Evidence concerning conduction in smooth muscle has been obtained by comparing the electrical properties of a variety of visceral muscles. Correlations with morphology permit some conclusions regarding interfiber conduction.

**Methods**

Membrane potentials have been recorded by means of the sucrose gap electrode as described previously. An electrometer preamplifier was used in conjunction with a d.c. Tektronix oscilloscope. External recording of action potentials was by conventional wick-silver-silver chloride electrodes and a Grass polygraph. In the discussion, reference is made to previous evidence obtained with intracellular electrodes.

**Results**

**Membrane potential and configurations of electrical activity.** The mean values of membrane depolarization by K$_2$SO$_4$ for the different muscles are given in Table I. These depolarizing potentials fell between 50 and 70 mv for all muscles; the lowest value was for longitudinal intestinal muscle and the highest for dog retractor penis. In general, the membrane potentials were less for the spontaneously active preparations (e.g. taenia coli and cat intestine) than for the inactive muscles. Depolarization by isotonic KCl was one-half to two-thirds that by K$_2$SO$_4$ in the gut muscles, as previously reported, and two-thirds the K$_2$SO$_4$ depolarization in ureter and dog retractor penis.

The configuration of spontaneous activity recorded diphasically with paired external wick electrodes is shown in Figure 1. A transition from simple to complex spikes in the different muscles is illustrated. In the pig esophagus, spontaneous activity was rare, but when spikes did appear, they were fast and simple. Typical spontaneous activity in the taenia coli consisted of regular trains of simple spikes. In the cat intestine, the spikes rarely appeared singly but rather in a complex form, particularly in the longitudinal layer. In the rabbit bladder and guinea pig vas deferens, complex trains of fast spikes, often accompanied by depolarization, formed the characteristic pattern preceding contraction. The rat ureter showed a plateau-type response as reported previously and in addition the guinea pig ureter spike potential was characterized by initial oscillations. The dog retractor penis shows prominent slow waves, often capped by fast spikes. Irregular slow waves sometimes appear in cat nictitating membrane and pig renal vein especially on lowering the temperature.

Configurations of individual spikes recorded both spontaneously and in response to stimulation with the sucrose gap technique are shown in Figures 2 and 3.
results indicate that the muscles fall into two, or perhaps three, distinct groups.

The spikes recorded from the various gut muscles, i.e. pig esophagus muscularis mucosae, guinea pig taenia coli and cat intestine circular and longitudinal muscle were similar (fig. 2). Both slow waves and simple spikes occurred rhythmically once every few seconds either spontaneously or as a result of being 'driven' electrically (1). The spikes usually arose from the crests of slow waves (e.g. fig. 2c) but occasionally appeared to fire independently of them (e.g. fig. 2g). The slow waves rarely exceeded 5 mv, while spikes of 25-45 mv were observed in this group of muscles (see table 1). In cat longitudinal intestinal muscle, spikes sometimes appeared on the crests of plateau-like depolarizations (fig. 2e) (4). All the gut muscles produced spike potentials characterized by an initial slow depolarization, followed by approximately equal rate of rise and fall, and by after-hyperpolarization (fig. 2g, h, i). In the pig esophagus muscle where the spikes were large and the conduction velocity fast, the rate of rise was somewhat faster than the rate of decay (fig. 2g). The duration of the spike at half peak height was shorter for the faster conducting muscles (table 1).

In the dog retractor penis muscle large slow waves (10-18 mv) and spikes of up to 110 mv were recorded with the sucrose gap method (fig. 3a-h). Slow waves appeared spontaneously or on stimulation, but spikes were obtained only in response to stimulation. The conduction velocity was nearly always preceded by a small diphasic or negative wave (fig. 3m). Some slow waves up to 40 mv were detected.

**TABLE 1. Electrical Parameters of Smooth Muscles**

<table>
<thead>
<tr>
<th>Conduct. Veloc.</th>
<th>Depolarization in isotonic KSO4</th>
<th>Spike (Sucrose Gap)</th>
<th>Muscle in Sucrose Gap, 10 mm by 0.5 mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pig esophagus muscularis mucosae</td>
<td>15.2 ± 0.09</td>
<td>63 ± 0.81</td>
<td>49 ± 0.31</td>
</tr>
<tr>
<td>Guinea pig taenia coli</td>
<td>7.2 ± 0.19</td>
<td>51 ± 0.93</td>
<td>31 ± 0.82</td>
</tr>
<tr>
<td>Cat circular intestinal muscle</td>
<td>4.4 ± 0.08</td>
<td>32 ± 0.42</td>
<td>38 ± 0.92</td>
</tr>
<tr>
<td>Cat longitudinal intestinal muscle</td>
<td>3.8 ± 0.11</td>
<td>49 ± 0.71</td>
<td>22 ± 1.36</td>
</tr>
<tr>
<td>Dog retractor penis muscle</td>
<td>1.6 ± 0.33</td>
<td>68 ± 1.62</td>
<td>80 ± 1.61 (spike)</td>
</tr>
<tr>
<td>Rat ureter</td>
<td>2-10</td>
<td>57 ± 0.1</td>
<td>68 ± 2.35</td>
</tr>
<tr>
<td>Pig renal vein none</td>
<td>53 ± 0.1</td>
<td>4.8 ± 0.2</td>
<td>12</td>
</tr>
<tr>
<td>Pig cecal artery none</td>
<td>50 ± 0.8</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

