(Figure 3). At small distending fluid volumes (1 to 4 ml), the sino-atrial conduction increased while at high distending volumes (5 to 8 ml) atrioventricular complex decreased. Release of distension by cutting open the pericardium reversed the chronotropic (Figure 1 B) and electrical (Figure 3) changes, i.e. the heart rate, voltage of ventricular complex and conduction changes tended to return to control values and arrhythmia tended to disappear.

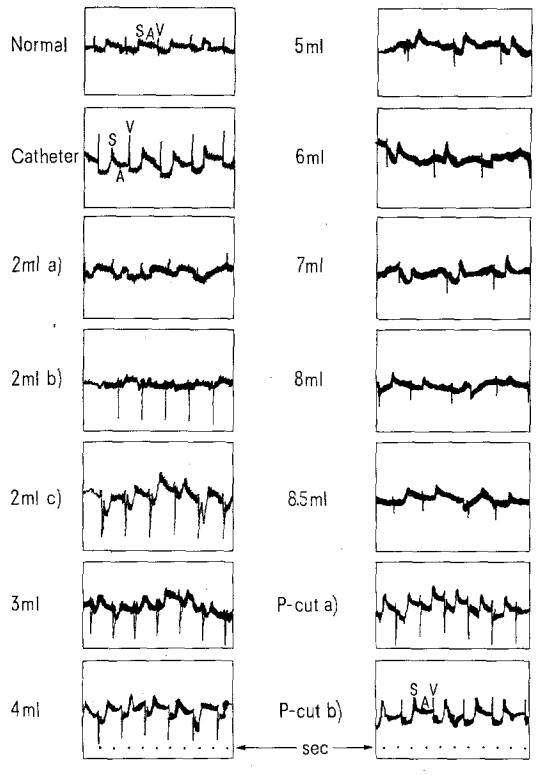

Fig. 3. Electrocardiographic changes with pericardial distension. Slight acceleration occurred when catheter was placed in the pericardium. Acceleration increased with increasing fluid volume in the pericardium upto 4 ml. Injection of more fluid caused bradycardia. S, A, V, sinus, atrial and ventricular complexes. S-A conduction increased upto 4 ml and both S-A and A-V conduction increased at 5, 6 and 7 ml. At 8 and 8.5 ml bifocal sinus discharge, arrhythmia and reduced voltage of ventricular complexes are seen. Immediately after cutting open the pericardium, rebound acceleration occurred with reversion of conduction changes and arrhythmia (P-cut, a). The rate and direction of ventricular complex reverted towards controls 10 min afterwards (P-cut, b).

The chronotropic changes in heart rate and impulse parameters due to distension were also reversed by sucking the fluid out of the pericardial sac into the syringe. Injection of air into the pericardial cavity produced changes similar to those observed by injecting Ringer's solution, and these changes were reversed by suction of air back into the syringe. The pericardium usually gave way or ruptured when 6 to 8 ml of fluid had been injected. On an average, with graded increase in fluid volume upto 5 ml the pericardial pressure rose slowly to 6–8 mm Hg. After this even small increments caused a very steep rise in the pericardial pressure to 15–25 mm Hg or more.

Discussion. The thin pericardial sac of frog heart can accommodate 6 to 8 ml of fluid. Compression of sinus venosus would alter the dimensions and configuration of pacemaking cells. It has already been shown that intraluminal pressure-stretch alters pacemaker frequency (PATHAK[1–3, 6, 7]). The present work demonstrates that extramural stretch due to pericardial distension also changes the pacemaker response. It is of interest to note that, in the hearts showing initial acceleration followed by deceleration, the pattern of chronotropic responce due to pericardial distension observed during the present work, is similar to that observed previously by intraluminal distension (PATHAK[1–3, 6, 7]). These investigations support the view that mechanical stretch of pacemaker from within or from without alters the impulse frequency and determines the chronotropic response of the heart. Moderate distension of pericardium is associated with cardio-acceleration. Relaxation of pacemaker due to compression and altered anatomy of other chambers and/or overstretch of the pacemaker appear to be responsible for bradycardia, conduction changes, atrioventricular block and arrhythmia observed at high distending fluid volumes.

