and waned. On other occasions the slow waves were discharged in distinct bursts with intervening periods of quiescence. In this case it was apparent that each burst of slow waves was accompanied by an increase in the rate of tension development. On rare occasions each slow wave was associated with a very small increment of tension.

The peak tension spontaneously developed by the tissue was in the range 0.5–1.5 g. In some tissues slow wave activity apparently ceased once the peak tone had been reached. Despite this the developed tension was moderately well maintained. In the majority of tissues slow wave activity continued after peak tone had been reached, and the pattern of slow wave discharge again was quite variable.

Measurements of the amplitude and frequency of spontaneous slow waves were made as tissue tone reached its peak. Slow wave amplitude was $10.1 \pm 0.6\,\mu V$ and frequency was $1.38 \pm 0.02$ Hz (mean ± s.e.; $n = 34$ in each case). The amplitude of the extracellularly recorded slow waves was, as expected, much smaller than that of the intracellularly recorded events. The frequency of the extracellular waves and their tendency to wax and wane was, however, very similar to that of the intracellular waves (Figure 1 and Clark & Small, 1979).

### *The effects of cooling and rapid rewarming*

The effects of cooling were studied in tissues which had already developed spontaneous tone. Cooling

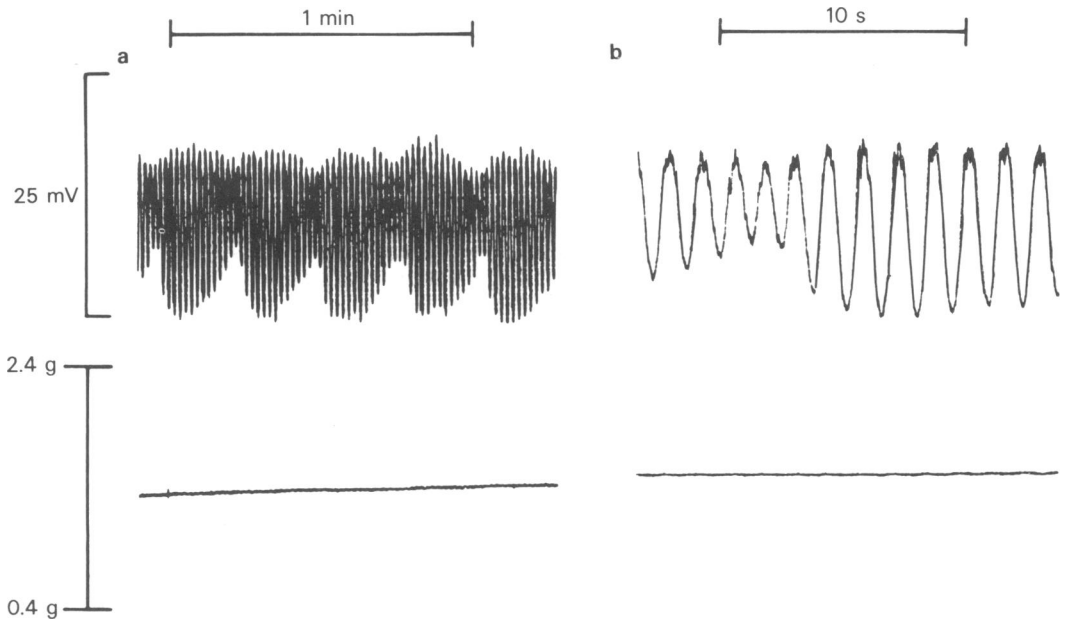


**Figure 1** Intracellular electrical activity (upper trace) and simultaneous recording of mechanical activity (lower trace) from adjacent, contiguous segment of guinea-pig trachealis. (a) Spontaneous slow wave activity with prominent waxing and waning, a pattern similar to that of the extracellular recordings of slow waves shown in Figure 6. (b) Continuation of recordings shown in (a) but at higher chart speed. Note the small, rapid oscillations of potential on the crests of the slow waves.

markedly lowered the frequency of slow waves. Slow wave amplitude also fell and in most cases slow waves were not detectable at 27.5°C. These electrical changes were accompanied by a slowly developing and partial relaxation of the tissue (Figure 2 and Table 1).

