known that the action of angiotensin on this tissue can be separated into a direct and indirect component (Khairallah & Page, 1961) experiments are in progress to clarify with which component the glucose-dependent oxidative step is involved.

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Slow contraction of the guinea-pig proximal colon in response to the stimulation of an unidentified type of nerve

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Characteristic movements, notably anti-peristalsis, distinguish the proximal colon from other parts of the guinea-pig intestine (Elliott & Barclay-Smith, 1904; Hukuhara & Neya, 1968). This part of the gut is also unusual in that adrenergic neurones are present in the myenteric plexus (Furness & Costa, 1971).

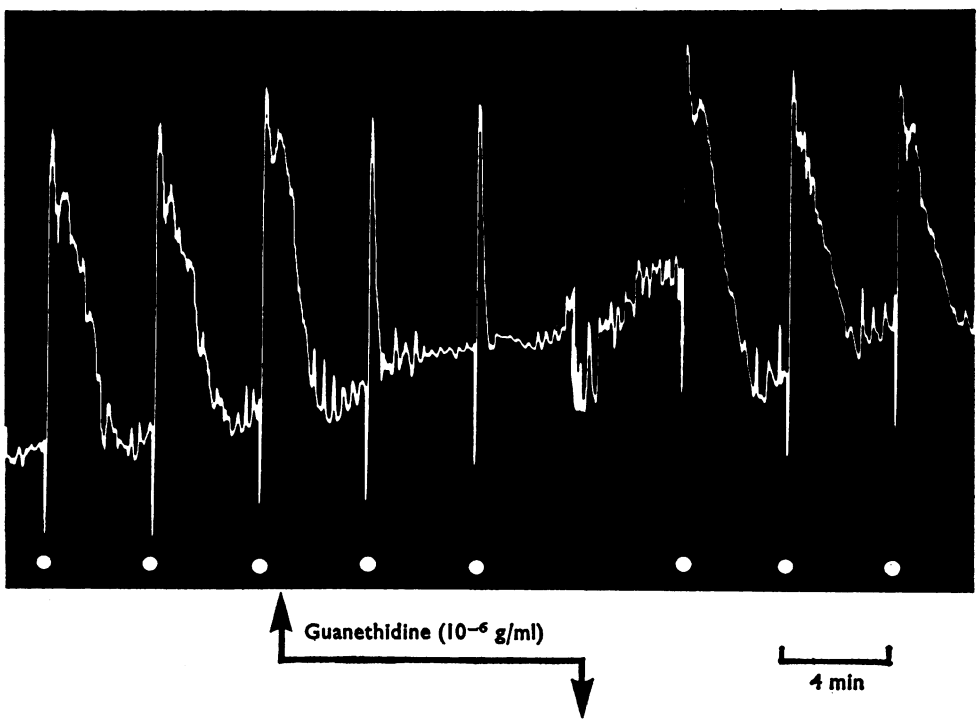

FIG. 1. Responses of the longitudinal muscle of the proximal colon to transmural stimulation at 20 Hz for 10 sec each 4 min (at the dots). The muscle relaxed during the stimulation. At the end of the stimulus, there was a rapid contraction which declined only slowly. The slow phase of this contraction was blocked by guanethidine (10^{-6} g/ml), applied between the arrows. The slow contraction returned soon after the guanethidine was washed from the bath.

In the present work, we have examined mechanical responses of the longitudinal muscle of isolated segments of the proximal colon. Stimulation of intrinsic nerves with transmural electrodes resulted in complex responses to which at least three nerve types contributed, these being, 1, cholinergic nerves which gave primary contractions, 2, inhibitory, but not adrenergic, nerves which gave primary relaxations followed by rebound contractions of the muscle, 3, excitatory nerves which gave slow contractions after long latencies. There was generally little contribution of adrenergic nerves to the response to transmural stimulation. After blockade of muscarinic receptors by hyoscine (10^{-7} g/ml) there was occasionally evidence of a brief, apparently non-cholinergic, contraction during short (10 s) bursts of stimuli.

The slow contraction (Fig. 1) was observed at stimulation frequencies from 5 to 50 Hz. It began 10–15 s after the beginning of trains of stimuli lasting 10–30 s. The contractions lasted 0·5–4 min. Slow contractions were very susceptible to blockade by guanethidine and were readily restored following the washout of this drug (Fig. 1). The contraction is considered to be nerve-mediated in that it was blocked by tetrodotoxin (10^{-7} g/ml) and non-cholinergic in that it was unaffected by hyoscine or atropine in sufficient concentration to block the primary cholinergic contraction elicited by transmural stimulation. It is apparently not due to the release of noradrenaline, because directly acting sympathomimetic amines all relax the muscle and none of these relaxations could be reversed by α- or β-adrenoceptor blockade. The slow contraction can be distinguished from the rebound contraction following stimulation of intrinsic inhibitory neurones by the selective blocking action of guanethidine and by the fact that it occurs during, rather than after, an extended period of stimulation (see Furness, 1970).

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Effects of metformin on glucose uptake by the isolated rat diaphragm

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The biguanide antidiabetic drugs do not produce significant hypoglycaemia in non-diabetic subjects. In diabetic patients phenformin increases glucose uptake into muscle in the human forearm (Butterfield, 1968). Previous *in vitro* studies on the effects of buformin and phenformin on glucose uptake by the isolated rat diaphragm preparation (Vallance-Owen & Hurlock, 1954) have been inconclusive due to the use of high drug concentrations (Daweke & Bach, 1963).

The effects of metformin on the isolated rat diaphragm preparation have been studied under normal and diabetic conditions (Table 1). Metformin at a therapeutic concentration (10 μg/ml) did not affect glucose uptake by this preparation under normal conditions. A tenfold increase in the concentration of metformin, however, caused a significant depression of uptake. This emphasizes the danger of extrapolation from results obtained with high drug concentrations. Diaphragms taken