Résumé. On a démontré que la distension péricardiale produit des changements chronotropiques dans le cœur de grenouille isolé en perfusion. Sur 26 cœurs, l'accélération cardiaque (18 a 148%) se produit dans 12 avec un volume de fluide péricardique atteignant 4 ml. Dans les 14 cœurs restant nous avons observé une bradycardie, des irrégularities de conduction, un blocage cardiaque et une arythmie. On en conclut que ces effects chronotropiques et les variations du paramètre d'impulsion sont dues aux changements dans l'activité du «pacemaker».

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The Effect of the Gastrointestinal Hormones on Small Intestinal Motility and Blood Flow

Recent studies give evidence that gastrin, cholecystokinin and secretin might be involved in the regulation of intestinal motility and blood flow, both in animals and in man[1–3]. Whether these effects are brought about by a direct influence on the smooth intestinal and vascular muscles, or might largely be secondary to the release of intermediary substances, is still, however, a matter of dispute. The aim of the present investigation was therefore to study in more detail the effect of graded intra-arterial infusion of the gastrointestinal hormones on the small intestinal motility and blood flow.

Methods. Experiments were performed on anaestetized cats weighing 2.5–5.2 kg and fasted for 24 h. A femoral artery was connected to a mercury manometer for recording of arterial blood pressure. The abdomen was opened along the midline and the greater omentum and the spleen were extirpated. A small intestinal segment weighing 10–20 g was isolated and the remaining parts of the intestine were extirpated. The adrenals were excluded from the circulation by encircling ligatures. The splanchnic nerves were cut just beneath the diaphragm.

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Recordings of motility. Intestinal motility was studied by a volume recording device. The distal end of the intestinal segment was connected to a plastic tube in turn connected by a rubber tubing to a pressure reservoir of wide dimensions. The system was filled with bodywarm 0.9% saline. By means of such an arrangement the intraluminal pressure could be kept constant at about 10 cm H_2O despite wide variations in volume. The pressure reservoir was coupled to a piston recorder operating on a kymograph.

Recording of blood flow. To measure quantitatively the overall intestinal blood supply, the total superior mesenteric arterial inflow was recorded. For this purpose, a wide bore polyethylene tube was inserted in the carotid artery and the blood flow diverted to a closed perspex drop chamber filled with silicone oil, in turn connected to the proximal end of the centrally cut superior mesenteric artery. By using siliconized tubes of wide dimensions and of short length, the resistance of this device was kept minimal.

Administration of drugs. Secretin and cholecystokinin-pancreozymin (CCK) were obtained from the Gastrointestinal Hormone Laboratory, Karolinska institutet, Sweden. Solutions were prepared in isotonic NaCl just before use. Pentagastrin (Pentavlon) was obtained from Scanmeda. The hormones were administrated close intra-arterially utilizing an automatic pump. Atropine, when used, was given i.v. in a dose of 1 mg/kg.

Results. 1. Pentagastrin. As shown in Figure 1 (left panel), close intra-arterial infusion of pentagastrin in a dose of about 3 µg/kg/min evoked a slow tonic and sustained contraction in the small intestine. Concomitantly there was also a significant and immediate decrease of vascular resistance, which was only transient, however. The peak flow, corresponding to at the most a 50% increase, vanished despite continuous infusion. After atropine (Figure 1, right panel) there was sometimes a delayed and markedly reduced motor contraction, but in most experiments the motor response was completely abolished. The blood flow increase was often more pronounced and sustained, however, but even on high doses of pentagastrin blood flow increase did not exceed 150%.

2. CCK. As shown in Figure 2 (left panel), intra-arterial infusion of CCK evoked a strong and sustained tonic intestinal contraction and an immediate but shortlasting increase of blood flow. The motorcontraction remained several min after cessation of the infusion. The blood flow increase, on the other hand, vanished within $^1/_2$ min and was then considerably decreased before returning to resting level. Atropine abolished the motor contraction completely (right panel). The decrease of vascular resistance was now well sustained, however, and the blood flow did not reach resting level until several min after cessation of the infusion. The maximal peak response corresponded to about 150% increase of blood flow.

3. Secretin. Secretin had no effect whatsoever on small intestinal motility. As shown in Figure 3, there was a significant increase of blood flow, however. This blood flow increase was immediate and returned to resting level on cessation of the infusion. The maximal increase amounted to about 150%.

