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A preliminary investigation into the metabolic requirements of the contractile response of guinea-pig ileum to angiotensin

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The contractile response of many smooth muscle preparations to angiotensin is well documented and has been reviewed recently (Khairallah, 1971). In this study the metabolic requirements for this action of angiotensin on guinea-pig ileum have been investigated.

The terminal ileum, removed from male albino guinea-pigs that had been starved overnight, was suspended in Tyrode solution containing 1 g/l. glucose at 28° C and gassed with air. Contractions were recorded on a kymograph using an isotonic, frontal-writing lever. In all experiments, concentrations of acetylcholine and angiotensin were selected which produced responses approximately equal to the 50% maximum acetylcholine response.

Initially the effect of altering the glucose concentration of the Tyrode solution, for 20 min periods, upon the responses to acetylcholine and angiotensin, was investigated. It was found that an increase to 8 g/l. glucose had no effect on the responses to either agonist. A decrease in glucose concentration to 0.25 g/l. reduced the response to acetylcholine by 12% but to angiotensin by 48%. The difference between the percentage reduction of the responses was highly significant ($P < 0.001$). There was a significant difference ($P < 0.001$) between the reduction of the acetylcholine response (60%) and the angiotensin response (92%) when glucose was completely removed from the Tyrode solution for 15 minutes. The effect of other hexoses was tested by replacing glucose in the Tyrode solution with either galactose or fructose at a concentration of 1 g/l. for 20 min. With galactose or fructose the responses to acetylcholine and angiotensin were similarly reduced (75–85%). These findings suggested that a glucose-dependent mechanism might be implicated in the angiotensin response.

The possibility that this mechanism utilized an oxidative pathway was investigated by comparing the responses to acetylcholine and angiotensin when the Tyrode was gassed with nitrogen for 110 min. There was a progressive reduction in the responses to both agonists which was greater for angiotensin (78%) than for acetylcholine (45%). Exposure of the tissue to carbon monoxide decreased the angiotensin response by 26% while the response to acetylcholine was unaffected or slightly increased.

These findings indicate that the contractile response of guinea-pig ileum to angiotensin might involve a glucose-dependent oxidative mechanism. Since it is well

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).

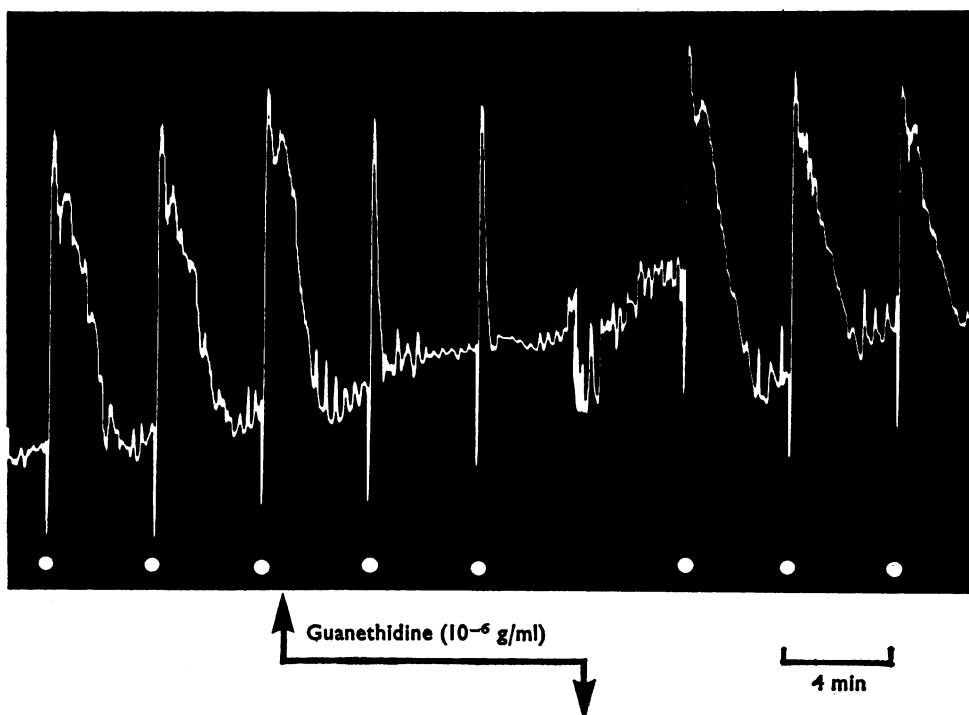


FIG. 1. Responses of the longitudinal muscle of the proximal colon to transmural stimulation at 20 Hz for 10 sec each 4 min (at the dots). The muscle relaxed during the stimulation. At the end of the stimulus, there was a rapid contraction which declined only slowly. The slow phase of this contraction 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.