The initial effect of rapidly rewarming the tissue was a rapid, transient and more profound relaxation. This was followed by an intense discharge of slow waves as the developed tension then rapidly rose again back to the pre-cooling value.

*The effects of relaxant drugs*

Relaxant drugs were tested on tissues which had generated spontaneous tone. Isoprenaline was chosen as a standard relaxant agency and the actions of the other drugs were compared with the maximal relaxation evoked by isoprenaline in the same tissue.

Isoprenaline 0.01 μmol/l evoked a mild relaxation of the tissue together with a slight reduction in slow wave frequency (Table 2). A reduction in slow wave amplitude sometimes accompanied these effects. Higher concentrations of isoprenaline produced a more rapid reduction in the frequency and amplitude of slow waves and subsequently their abolition. Such electrical changes were associated with profound relaxation. In general the electrical and mechanical effects of isoprenaline were reversible following the removal of the drug from the perfusion fluid (Table 2 and Figure 3).

The relaxant effects of sodium nitrite 0.04–4 mmol/l were associated with electrical changes similar to those described for isoprenaline (Table 2). However, sodium nitrite sometimes failed to abolish the slow waves even when relaxation was quite profound. In such cases slow wave amplitude and frequency were both markedly reduced. The actions of sodium nitrite were reversible.

Adenosine and ATP relaxed the trachealis at concentrations in the range 0.01–10 mmol/l (Table 2 and Figure 4). The relaxant effects of these agents were also associated with abolition of slow waves or a marked reduction in their amplitude and frequency. In a few preparations ATP at 0.1 mmol/l caused a slight spasm and increased slow wave amplitude prior to the onset of the relaxant effect. The actions of adenosine and ATP were reversible.

The effects of D600 (1 μmol/l) were studied by incubating tissue with the drug for 15 min. D600 consistently abolished slow wave activity within this period. The electrical effects of D600 were accompanied by a small and slowly developing relaxation (Figure 5) which at the end of the drug contact time represented 22.4 ± 3.7% ($n = 9$) of the maximal relaxation evoked by isoprenaline. In several experiments the reversibility of the action of D600 was examined. Slow wave activity and the initial level of

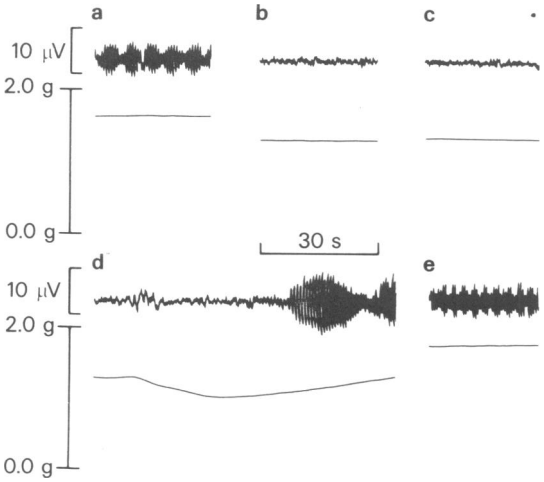


**Figure 2** The effects of cooling and rapid rewarming on the extracellular electrical (upper trace) and mechanical (lower trace) activity of guinea-pig trachealis. All records from the same preparation. (a) Control activity at 37.5°C with waxing and waning of slow waves; (b) activity on cooling to 32.5°C; (c) activity on cooling to 27.5°C; (d) effects of rapidly rewarming from 27.5°C (start of trace) to 37.5°C (end of trace); (e) later stage (at 37.5°C) in recovery from cooling and rewarming.