All experiments were carried out at 35-37°C. Mean values and S.E.'s given where possible. * Minimum values (covering not less than 5 preparations of each muscle) only are given, since these values depended on spontaneous fluctuation in excitability.

The spikes usually arose from the crests of slow waves (e.g. fig. 2c) but occasionally appeared to fire independently of them (e.g. fig. 2g). The slow waves rarely exceeded 5 mv, while spikes of 25-45 mv were observed in this group of muscles (see table 1). In cat longitudinal intestinal muscle, spikes sometimes appeared on the crests of plateau-like depolarizations (fig. 2e) (4). All the gut muscles produced spike potentials characterized by an initial slow depolarization, followed by approximately equal rate of rise and fall, and by after-hyperpolarization (fig. 2g, h, i). In the pig esophagus muscle where the spikes were large and the conduction velocity fast, the rate of rise was somewhat faster than the rate of decay (fig. 2g). The duration of the spike at half peak height was shorter for the faster conducting muscles (table 1).

In the dog retractor penis muscle large slow waves (10-18 mv) and spikes of up to 110 mv were recorded with the sucrose gap method (fig. 3a-h). Slow waves appeared spontaneously or on stimulation, but spikes were obtained only in response to stimulation. The conduction velocity was nearly always preceded by a small diphasic or negative wave (fig. 3m). Some slow waves up to 40 mv were detected.

**FIG. 1. Comparison of characteristic patterns of spontaneous spike activity recorded diphasically with external wick electrodes from various smooth muscles 35°C.** Mechanical (upper) and electrical (lower) records in b, e, g, j, electrical only in a, c, f, h, k, l; a, pig esophagus muscularis mucosae; b, c, taenia coli of guinea pig and rabbit; d, cat intestine circular muscle; e, cat intestine longitudinal muscle; f, guinea pig vas deferens; g, rabbit bladder; h, dog retractor penis; i, j, rat and guinea pig ureters; k, cat nictitating membrane under influence of cold; l, pig renal vein.

Conduction velocity; distance; threshold. Velocity of conduction was measured between two pairs of recording electrodes (fig. 4, table 1). The velocity of pig esophagus was 15.2 cm/sec., which is the fastest velocity ever observed in vertebrate visceral smooth muscle (table 1, fig. 4a). Velocities of the other muscles ranged from 7.1 cm/sec. in taenia coli (fig. 4b) and 4.1 cm/sec. in cat
Comparative Electrical Properties, Smooth Muscles

The muscles present a graded series of increasing resistance and capacitance. Resistance of strips of various smooth muscles (0.5 mm in diameter and 10 mm long) was measured across the sucrose gap. Square pulses were applied across the preparation in series with known variable resistances and the signal across the preparation was measured on the oscilloscope. The unknown (preparation) resistance ($R_2$) was given by

$$R_2 = \frac{V_2R_2 - V_1R_1}{V_1 - V_2},$$

where $V_1$ and $V_2$ are amplitudes of the same square pulse on the oscilloscope at the known resistances $R_1$ and $R_2$.

In preliminary experiments the resistance was measured at 5-10-minute intervals during 3 hours. Within the first few minutes of sucrose flow the resistance reached a steady level which was maintained for from 15 to 60 minutes depending on the preparation. Thereafter the resistance increased further, probably because of sucrose penetration into the cells. For comparison of the different muscles, resistances were measured during the period 25-30 minutes after starting the sucrose flow. Capacitance was measured by means of a General Radio a.c. bridge during the same period as the resistance.

