A NOTE ON AN EFFECT OF PYROGALLOL ON DUODENAL MOTILITY

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Pyrogallol injected intravenously exerts an initial depressor and a secondary stimulatory effect on the duodenal motility of dogs. The first effect is similar to that of adrenaline. The duodenal excitation is thought to be due to a peripheral cholinergic mechanism. Pyrogallol enhances the duration of the inhibitory action of adrenaline on duodenal motility and converts the action of histamine to an inhibition.

PYROGALLOL is known to be an inhibitor of catechol-*o*-methyl transferase (Axelrod and Laroche, 1959; Axelrod, 1960) and its action as a potentiator of the effects of catecholamines has thereby been explained (Axelrod, 1960). It has been shown to enhance actions of adrenaline (Wylie, Archer and Arnold, 1960; Axelrod, 1960; Bacq, 1935; Ludueña, 1938; Lembeck and Resch, 1960; Izquierdo, Izquierdo, Kaumann and Coussio, 1961a, b), noradrenaline (Wylie and others, 1960; Izquierdo and others, 1961a, b), sympathetic nerve stimulation (Bacq, 1935; Izquierdo and others, 1961b), isoprenaline (Konzett, 1960; Izquierdo and others, 1961a, and unpublished results) and is presumed to exert its own adrenergic effect by the potentiation of circulating catecholamines (Izquierdo and others, 1961a).

An entirely different action of pyrogallol is described in this paper, which refers to studies on the duodenal motility *in situ* of dogs.

METHODS

Twenty mongrel dogs of both sexes were used in this experiment. They were anaesthetised with intraperitoneal pentobarbitone (35–40 mg./kg.). Carotid blood pressure and duodenal motility, by intraduodenal balloon, were recorded on smoked paper.

All drugs were injected into a cannulated external iliac vein.

RESULTS

Pyrogallol (5, 10, 20, 25 and 50 mg./kg.) produced an initial and immediate reduction in tonus and a decrease or disappearance of duodenal contractions in all dogs. This effect closely resembled that of 1 or 2 μg./kg. of adrenaline injected as a control, and lasted 1 to 3 min.

Also the duration of the inhibitory action of adrenaline upon the duodenal activity was always increased.

Two to 10 min. after its injection, pyrogallol provoked a marked increase in the amplitude of contractions (Fig. 1), which sometimes reached very high levels. This was seen in 19 out of 20 dogs. The tonus was usually also increased. This effect lasted up to 15–40 min. from the injection of the polyphenol. A dose-response curve could not be obtained since all doses over 5 mg./kg. gave the same response.

This enhancement of duodenal motility was not inhibited by mepyramine (5 mg./kg., 2 dogs) or hexamethonium (3–8 mg./kg., 4 dogs) but was completely abolished by atropine (0·5–2 mg./kg., 9 dogs) (Fig. 2). It appeared in animals with their vagi intact or with one or both of them sectioned. It was also observed in animals previously treated with hexamethonium but it was not possible to evoke it after the administration of atropine, unless (1 dog) large doses of neostigmine were given beforehand.

The potentiating effect of pyrogallol on the duodenum was intensified after the administration of tolazoline (5 mg./kg., 3/3 dogs), phentolamine

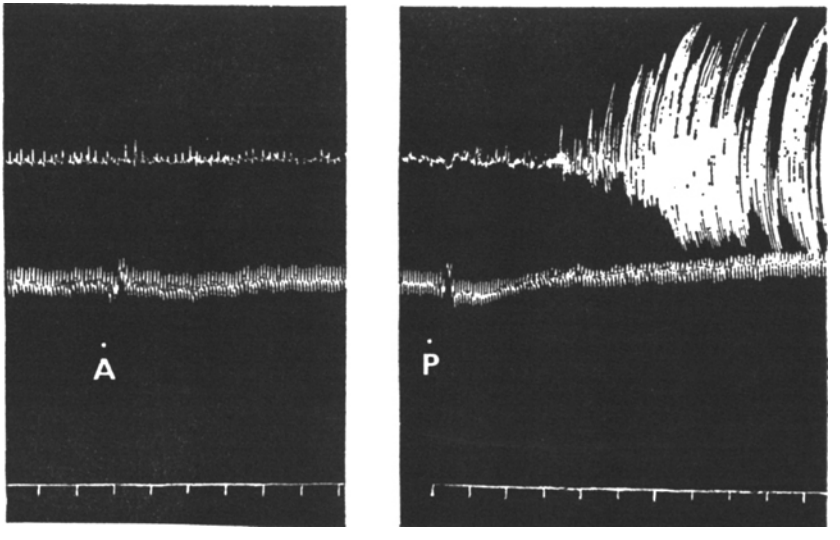

FIG. 1. From above down: duodenal motility, blood pressure, time (min.). A: 3 ml. 1 per cent ascorbic acid. P: pyrogallol, 20 mg./kg. Note the increase in duodenal motility seen after pyrogallol.

(10 mg./kg., 1/2 dogs) and yohimbine (0·5 mg./kg., 1 dog). It could be evoked in the presence of one or more of these drugs, or of dichloroisoprenaline (3 mg./kg., 1 dog).

