The effect of TK174 on sympathetic nerve stimulation was tested on the guinea-pig isolated hypogastric nerve-vas deferens preparation[2]. Contractions were markedly increased by $5.0 \cdot 10^{-6}$ g/ml concentrations of both TK174 and cocaine, while those induced by direct muscular stimulation of the organ remained uninfluenced. Thus the effect of TK174 seems to be elicited specifically on the sympathetic nerve endings. This view is further supported by the fact that pressor responses of spinal cat preparations to vasopressin, which contracts vascular smooth muscle independently from sympathetic receptors[3], also failed to be increased significantly by 2.5 mg/kg of TK174 (Table I).

There are, however, exceptions to the potentiation of noradrenalin effects by TK174, inasmuch as direct cardiac actions such as the positive chronotropic action of noradrenalin failed to be enhanced by $5.0 \cdot 10^{-6}$ g/ml of TK174, a concentration highly effective in other tests mentioned.

The actions of tyramine, an indirectly acting sympathomimetic agent[4], are inhibited by TK174. This was demonstrated on pressor responses to this amine of rats under thiobarbiturate anaesthesia (Table I). From this point of view TK174 is also similar to cocaine[5].

The results obtained in our experiments suggest that the site of action of TK174 should be searched for in the peripheral sympathetic nerve endings supplying different organs, first of all those containing smooth muscle.

Table II. Effects of TK 174 and cocaine on guinea-pig isolated vas deferens preparations

A) Chemical stimulation by noradrenalin

Concentration of noradrenalin	No. of experiments	Contractions[a] recorded in the presence of		
		No other drug	TK 174 ($2.0 \cdot 10^{-7}$)	Cocaine ($2.0 \cdot 10^{-7}$)
$5.0 \cdot 10^{-7}$	6	3.2 ± 1.0	33.5 ± 14.5	14.8 ± 2.0
$2.0 \cdot 10^{-6}$	6	26.3 ± 2.8	100.3 ± 8.3	49.5 ± 5.2

(B) Electrical stimulation of the hypogastric nerve-vas deferens preparation

Drug to be tested	No. of experiments	Art of stimulation	Contractions[a] recorded	
			Before addition of the drug to be tested	After
TK 174 ($5.0 \cdot 10^{-6}$)	8	Muscular	22.9 ± 2.7	27.8 ± 2.1
		Neural	23.6 ± 4.4	44.1 ± 4.4
Cocaine ($5.0 \cdot 10^{-6}$)	6	Muscular	23.8 ± 5.3	23.1 ± 6.5
		Neural	18.8 ± 5.5	32.1 ± 6.0

[a] in mm; mean values $\pm$ S.E.

Résumé. Par le composé 1,1-*bis*-(4-amino-phényl)-propyl-(3)-amine (TK174), de même que par la cocaïne, les actions de la noradrénaline sont considérablement augmentées tandis que celles de la tyramine sont bloquées. Les autres effets pharmacodynamiques de la cocaïne ne sont pas produits par TK174.

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Effect of Secretin on Bicarbonate Secretion in Fluid Perfusing the Rat Ileum

Intravenous secretin increases the rate of bicarbonate secretion in both bile and pancreatic juice. Bicarbonate secretion also occurs in the rat ileum and colon[1]. The common embryologic origin of the liver, pancreas, and intestine suggested that secretin might also influence bicarbonate secretion in fluid perfusing the rat ileum. This study reports the effect of secretin on bicarbonate secretion and the net transport of sodium, potassium and chloride in the rat ileum.

Method. Sprague-Dawley rats of either sex, weighing 350–450 g, were anesthetized with 0.7 ml/kg of Dial-Urethane given i.p., and a femoral vein was cannulated for injections. The terminal 25 cm of the small intestine was cannulated at both ends, washed with 40 ml of perfusion fluid at a pressure of less than 10 cm of saline, and flushed with air. There followed two 30 min perfusion periods in which 8 ml of fluid was circulated from a reservoir at a rate of 2 ml/min with a Bowman pump (Process and Instruments Company, Brooklyn, New York). At the end of each period, the contents of the ileum and tubing were collected in the reservoir. After the first collection period, the system was washed for 5 min with fresh perfusion fluid and flushed with air. For the second period, 8 ml of fresh perfusion fluid was added to the system. 5 min after the start of each period, 2 ml of fluid was removed from the reservoir for determination of 'initial concentration' and was replaced with 2 ml of fresh perfusion fluid. 'Final concentration' was determined using the fluid collected in the reservoir at the end of each period. The perfusion fluid contained: NaCl 102.8 m*M*/l, KCl 4.7 m*M*/l, KH_2PO_4 0.8 m*M*/l, $NaHCO_3$ 28.2 m*M*/l,

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$MgCl_2 \cdot H_2O$ 1.2 mM/l, glucose 16.7 mM/l, and polyethylene glycol (PEG) 2 g/l.