Discussion. Both gastrin and CCK induce a motor contraction in the small intestine. The motor response was abolished after atropine treatment, however, indicating that the hormones probably exert their effects on the intestinal smooth muscles indirectly involving some cholinergic neuronal pathway. This is in accordance with HEDNER et al[2], who suggested that the effect of CCK on

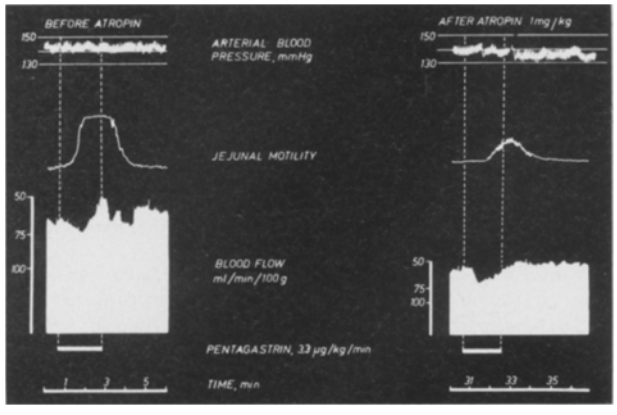

Fig. 1. The effect of pentagastrin on small intestinal motility and blood flow. Note the tonic contraction and phasic reduction of blood flow (left panel) and the sustained blood flow increase after atropine when the motor response is virtually absent (right panel).

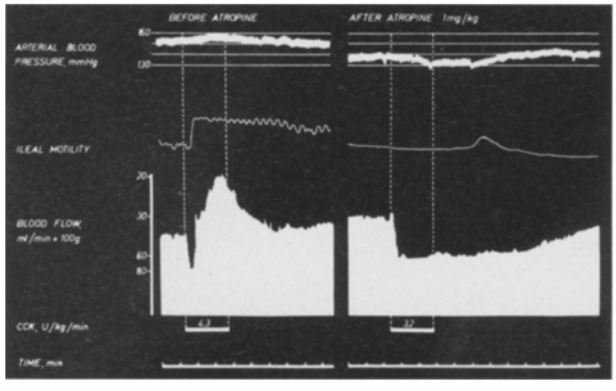

Fig. 2. The effect of CCK on small intestinal motility and blood flow. There is a sustained tonic contraction which declines over several min after cessation of the infusion (left panel). The initial blood flow increase is followed by a phasic decrease. After atropine (right panel) the motor response is abolished. Note the prolonged effect on blood flow.

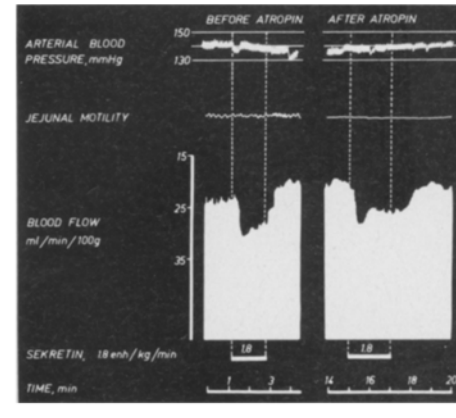

Fig. 3. The effect of secretin on small intestinal motility and blood flow. Note the immediate increase of blood flow, whereas the motility is unaffected.

intestinal motility is probably brought about by a secondary release of 5-HT.

Secretin had no effect on small intestinal motility. This is in contrast to many recent observations[3] where secretin was often shown to inhibit intestinal motility. Secretin is structurally strikingly similar to glucagon and might therefore have certain similar functional activities. It has been shown previously[4] that the pronounced intestinal inhibition evoked by glucagon is in fact induced by a secondary release of catecholamines from the adrenal medullae. In the present experiments, the catecholamines secretion from the adrenals, known to interfere considerably with intestinal motility, had however, been removed, which might explain the diverging results in this respect.

Gastrin, CCK and secretin caused a significant increase of the regional blood flow. Insofar as gastrin and CCK are concerned, this response was however only transient. After atropine, which abolished the motor response, the blood flow was well sustained and often more pronounced. It appears, therefore, most likely that the tonic contraction on higher concentration might interfere mechanically with the intramural blood flow.

