were obtained in a second experiment using the conditions described above, except that the buffers were free of Mg and Ca ions. Finally, in studies performed as above but with buffers in which the alkali metal cations were replaced by 100 mM of the chloride salts of the alkali earth cations, the following effect was found on the degree of hemolysis (Mean $\pm$ S.E., 8 experiments). Tr: Ca, 84.7 $\pm$ 2.8; Sr, 58.6 $\pm$ 6.0; Ba, 58.1 $\pm$ 8.8; and Mg, 18.0 $\pm$ 4.5. DOC: Ca, 90.6 $\pm$ 4.1; Sr, 51.6 $\pm$ 10.0; Ba, 38.4 $\pm$ 11.0; and Mg, 7.2 $\pm$ 0.5. In contrast, the degree of M solubilization caused by the detergents was unaffected by the various alkali earth cations.

The observation that the alkali cations modify the degree of detergent-induced lysis of intact E is of interest in regard to the multiple effects of such ions on M phenomena. It is unclear why there is a selectivity effect of the alkali cations on hemolysis but not on M solubilization caused by Tr and DOC. M solubilization reflects a profound disruption of M structure and thus may be independent of the relatively subtle changes imparted on the M surface by the alkali cations. These modifications are, however, sufficient to alter the degree of hemolytic processes caused by relatively minor, often localized, alterations produced by hemolysins on M structure. The finding of similar degrees of E M solubilization by the detergents in the various cationic media indicates that the modifications caused by the alkali cations on the degree of lysis of intact E result from their interaction with the M itself rather than from a fluid phase effect of the cations on the solubility or micellar arrangement of the detergent. The activity series of alkali metal ions upon C lysis[1,3] is unrelated to those found in lysis caused by Tr and DOC. However, the series obtained with alkali metal cations on the final stage of C lysis[2] was similar to that obtained in Tr induced lysis.

Resumen. Los distintos cationes alcalinos monovalentes (145 mM) y divalentes (100 mM) modifican marcadamente el grado de hemólisis de eritrocitos humanos provocado por Triton X-100 y por desoxicolato de Na (DOC). La serie de actividad con cationes monovalentes en hemólisis por Triton es K > Rb = Cs > Na $\geqslant$ Li, y por DOC es Li > Rb = Cs > K > Na. Por el contrario, el grado de solubilización de membranas eritrocitarias producido por Triton o DOC es independiente de los distintos cationes alcalinos.

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Vascular Effects of Periarterial Mesenteric Nerve Stimulation After Adrenergic Neurone Blockade

During an investigation of the vascular effects of 6-hydroxydopamine in cats, it was observed that stimulation of the periarterial mesenteric nerves after adrenergic blockade increased blood flow in the superior mesenteric artery. This observation led to the studies reported below.

Methods. 13 cats of either sex weighing 3–4.5 kg were anaesthetized with i.p. pentobarbital sodium 40 mg/kg Polyethylene catheters were inserted into an external jugular vein and a common carotid artery for drug administration and systemic arterial pressure measurement respectively. The abdomen was opened in the midline and the adrenal glands were excluded from the circulation by ligatures. The nerve plexus surrounding the main trunk of the superior mesenteric artery was dissected from the vessel and divided. The distal end was laid over bi-polar platinum electrodes and rectangular pulses of 1 msec duration at frequencies of 5–15/s and voltages of 5–15v were delivered for periods of 1–5 min. Blood flow in the superior mesenteric artery was measured with a Biotronex electromagnetic flowmeter using cuff-type probes. Vascular connections between the superior and inferior mesenteric arteries were divided. Intestinal motility was recorded in some animals by means of a balloon inserted into the small intestine and connected to a Statham pressure transducer. Mesenteric vascular resistance (mm/Hg/ml/min) was calculated by dividing arterial pressure by mesenteric arterial flow. Portal venous pressure changes were neglected since this variable changed by less than 2 mm Hg in preliminary experiments in 2 cats. Adrenergic neurone blockade was produced acutely in 9 animals by infusions of bretylium tosylate 1–3 mg/min via a polyethylene catheter tied into the pancreatico-duodenal branch of the mesenteric artery.

Adrenergic neurone blockade was produced in the other 4 cats by giving i.v. 6-hydroxydopamine 50 mg/kg and 75 mg/kg respectively 14 and 7 days prior to the blood flow studies.

Results. The control values (means $\pm$ SE, n = 13) for mean arterial pressure and superior mesenteric arterial flow were 127 $\pm$ 4 mm Hg and 12.4 $\pm$ 1.6 ml/min/kg cat.

Effects of mesenteric nerve stimulation after blockade with 6-hydroxydopamine (4 cats). Stimuli below 8v produced no changes. Stronger stimuli up to 15v, 15/s increased mesenteric blood flow and produced either no change or a slight fall (5-10 mm Hg) in systemic arterial pressure (Figure 1). Intestinal tone and motility were not significantly affected. The mesenteric flow increase was small in magnitude and often slow in onset and development (Figure 1D). Furthermore it usually outlasted the period of stimulation by 2–15 min (mean 5.2 min). The calculated maximum reductions in the vascular resistance of the mesenteric bed in each of the four animals were 41%, 25%, 16% and 12%. These reductions were not significantly altered by pre-treatment with intravenous atropine 0.5 mg/kg.

