The effect of 5 μM lanthanum on calcium uptake and on the restoration of contractile force in calcium depleted hearts

	Control (5)		Lanthanum (5)	
	Ca_1	Ca_2	Ca_1	Ca_2
$T_1/_2$ (sec)	5.6 ± 1.7[a]	46.2 ± 6.2	—	33.4 ± 7.9
Calcium content (mEq/kg tissue wet wt.)	0.92 ± 0.13	2.87 ± 0.33	—	3.96 ± 0.38[b]
Contractile force (g)	19.1 ± 3.1		0	

Figures in parentheses indicate the number of hearts. [a] Mean ± S.E. [b] Differs significantly from control ($P < 0.05$).

proached a steady state at approximately the same rate[2], the calcium taken up probably entered the same pool, Ca_2. Thus, on the basis of this criterion, Ca_1 was absent in the calcium uptake curve in lanthanum treated hearts. The quantity of calcium taken up by Ca_2 during reperfusion in the presence of 5 μM lanthanum was greater ($P < 0.05$) than the quntitiy of calcium taken up by Ca_2 alone, but was not significantly different ($P > 0.05$) from the total quantity of calcium (Ca_1 + Ca_2) by the control hearts.

It can be concluded from these results that 5 μM lanthanum blocked the uptake of calcium by Ca_1 but not by Ca_2, and moreover, when calcium uptake into Ca_1 was blocked, contractile force was not restored even though significantly more calcium was taken up by Ca_2. Since this concentration of lanthanum has been shown to have little or no effect on electrical activity in the myocardium[3], these results indicate that there are at least 2 pools of calcium involved in the process coupling excitation to contraction in the heart. First, a compartment which we have identified as Ca_2, and have shown to be necessary, but not sufficient by itself, to maintain contractile force.

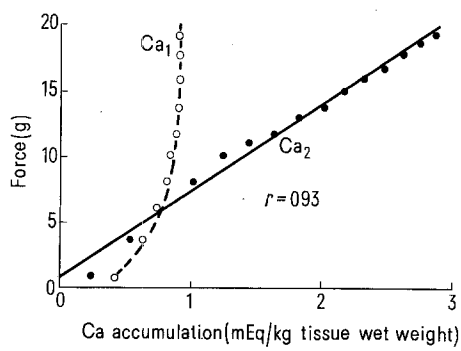

Fig. 2. The relationship between the accumulation of calcium during reperfusion by Ca_1 and Ca_2 and the restoration of contractile force. The mean coefficient of correlation, r, between the accumulation of calcium by Ca_2 and restoration of contractile force for the 5 hearts was 0.93.

Second, a smaller calcium compartment, Ca_1, whose calcium content was not related directly to the restoration of contractile force, but which was absolutely essential to the coupling process in cardiac muscle. One possible interpretation of these results is that the calcium contained in Ca_1 in some way mediates the release of calcium from Ca_2 which in turn activates the contractile mechanism. A mechanism similar to this has been proposed for skeletal muscle where it has been shown that the release of activator calcium from the sarcoplasmic reticulum of skinned skeletal muscle fibres is a regenerative process initiated by free calcium in the bathing solution[5,6]. Presumably the free ion represents calcium liberated from the sarcolemma and transverse tubular system by depolarization of the cell. According to this hypothesis, the free calcium then 'triggers' the release of reticular calcium to activate the contractile mechanism[7]. However, one can only conclude from the present results that the 2 calcium pools, Ca_1 and Ca_2, are both intimately involved in the coupling process in the heart and that their roles in this system are different.

Zusammenfassung. Es wird angenommen, dass mindestens zwei Fraktionen von intrazellulärem Kalzium am Kupplungsprozess zwischen Reizung und Kontraktion des Herzens beteiligt sind.

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Neurohumoral Regulation of Motility and Blood Flow in the Colon

The extrinsic nervous control of colonic motility and blood flow has recently been studied[1]. Electrical stimulation and reflex activation of the pelvic nerves produce an intense flushing of the mucosa in the distal two thirds of the colon. Corresponding in time with this mucosal flush there is a marked but transient increase of venous outflow and concomitantly with the vasodilatation a mucoid secretion. Intravenous administration of atropine (1 mg/kg) did not significantly interfere with the vasodilation and the motility response indicating that both might be

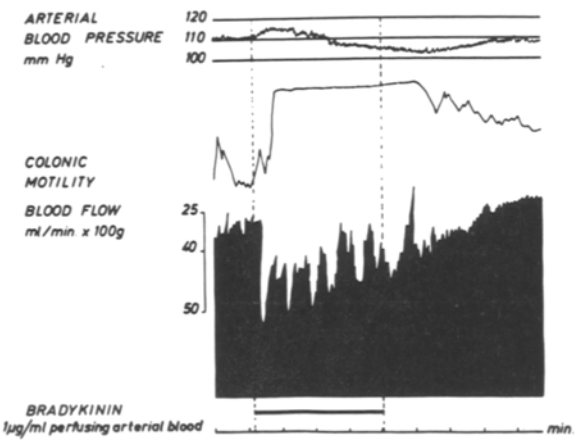

Fig. 1. The effect of supramaximal, intraarterial doses of bradykinin (left panel) and supramaximal pelvic nerve stimulation (right panel). Note the almost identical responses.