Resistance and capacitance data are given in table 1. The muscles present a graded series of increasing re-
abruptly when the strip was cut down, but sometimes a graded reduction of conduction distance was seen (taenia coli section). Loss of conduction usually occurred resistance of 0.8 megohms as compared with

The resistances in table I are for 0.5-mm diameter strips and renal vein failed to conduct, regardless of width. Nonconducting strips, checked histologically, usually

Conduction in strips of different thickness. Conduction distance was measured in strips of different diameters (table 2B). It was found that the thicker the preparation, the more consistent was conduction. Conduction occurred for distances of 25–40 mm in all strips wider than 100–200 μ. In smaller strips (<100 μ) conduction distance was not greater than 1–3 mm, although the strips were capable of local contraction and spontaneous activity. Nonconducting strips, checked histologically, usually contained several bundles and less than 200–300 cells in cross section. Loss of conduction usually occurred abruptly when the strip was cut down, but sometimes a graded reduction of conduction distance was seen (taenia coli and cat intestine, table 2B). Strips of carotid artery and renal vein failed to conduct, regardless of width.

DISCUSSION

Bozler (6) classified smooth muscles into unitary types, which include visceral muscles, and multiunit types, which include cat nictitating membrane, pilomotor and pupillary muscles. In unitary muscles, conduction occurs in the absence of nerves, while in multiunit muscles it does not. This division has been confirmed in the present work. In addition there is evidence of a further division within the visceral group. The gut muscles, including the muscularis mucosae, taenia coli, longitudinal and circular intestinal muscles clearly belong to one group, together with uterine muscle. The dog retractor penis and ureter muscles show characteristics of a different nature from these muscles.

Smooth muscles of the gut and uterus show two kinds of electrical activity—(1) graded slow waves (up to 5 mv with the sucrose gap) which may be local generator potentials or pacemaker potentials and (2) spikes which are usually all-or-none (45 mv in sucrose gap, 60 mv with microelectrodes). Slow waves are not associated with conduction, but appear to propagate decrementally for short distances at the same velocity as spikes which are associated with conduction. Spikes usually arise from the crests of slow waves, but occasionally appear independently of them. During maintained depolarization (stretch, acetylcholine) slow waves may be lost while spikes persist. It appears that slow waves and spikes result from different membrane processes, that they may be separated yet are interdependent. The similarity to generator potentials and spikes in mechanoreceptors (7) and to pacemaker potentials and spikes in crustacean heart ganglion cells (8, 9) is striking.

In the ureter and dog retractor penis, the electrical characteristics are different from those recorded in the more spontaneous gut and uterine muscles. In dog retractor the slow waves are prominent, as large as 18 mv (sucrose gap) and they conduct greater distances. No slow waves appear in the ureter. The pure spikes from both ureter and dog retractor are also larger (up to 110 mv by sucrose gap), their shape shows faster rate of rise, rarely an initial slow rising phase and only occasional after-hyperpolarization such as is common in the gut muscles. The ureter spikes tend to plateau and are topped by oscillations in the guinea pig. The range of membrane potential in which ureter and dog retractor are excitable is narrow; they tend to give only one spike in response to stretch (10) and only one or two spikes during the initial stage of K_2SO_4 depolarization whereas the gut muscles continue to fire for about 30 mv of such depolarization. Also, there is less difference between K_2SO_4 and KCl depolarization than in gut muscles.

Comparison of different muscles, and in particular of the series of four gut muscles, shows certain correlations between speed of conduction and electrical and morphological parameters of the membranes (11). Conduction is fastest in the muscles with long fibers, hence fewest cell junctions, e.g. esophagus muscularis mucosae. This result implies that the velocity in smooth muscle is not uniform.
and that the slow velocity may result from the many intercellular junctions, while conduction within a fiber may be rapid. This is supported by the following: conduction distance is greater in a muscle lengthened by stretch; that is, with the same number of junctions for a longer length. Conducted responses show long refractory periods longer length. Conducted responses show long refractory periods (1-5 sec.), whereas intracellular records show that single fiber membranes can give spikes separated by as little as 50 msec. (2, 3). Further evidence for some conduction barrier between cells is the correlation of high velocity with close packing of fibers, low extracellular space, and long bundles of parallel fibers. In multiunit arterial muscles where the cells are widely separated, no interfiber conduction has been recorded.

Conduction velocity is also correlated with the excitability of the fibers. The faster muscles are excited by short-duration pulses, have shorter relative refractory periods and brief spikes than the slower muscles.

Many cells arranged in parallel are necessary for conduction to occur in visceral smooth muscle. Strips of muscle conducted distances up to 25-40 mm until the size of strip was reduced to about 100 µm diameter when no conduction occurred, no matter what strength of stimulus was applied. This requirement of interaction among many cells is supported by the observation that when a stimulating pulse is applied by a low resistance microelectrode to one or a small group of cells of the taenia, conduction up to only 0.7 mm is possible, whereas stimulation by widely spaced electrodes readily elicits a response conducted for 20 mm or more (2). Simultaneous contraction of even larger units of circular intestinal muscle has been observed microscopically in intact muscle rings (3). Further, conduction can occur across the axis of fiber orientation at about one-tenth the velocity in the long axis (2, 12). The difference in latency of responses at two microelectrodes within a bundle is less than when the electrodes are in fibers in separate bundles (2). The conducting unit may not be a morphological entity. For example, in esophagus muscle, conduction over 25 mm failed when strips were cut down to widths containing several naturally occurring bundles of 60-100 fibers each. However, these bundles branch every few millimeters. Thus it may be that while the naturally occurring bundle has the minimum specifications to be the conducting unit, a number of interlocking and branching bundles are necessary for conduction to occur over long distances. In some muscles, increasing the stimulus duration above threshold may increase conduction distance by 5 mm, presumably by bringing in more conduction paths.