The excitatory action of histamine (1, 2, 4 μg./kg.) on the duodenum is converted into a brief inhibition after pyrogallol. This inhibition resembles that produced by adrenaline.

Pyrogallol produces its excitatory effect on duodenal activity either when dissolved in 1 per cent ascorbic acid or when diluted, a few seconds before its injection, in saline solution. 3 ml. 1 per cent ascorbic acid did not itself exert any appreciable effect on duodenal motility (2 dogs).

DISCUSSION

The explanation of the initial sympathomimetic-type effect of pyrogallol on the duodenum may be an enhancement of the action of circulating catecholamines. In fact, it also potentiates the intestinal effect of exogenous

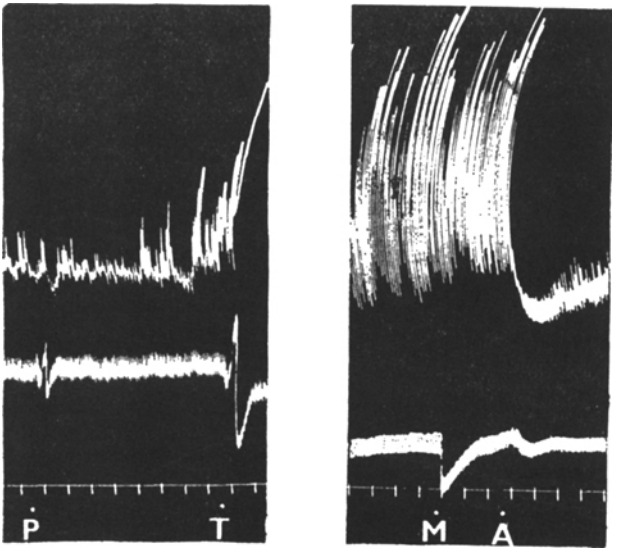

FIG. 2. P: pyrogallol, 10 mg./kg. T: tolazoline, 5 mg./kg. M: 11 min. afterwards, 4 mg./kg. hexamethonium. A: atropine, 1 mg./kg. Note that tolazoline exaggerates the effect of pyrogallol on the duodenum; hexamethonium does not inhibit it, and atropine does.

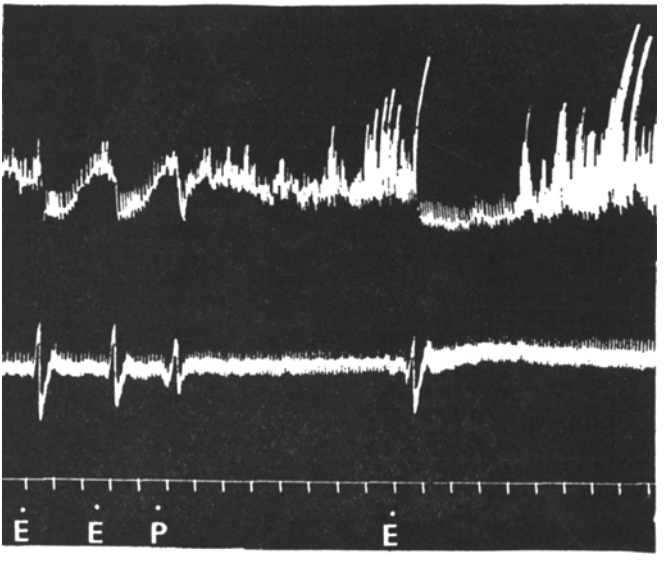

FIG. 3. E: Adrenaline, 1 μg./kg. P: pyrogallol, 20 mg./kg. Note the enhancement by pyrogallol of the effect of adrenaline on duodenal motility as well as the effect of pyrogallol itself.

adrenaline. However, an adrenaline-like effect in its own right cannot be wholly discarded.

The secondary enhancement of intestinal motility seen 2–10 min. after pyrogallol seems acetylcholine-like in nature for it is readily abolished by atropine and cannot be provoked in its presence unless neostigmine is first administered. It appears to be peripheral, because it happens in spite of vagotomy and after hexamethonium and is not inhibited by the latter.

The augmentation of this effect seen with tolazoline, phentolamine and yohimbine may be due to the complex actions on the intestine of these drugs, part of which action is acetylcholine-like and histamine-like.

The potentiator effect of pyrogallol on duodenal motility is independent of its acetylcholine-like action. In fact, it enhances the duration of the effect of adrenaline on duodenal motility while this is, at the same time, much potentiated by pyrogallol itself (Fig. 3). Moreover, the latency of this effect is much longer (2–10 min.) than that of the adrenaline-like potentiating effect, which is immediate according to the results of Wylie and others (1960).

The reversal of the effect of histamine on duodenal motility may be thought to be due to an unmasking of its known stimulatory action on the adrenal medulla by pyrogallol. An inhibition of histamine-like effects on duodenum has been observed by Juorio (unpublished results) using isolated organs.

In summary, an intense acetylcholine-like effect of pyrogallol is described on the intact duodenum of dogs, and which does not prevent the simultaneous potentiation of the action of adrenaline-like agents upon it.

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