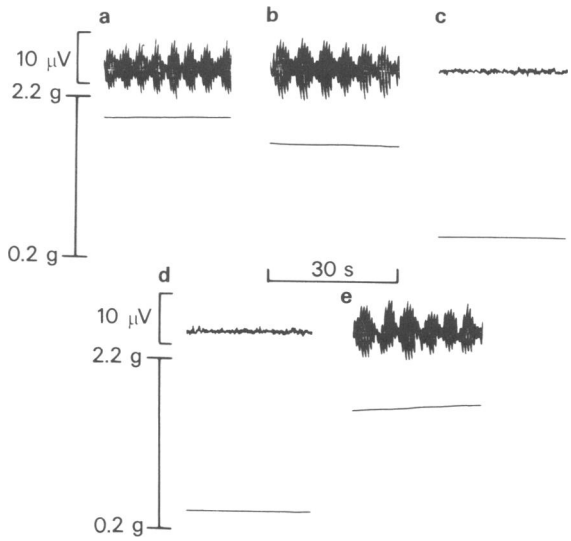


**Figure 3** The effects of isoprenaline on the extracellular electrical (upper trace) and mechanical (lower trace) activity of guinea-pig trachealis. All records from the same preparation. (a) Control activity; effects of isoprenaline: (b) 0.01 μmol/l; (c) 0.1 μmol/l and (d) 1.0 μmol/l; (e) stage in recovery from the effects of isoprenaline.

**Table 1** The effects of cooling and rapid rewarming on slow wave frequency and tone of guinea-pig trachealis

| | *Temperature* (°C) | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | *On cooling* | | | *On rewarming* | |
| | 37.5 | 35.0 | 32.5 | 30.0 | 27.5 | 30.0 | 37.5 |
| Slow wave frequency (Hz) | 1.43 ± 0.06 | 0.97 ± 0.19 | 0.33 ± 0.21 | 0.23 ± 0.15 | 0.10 ± 0.09 | 0.00 ± 0.00 | 1.65 ± 0.05 |
| Relaxation as % of isoprenaline maximum | 0.00 ± 0.00 | — | — | — | 34.8 ± 6.2 | 64.9 ± 7.2 | 0.00 ± 0.00 |

Results indicated in the table are the means of data from tissues from six animals ± s.e. Dashes indicate that measurements of relaxation were not made at the indicated temperature.