It is concluded that conduction depends on a) nature of intercellular barriers, b) excitability of individual cell membranes and c) interaction among groups of cells.

Despite the requirement for interaction among a large number of parallel fibers for conduction, the individual fibers constitute the electrical units. Resting potentials are found across membranes of single cells and not within the bundle sheaths. The responses recorded extracellularly and by the sucrose gap are compounded from the single fiber potentials. Even when microelectrodes less than 500 µ apart recorded spike discharges at about the same frequency, the spikes did not necessarily coincide (2).

The results reported in this paper do not permit a definite decision as to relative importance of chemical and electrical factors in interfiber transmission, but they do give strong support for electrical transmission. The abundant vesicles, especially in protruding rows close to the cell membranes, might be interpreted as sources of a chemical transmitter (11). Yet vesicles are abundant not
only at chemical synapses but also at postganglionic endings of an electrical synapse (13), at cell membranes of nonexcitable tissues, and in smooth muscles in which conduction is entirely by nerves. The slow graded potentials which often precede spikes might be interpreted as synaptic potentials, yet they resemble generator potentials of mechanoreceptors where there is no evidence as synaptic potentials, yet they resemble generator potentials, transmitters, motor activities.

A useful working model is that smooth muscle resembles a number of parallel core-conductors connected by moderate-resistance barriers. Delays in conduction may occur at these interfiber barriers. The facts that injury potentials can be measured, monopolar action potentials can be recorded externally and the sucrose gap used, indicate relatively low resistance paths. Also the wave length of a conducted action potential is many cells long, particularly in muscles which show plateaus (5). The resistance across sucrose in the 1-cm gap is 84 megohms, across a sucrose gap preparation of conducting smooth muscle 1 megohm, across a strip of long-fibered striated muscle (frog sartorius) less than 0.1 megohm and in nonconducting preparations, either small-sized gut muscle strips or nonconducting blood vessels, it is some 12 megohms. In intact muscle where the extracellular fluid is a good conductor rather than sucrose there must be much short-circuiting of the fiber currents in the wide spaces.

Direct measurement by intracellular electrodes in resting cells gives a value of total cell resistance of 115 megohms which corresponds to 1100 ohms cm²; current distribution in these measurements is uncertain, but the order of magnitude of resistance is similar to that in striated muscle. In nerve (15). No low resistances were seen between two internal microelectrodes several cell apart (15). However, if two cells were connected by a resistance path equal to the total resistance of one cell, an action potential in one would be divided across the second so that it would be half the amplitude across the first cell. The longitudinal extracellular resistance around a smooth muscle fiber calculated from the narrow spacings is high (about 65 megohms), hence favoring current flow through adjacent cell membranes. Effective resistance (and capacitance) may vary with amount of intercellular contact, also with activity. The 'bridges' and also the regions where rows of vesicles are close together, may provide regions of 'relatively' low resistance during activity (11).

Conduction in smooth muscle varies with excitability. There are many ways in which smooth muscle is normally poised for conducted discharge: stretch alters responsiveness and may depolarize and stimulate (10); acetylcholine is continually released in the gut wall (16, 17) which depolarizes the membrane, thereby increasing excitability; impulses in autonomic nerves similarly regulate responsiveness. In the uterus propagation depends on hormone levels (6, 18, 19); estrogen decreases membrane potential from inactivity into a zone of firing. Acetylcholine (and adrenaline in esophagus muscularis mucosae) can reduce threshold duration from 100 to 1 msec. Local pacemaker regions may occur at random and when sufficient excitable cells are involved, a propagated wave results. When autonomic nerves degenerate, the muscle is more active spontaneously and more sensitive to drugs (30). In general, increase in excitability and in ability to
propagate is associated with depolarization of cell membranes.

It is concluded that propagation in smooth muscle depends on more than one factor. Transmission, per se, appears to be electrical, but it occurs best when the muscle is made excitable by stretch or by chemical transmitters. The electrical unit appears to be the fiber, but the conducting unit involves interaction among many parallel fibers which provide a relatively low resistance path, and a 'front' of depolarization.

REFERENCES


15. BARK, L. M.