Effects of mesenteric nerve stimulation after blockade with bretylium (9 cats). Mesenteric nerve stimulation before bretylium produced the expected reduction in mesenteric arterial flow (Figure 1A). Infusions of bretylium 1–3 mg/min into the mesenteric artery increased systemic arterial pressure and mesenteric blood flow in parallel. Both variables returned to pre-infusion values within 20 min of stopping the infusion. After total bretylium doses of 18–40 mg mesenteric nerve stimulation, at 8v or above increased mesenteric blood flow in 6 of the 9 cats. The response resembled that seen in the four cats given

6-hydroxydopamine, i.e. it was of small magnitude and outlasted the period of stimulation, arterial pressure fell slightly or did not change, intestinal motility was unaltered and pretreatment with intravenous atropine 0.5 mg/kg failed to affect it (Figure 1). The maximum reduction in mesenteric vascular resistance (mean ± SE, $n = 6$) was 17 ± 4% of the pre-stimulation value. No mesenteric flow or resistance changes could be induced by nerve stimulation in three of the nine cats even after increasing the total dose of bretylium to 60 mg.

Discussion. These experiments have shown that stimulation of the nerves surrounding the superior mesenteric artery after adrenergic neurone blockade produces vasodilatation within the area of distribution of this vessel. Since the pancreatico-duodenal branch was tied and the branches to the large intestine were divided, it seems likely that the dilatation occurred in the small intestine although it cannot be excluded that dialtation also occurred in the vessels supplying the fat and lymph nodes of the mesentery. The response was not secondary to changes in intestinal tone or motility since no significant alteration in these variables occurred. Cholinergic mechanisms were probably not involved since the response was unaltered by atropine. Moreover, mesenteric vasodilatation does not occur when the abdominal vagi are stimulated[1].

The present study provides additional evidence indicating the possible existence of intestinal neurogenic vasodilator mechanisms which are neither adrenergic or cholinergic. This possibility was suggested by the previous observation that pelvic nerve stimulation in cat produced an atropine-resistant dilatation of the mucosal vessels of the colon[2]. Moreover mechanical stimulation of the small intestinal mucosa in cats induces a non-cholinergic vasodilatation possibly mediated by an intramural nerve reflex[3].

There are several possible explanations of the vasodilatation observed in my experiments:

1. The mesenteric nerves may contain specific efferent fibres which release a vasodilator transmitter. Recent studies suggest that the vasodilator agent adenosine triphosphate may be released by non-adrenergic inhibirotory nerves innervating the gut of several species[4,5]. However, inhibition of gut motility was not observed in the present study. The slow onset of the dilator response and its persistence after the stimulus is withdrawn is also rather uncharacteristic of a neurotransmitter.

2. A vasodilator substance may be released from the pre-terminal portions of adrenergic nerves during stimulation but can only produce vasodilatation when the release of the vasoconstrictor transmitter, noradrenaline, is prevented. One possible vasodilator which might be involved is prostaglandin E 1 which occurs in sympathetic nerves[6] is a mesenteric dilator[7] and is released when sympathetic nerves are stimulated[8].

3. The dilatation may be associated with secretory changes induced in the gut by stimulation of non-adrenergic nerve fibers in the periarterial nerve plexus. No evidence bearing on this possibility is available[9].

Resume. La stimulation électrique du plexus nerveux périartérial mésentérique provoque une vasodilatation résistante à l'atropine de la couche vasculaire mésentérique chez le chat anesthésié après blocage des neurones adrénergiques.

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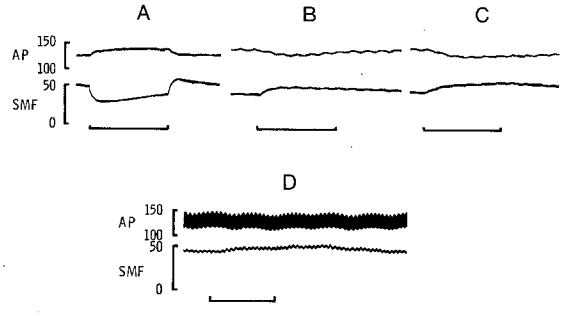

Effects of mesenteric periarterial nerve stimulation (10 v, 2 ms, 10/s) on arterial pressure (AP, mm Hg) and superior mesenteric arterial flow (SMF, ml/min), A) no drugs; B) after bretylium tosylate 30 mg infused into the superior mesenteric artery; C) same as B) but i.v. atropine 0.5 mg/kg also given; D) after chronic pre-treatment with 6-hydroxydopamine. The bars under panels A), B), C) indicate a period of 3 min stimulation and the bar under panel D) indicates 2.5 min stimulation.

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Histamine Sensitizing Activity of Lentinan, an Antitumour Polysaccharide

Lentinan, a β-(1 → 3) glucan obtained from *Lentinus edodes*, an edible mushroom, exhibits an excellent antitumour activity against Sarcoma 180 of mice[1,2]. As one of new biological properties of this substance, we found that lentinan was able to increase the susceptibility of the mice to histamine. The finding caused us to investigate the histamine sensitizing (HS) activity of lentinan.

Lentinan was administered i.p. in the total amounts of 100 to 500 μg fractionated for several days to the female 5-week-old mice (ddY strain). Three or 4 days after the last administration of lentinan, the mice were treated with the i.p. injection of 6 mg histamine (as histamine dihydrochloride, Sigma Co.) and 2 h later the death of the mice was observed. As shown in Table I, a number of dead mice were observed in the lentinan-histamine treatment group, but not in both control groups treated only with lentinan or histamine. The mortality of mice due to lentinan-histamine treatment was rather irregular. The