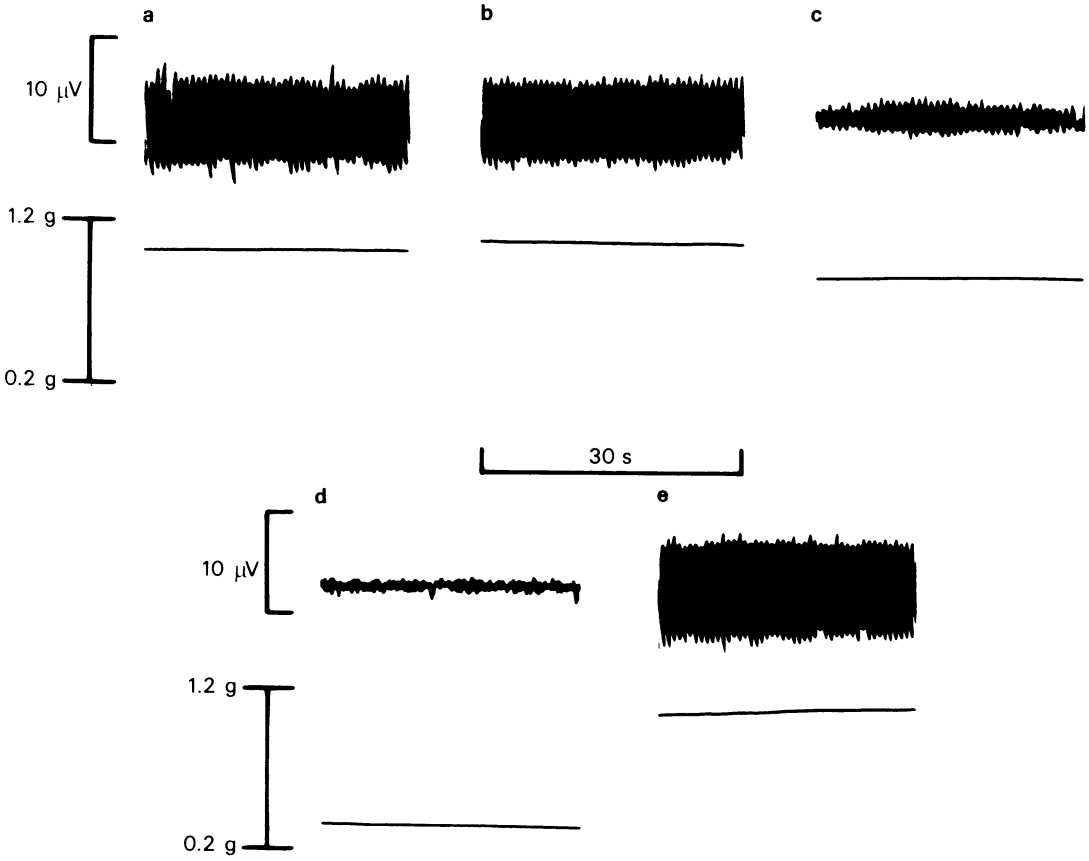


**Figure 4** The effects of ATP on the extracellular electrical (upper trace) and mechanical (lower trace) activity of guinea-pig trachealis. All records from the same preparation. (a) Control activity; effects of ATP: (b) 10 μmol/l (note the slight spasmogenic effect); (c)100 μmol/l; (d) 1 μmol/l; (e) stage in recovery from the effects of ATP.

**Table 2** The effects of some relaxant drugs on slow wave frequency and tone of guinea-pig trachealis muscle

| | | *Slow wave frequency* (Hz) | *Relaxation* | n |
|---|---|---|---|---|
| Control | 0.00 | 1.53 ± 0.05 | 0 | |
| Concentration of | 0.01 | 1.38 ± 0.04 | 212 ± 45 mg | |
| isoprenaline | 0.1 | 0.00 ± 0.00 | 1062 ± 124 mg | 9 |
| (μmol/l) | 1.0 | 0.00 ± 0.00 | 1154 ± 99 mg | |
| Recovery | 0.00 | 1.51 ± 0.04 | — | |
| Control | 0.00 | 1.54 ± 0.05 | 0 | |
| Concentration of | 0.04 | 1.53 ± 0.05 | 3.4 ± 1.7% | |
| sodium nitrite | 0.4 | 0.85 ± 0.22 | 53.3 ± 8.2% | 8 |
| (mmol/l) | 4.0 | 0.33 ± 0.17 | 79.2 ± 6.7% | |
| Recovery | 0.00 | 1.45 ± 0.04 | — | |
| Control | 0.00 | 1.53 ± 0.03 | 0 | |
| Concentration of | 0.01 | 1.51 ± 0.05 | 5.7 ± 3.1% | |
| ATP | 0.1 | 1.00 ± 0.30 | 18.7 ± 5.1% | 8 |
| (mmol/l) | 1.0 | 0.21 ± 0.21 | 64.2 ± 8.9% | |
| Recovery | 0.00 | 1.56 ± 0.04 | — | |
| Control | 0.00 | 1.53 ± 0.07 | 0 | |
| Concentration of | 0.1 | 1.50 ± 0.05 | 0.8 ± 0.8% | |
| adenosine | 1.0 | 0.43 ± 0.28 | 55.5 ± 12% | 6 |
| (mmol/l) | 10 | 0.18 ± 0.17 | 89.3 ± 4.1% | |
| Recovery | 0.00 | 1.47 ± 0.08 | — | |

Data are means ± s.e. of results from tissues from *n* animals. Relaxation is expressed in mg (isoprenaline) or as a percentage of the maximal relaxation evoked by isoprenaline (other agents).