Gastrin, CCK and secretin increased blood flow about 150% at the most. This is a very moderate effect, particularly as compared with the maximal blood flow figures of about 250 ml/min × 100 g tissue recorded when the vascular bed is brought to maximal relaxation by means of supramaximal amounts of isoprenaline. The moderate blood flow increase evoked by the gastrointestinal hormones might be secondary to their metabolic effects on the intestinal glandular tissue, in turn due to the release of vasoactive intermediary substances. This is in accordance with BIBER et al[5], who showed evidence that the 5-HT and α-receptor antagonist dihydroergotamine abolished the blood flow responses to CCK and secretin.

Conclusion. Pentagastrin, CCK and secretin evoke a moderate increase of intestinal blood flow in the cat. Since the tonic contraction interferes mechanically with the blood flow, the increase is only transient following pentagastrin and CCK. After secretin, however, which has no effect on motility, the blood flow increase is sustained.

Zusammenfassung. Nachweis, dass Pentagastrin und CCK, in physiologischen Dosen bei der Katze infundiert, nur geringfügige Durchblutungseffekte im Dünndarmgebiet zeigen, während Sekretin über einen offenbar verschiedenen Mechanismus die Durchblutung erhöht.

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The Effects of Glycine on the Rabbit Retina: Averaged ERG and Averaged Visual Evoked Responses

Evidence exists that glycine can act as an inhibitory neurotransmitter in the central nervous system[1–6]. The retina is the first structure in which the general morphology became known of the neurons putatively operating with glycine as a neurotransmitter. EHINGER and FALCK[7,8] showed in the rabbit retina that the glycine uptake was localized in the neurons and not in the glia. BRUUN and EHINGER[1] showed the characteristics of the glycine uptake into the retinal neurons in in vitro incubation. The uptake mechanism for glycine seems to be specific for retinal neurons. The autoradiographic studies showed that there was a significant accumulation of radioactivity only in certain cells, mainly in the amacrine cells, and diffusely in the inner plexiform layer. Radioactivity was also seen in the ganglion cells, but clearly less than in the amacrine cells. There was very little uptake into other cells, glia included[1].

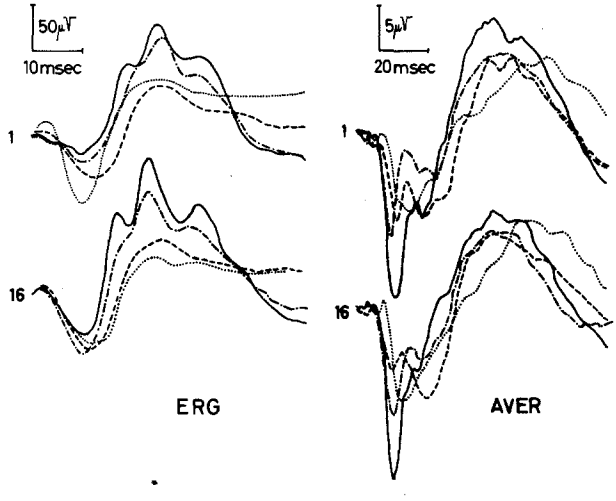

Fig. 1. Simultaneously recorded averaged ERG (left) and averaged VER (right) at different intensities (1: upper, and 16: lower), with a frequency of 1 Hz. Normal ERG and normal AVER. The progressive effect of 0.005 g of glycine after 10 min, 1½ h, and 4 h. Abolition of the ERG's oscillatory potentials and depression of the early components of the the AVER (Rabbit Nr. 70). —, normal; ·-·-·, 10 min; ----, 90 min; ·····, 4 h.

Material and methods. The experiments were carried out on both eyes of six unanesthetised rabbits (i.e. 12 eyes). Averaged photopic ERG and AVER were performed and analysed as previously described (STANGOS[9], KOROL[10]). Glycine 0.005 g was injected into the vitreous body of 10 eyes and 0.002 g into 2 eyes.

The following results have been found (Figure 1 and 2): ERG (Averaged Electroretinogram). 1. A total suppression of the oscillatory potentials (OP) 30 min after the injection of 0.005 g and 90 min after the injection of 0.002 g). 2. The third OP starts to disappear, then the first OP and lastly

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