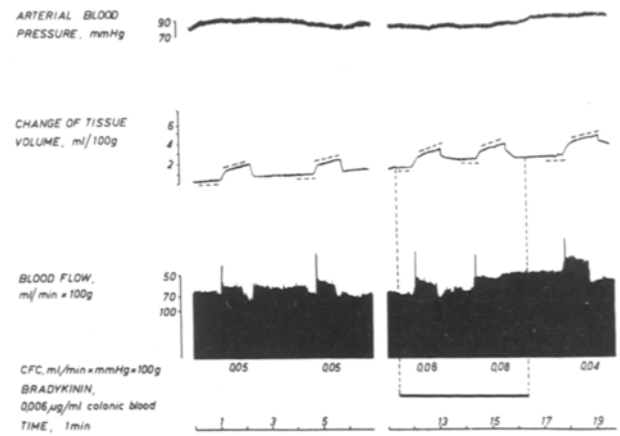

Fig. 2. The effect of subthreshold doses of bradykinin (left panel) and subthreshold stimulation of the pelvic nerves (right panel) on colonic blood flow, tissue volume and the capillary filtration coefficient (CFC). Note the almost identical responses.

brought about by a non-cholinergic mechanism largely secondary to an augmented secretion. The release of kinin-like substances similar to those involved in the atropine-resistant vasodilatation in the salivary glands and the pancreas[2,3] is suggested.

In the present study the effects of bradykinin and pelvic nerve stimulation on colon motility and blood flow were compared in an attempt to obtain evidence for bradykinin as a possible mediator in the pelvic nerve response.

Methods. By recording tissue volume and total venous effluent simultaneously, the resistance, the capacitance and the precapillary sphincter segments of the circulation of the cat colon were studied. This pletysmographic method was described in detail in a previous work[1]. In some experiments colonic motility and blood flow were recorded simultaneously. Motility was recorded by a volumetric method keeping intra-colonic pressure constant at about 10 cm H_2O. The pelvic nerves to the colon were cut centrally and mounted on ringformed electrodes for subsequent graded electrical stimulation. Synthetic bradykinin was administered close-intra-arterially.

Results. As is shown in Figure 1, close intraarterial infusion of bradykinin in a large dose (1 µg/ml) produced a marked and shortlasting blood flow increase and concomitantly a sustained and powerful motor contraction (left panel), an effect which is in many respects similar to that produced by efferent electrical stimulation of the pelvic nerves (right panel). Close intraarterial infusion of bradykinin in low doses (0.006 µg/ml) decreased vascular resistance only moderately, while the capillary filtration coefficient (CFC) increased considerably. As is shown in Figure 2 (left panel), a marked increase in CFC occurred following infusion of bradykinin in doses that did not affect blood flow at all. When the pelvic nerves were stimulated at high rates, the motor response interfered with the tissue volume recordings and made CFC determiations impossible. On the other hand, pelvic nerve stimulation at a low rate which did not affect motility or blood flow resistance nevertheless increased CFC to a considerable extent, Figure 2 (right panel).

Discussion. Specific vasodilator fibres were previously assumed to be widely distributed throughout the gastrointestinal tract. In recent years this concept has changed, however, and it has been suggested that neurogenous vasodilatation, which occurs only in certain restricted parts of the gastrointestinal tract, i.e., the salivary gland, the pancreas and probably the stomach, is partly or mainly caused by the release of a stable vasodilator material, a plasmakinin[2-5]. The present results indicate that a similar mechanism might be involved, even in the regulation of colon blood flow and secretion.

The vasodilatation and the concomitant motor response following pelvic nerve stimulation are largely atropine-resistant. This coupled response is closely mimicked by infusion of bradykinin. Following infusion of subthreshold doses of bradykinin as well as after pelvic nerve stimulation at a frequency that did not affect motility or resting blood flow, CFC increased considerably. The magnificant increase in CFC which occurred despite unchanged blood flow might therefore be due to increased capillary permeability. CFC often reached figures comparable to those commonly recorded when the vascular bed is brought to maximal dilatation by an unspecific vasodilator drug.

Zusammenfassung. Indiz, dass Plasma-Kinin sowohl in den Regulationsmechanismus der Kolon-Motilität als auch der Blutströmung eingreift.

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