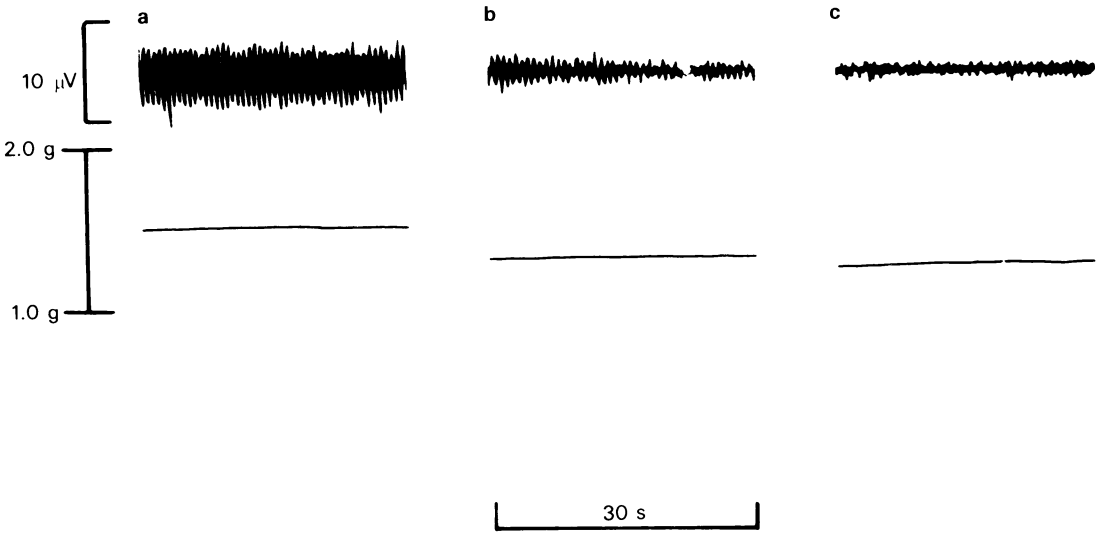


**Figure 5** The effects of D600 (1 μmol/l) on the extracellular electrical (upper trace) and mechanical (lower trace) activity of guinea-pig trachealis. All records from the same preparation. (a) Control activity; (b) activity seen after 7 min exposure to D600; (c) activity seen after 15 min exposure to D600.

tone were not restored by a period of 45 min superfusion with drug-free Krebs solution.

*Effects of spasmogens*

Spasmogens were tested on tissues which had already developed tone. Acetylcholine, histamine and TEA each increased the tension developed by the tissue. On removal of these drugs from the perfusion fluid the tissue generally relaxed below the initial level of tone. Subsequently tissue tension rose again towards the initial value.

Acetylcholine (0.001–1 mmol/l) did not usually induce slow wave activity in tissues which were electrically quiescent. When tested on tissues with ongoing slow wave activity it was apparent that the spasmogenic action of acetylcholine was associated with suppression of slow wave activity. Exposure of tissues to 0.01 mmol/l acetylcholine consistently disrupted the slow waves. An electrical discharge of relatively high frequency but very low amplitude was sometimes detectable following suppression of slow waves and exposure to high concentrations of acetylcholine.

Histamine had similar effects on tracheal electrical activity to those described for acetylcholine. Histamine rarely induced slow wave activity in electrically quiescent tissues. At a concentration of 10 μmol/l the drug usually reduced the amplitude of slow waves in tissues showing such activity. Higher concentrations of histamine abolished slow waves (Figure 6) and sometimes evoked the high frequency low amplitude electrical discharge observed with high concentrations of acetylcholine.

Among the three spasmogens examined, TEA was unique in consistently promoting slow wave activity. TEA 1 mmol/l always initiated slow waves in tissues that were electrically quiescent (Figure 7) and the drug greatly augmented the amplitude of slow waves. As the concentration of TEA was raised towards 8 mmol/l a variety of changes in the pattern of slow wave discharge occurred. At high concentration there was a tendency for extracellularly-recorded slow waves to become smaller or for spike activity to appear. The promotion of slow waves and spike

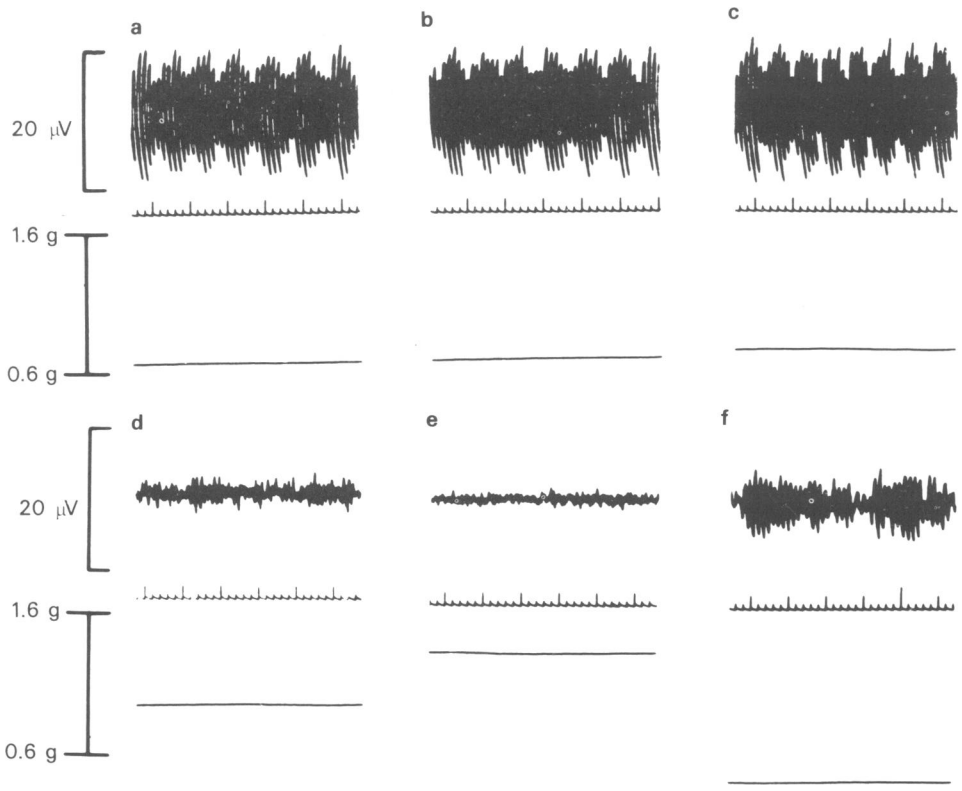


**Figure 6** The effects of histamine on the extracellular electrical (upper trace) and mechanical (lower trace) activity of guinea-pig trachealis. All records from the same preparation. The time trace is calibrated in seconds (smaller marks). (a) Control activity; effects of histamine: (b) 0.1 μmol/l; (c) 1 μmol/l; (d) 10 μmol/l; (e) 100 μmol/l; (f) early stage in recovery from effects of histamine.

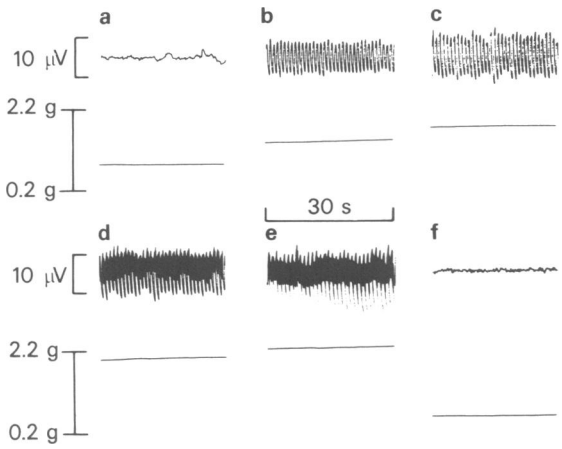


**Figure 7** The effects of tetraethylammonium (TEA) on the extracellular electrical (upper trace) and mechanical (lower trace) activity of guinea-pig trachealis. All records from a tissue which, before exposure to TEA, exhibited no slow wave activity. (a) Control activity; effects of TEA: (b) 1 μmol/l (note induction of slow waves); (c) 2 mmol/l; (d) 4 mmol/l (note appearance of small rapid oscillations on crests of slow waves); (e) 8 mmol/l (note spikes, recorded as fast downward deflections); (f) stage in recovery from effects of TEA.

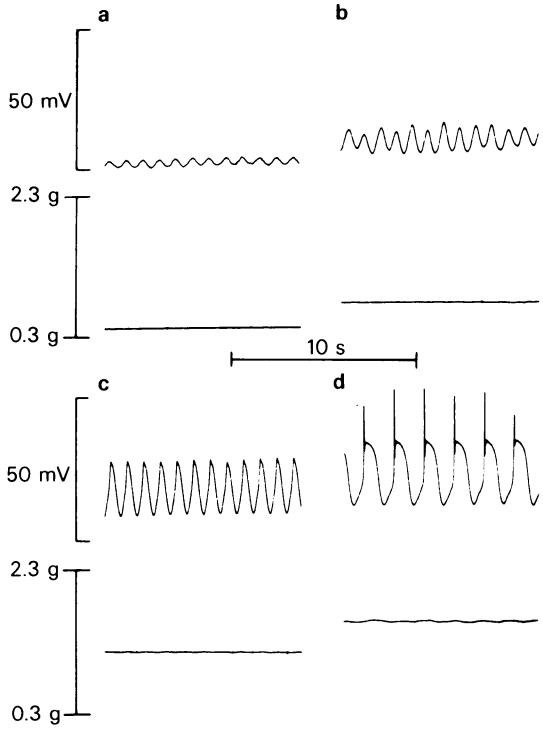


**Figure 8** The effects of tetraethylammonium (TEA) on the intracellular electrical activity (upper trace) and mechanical activity (lower trace) simultaneously-recorded from an adjacent, contiguous segment of guinea-pig trachealis. All electrical records from the same cell. (a) Control activity; activity after 5 min equilibration with TEA: (b) 2 mmol/l (note depolarization and enhanced slow wave amplitude); (c) 4 mmol/l (note further depolarization and increase in slow wave amplitude); (d) 8 mmol/l (note prominent spikes superimposed on slow waves). Compare with extracellular records of Figure 7.

activity by TEA was confirmed by intracellular recording (Figure 8).

During TEA-induced spasm each slow wave or burst of slow waves was often associated with an increment in tension. On reverting to perfusion with drug-free Krebs solution the spasm and electrical activity returned to the control pattern. However, the phase of relaxation was often interrupted by occasional tension waves and associated slow wave and/or spike activity. Although the electrical changes evoked by TEA were very different from those induced by acetylcholine and histamine, the spasmogenic effects of the three drugs were of similar magnitude (Table 3).

**Table 3** Spasm evoked by acetylcholine, histamine and tetraethylammonium (TEA) in guinea-pig trachealis muscle

| | *Acetylcholine concentration* (μmol/l) | | | | | n |
|---|---|---|---|---|---|---|
| | 0.1 | 1 | 10 | 100 | 1000 | |
| mg | 27 ± 27 | 163 ± 72 | 437 ± 131 | 895 ± 236 | 1354 ± 212 | 9 |
| | *Histamine concentration* (μmol/l) | | | | | |
| | 0.1 | 1 | 10 | 100 | | |
| mg | 21 ± 10 | 86 ± 34 | 452 ± 138 | 1161 ± 200 | | 9 |
| | *TEA concentration* (mmol/l) | | | | | |
| | 1 | 2 | 4 | 8 | | |
| mg | 315 ± 85 | 597 ± 130 | 804 ± 159 | 958 ± 172 | | 13 |

data represent the mean increase in tension (mg) ± s.e. from tissues from *n* animals.

## Discussion

The capillary technique (Golenhofen & v. Loh, 1970) for extracellularly recording electrical activity from smooth muscle registers the compound electrical activity of many cells beneath the recording electrodes. It follows that the record obtained will only reflect the activity of individual cells providing that the cells which contribute to the record generate similar activity and in a fairly synchronous manner.

The fact that the slow waves recorded extracellularly from guinea-pig trachealis were of similar waveform and frequency to those seen by intracellular recording (Clark & Small, 1979; present study) suggests that these membrane potential changes must be similar and reasonably synchronized throughout many cells. The simplest explanation for such a phenomenon is that the muscle cells of guinea-pig trachealis are electrically coupled. The nexi or gap junctions reported to exist in this tissue (Hoyes & Barber, 1980; Jones, Kannan & Daniel, 1980) may provide the structural basis for such coupling.

The extracellular recording technique revealed a close association between slow wave activity and spontaneous tension development, particularly in those tissues where individual slow waves accompanied individual tension increments or where bursts of slow waves accompanied an increase in the rate of tension development. Our present and earlier (Clark & Small, 1979) intracellular recordings failed to detect such a close association between electrical and mechanical activity. The reason for this may be that the microelectrode was inserted into the trachealis approximately 1.5 cm laterally from the tissue segment from which mechanical activity was recorded. It is possible that excitation is poorly conducted at right angles to the longitudinal axis of the smooth muscle bundles.

Although coordinated slow wave activity seemed important for the spontaneous development of tension, its role in the maintenance of developed tension was less clear. In some tissues slow wave discharge apparently ceased once peak tone had been reached. Cooling to 27.5°C and treatment with D600 could each apparently abolish slow waves and yet only evoked partial relaxation. These three observations may suggest that the trachealis muscle is able to sustain tension in the absence of slow wave activity. An alternative possibility is that, in the same three circumstances, slow wave activity occurs in some individual cells but is not synchronized in many cells and therefore is not detectable by the extracellular electrodes. Multiple impalements of the tissue with microelectrodes will be necessary to distinguish between these possibilities.

Relatively few studies have so far been made of the effects of spasmogenic drugs on the membrane potential of trachealis muscle. Early intracellular recordings from canine (Stephens & Kroeger, 1970) and bovine (Kirkpatrick, 1975) tissue suggested that the spasm evoked by acetylcholine was accompanied simply by a smoothly-developing depolarization of the cell membrane. However, the later sucrose gap experiments of Cameron & Kirkpatrick (1977) revealed slow wave activity superimposed on acetylcholine-induced depolarization of bovine trachealis. Histamine, too, can induce depolarization and slow wave activity in bovine trachealis (Kirkpatrick, 1975; 1981).

Although low concentrations of histamine occasionally induced or augmented slow wave activity in guinea-pig trachealis, the most consistent effect of both histamine and acetylcholine was suppression of slow wave activity. If these agents were causing significant depolarization of the tissue, then their suppression of slow waves might be a reflection of the dependency (Kirkpatrick, 1981) of slow wave discharge on resting membrane potential. The alternative explanation is that these spasmogens cause a desynchronization of cellular discharge. Again, microelectrode recording will distinguish between these possibilities.

Canine and bovine trachealis muscle both lack spontaneous electrical activity but depolarization, slow waves and spike activity can be induced by treatment of these tissues with TEA 30 mmol/l. The action of TEA on these tissues may largely be due to the drug's ability to reduce potassium conductance (Kirkpatrick, 1975; Kroeger & Stephens, 1975) though the formation of gap junctions may also be promoted by this agent (Kannan & Daniel, 1978).

The present study has shown that the guinea-pig trachealis exhibits spontaneous electrical activity and that this activity is enhanced by TEA in concentrations as low as 1 mmol/l. These observations may suggest that the potassium conductance in guinea-pig trachealis is normally lower than that of bovine or canine tissue. The lower resting membrane potential (Clark & Small, 1979) of guinea-pig trachealis compared with bovine (Kirkpatrick, 1975) or canine (Kroeger & Stephens, 1975) tissue is consistent with this suggestion.

Relatively little is known about the electrophysiological effects of catecholamine action on tracheal smooth muscle. Kirkpatrick (1981) has reported that the inhibitory effects of catecholamines in bovine trachealis are accompanied by hyperpolarization and that this hyperpolarization is reduced by propranolol. In our previous intracellular study of guinea-pig trachealis (Clark & Small, 1979) we performed some pilot experiments using noradrenaline. The relaxation evoked by this agent was accompanied by cessation of slow wave activity and hyperpolarization of the impaled cell. In most instances

electrode displacement occurred early in the action of the drug. Nevertheless these intracellular observations may suggest that the isoprenaline-induced abolition of slow waves seen in the present work represented their disappearance from individual cells rather than desynchronization of their discharge.

Sodium nitrite and the purine derivatives adenosine and ATP shared the ability of isoprenaline to relax the trachealis and to suppress co-ordinated slow wave activity. The latter effect of the purine derivatives contrasts with Kirkpatrick's (1981) observation that ATP has no effect on membrane potential changes in bovine trachealis. At present it is not possible to say whether the slow wave suppression induced by sodium nitrite and the purine derivatives is a feature seen in individual cells or represents desynchronization of discharge.

In concentrations in the range 1–10 μmol/l the calcium antagonist verapamil and its methoxy- derivative, D600, inhibit spontaneous spike activity in the taenia caeci and antral stomach of the guinea-pig (Golenhofen & Lammel, 1972) and in the portal vein of the rat (Jetley & Weston, 1980). However, the slow wave activity of antral stomach is relatively unaffected by verapamil (Golenhofen & Lammel, 1972). If the D600-induced suppression of slow waves seen in the present experiments is a reflection of their suppression in individual cells, then it would seem likely that the mechanisms underlying tracheal slow waves are similar to those underlying spontaneous spike activity in other smooth muscles.

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