The effect of i.v. secretin was determined by comparing the net electrolyte fluxes in the period following secretin (Boots Pure Drug Company, London) with those in the alternate period following i.v. saline. In Group I ($n = 5$), saline was injected 5 min after the start of the first perfusion period and secretin was injected 5 min after the start of the second. In Group II ($n = 5$), injections were given in the reverse order.

The net fluxes of sodium, potassium, chloride and bicarbonate were calculated as follows:

$$\text{ion flux} = \text{initial volume} \left(\text{final ion conc.} \frac{\text{initial PEG conc.}}{\text{final PEG conc.}} - \text{initial ion conc.} \right)$$

The sign of the flux denotes movement into (+) or out of (−) the perfusion fluid.

Statistical significance was assessed with a t-test for paired samples.

Results and discussion. The Table summarizes the mean net fluxes of bicarbonate, chloride, sodium and potassium that were measured after administration of saline and secretin. Large single doses of secretin failed to cause a significant change in the flux of any of the ions. Because a dose of 5 U elicits a near-maximal response in secretory rate from the rat pancreas[2], it was considered a stimulus sufficient to determine whether secretin affected intestinal bicarbonate secretion. The biologic effects of a single submaximal dose of secretin in the rat, as determined by its pancreatic exocrine activity, are maximal within 20 min and minimal after 30 min[2], so the period of observation used in this study should have detected any measurable change. There is little reason to doubt the activity of the preparation since vials from the same batch used in clinical studies elicited normal responses in humans.

Ion	Mean net flux (μEq)		S.E.	P
	Saline	Secretin		
HCO_3^-	+ 60.7	+ 55.9	3.44	> 0.10
Cl^-	− 190	− 173	15.3	> 0.10
Na^+	− 115	− 117	20.6	> 0.90
K^+	− 1.45	− 1.93	0.614	> 0.40

The Table compares the net fluxes of HCO_3^-, Cl^-, Na^+ and K^+ into (+) and out of (−) the fluid perfusing the ileum in 10 rats. The standard error (S.E.) and P-value are shown. (Student t-test.)

Conclusion. Single large i.v. doses of secretin failed to influence the net fluxes of bicarbonate, chloride, sodium or potassium in fluid perfusing the ileum of the rat. The results suggest that bicarbonate secretion in the ileum is controlled by a mechanism which differs from that of the pancreas and biliary tree.

Zusammenfassung. Es wird gefunden, dass einmalige, grosse i.v. Dosen von Sekretin keinen Einfluss auf den Netto-Flux von Bikarbonat, Chlorid, Natrium und Kalium in der Perfusionsflüssigkeit des Ileums der Ratte ausüben: offenbar ist der Kontrollmechanismus der Bikarbonatsekretion im Ileum von dem in Pankreas und Leber verschieden.

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Improved Impregnation of Degenerating Boutons in NAUTA-LAIDLAW Preparations

It is a well-known fact that the NAUTA method is not well suited for the demonstration of terminal boutons. It may well impregnate such structures[1], but the occurrence of impregnated particles, which for various reasons can be classified as degenerating boutons, seems to be rare.

In a preparatory NAUTA study on the spinal cord in the cat, in which we made use of that modification of the NAUTA method which incorporates the Laidlaw solution[2], we replaced the perfusion method of KOENIG, GROAT and WINDLE[3] with the method of HOLT and HICKS[4] which we have used for an electron microscopic study[5]. However we used 5% sucrose instead of 7.5%. We were struck by the presence of a great number of structures interpreted as degenerating boutons. Therefore we undertook a series of experiments with the methods of KOENIG, GROAT and WINDLE and HOLT and HICKS, respectively. In 1 of the 2 solutions, according to HOLT and HICKS, the pH of the solution was buffered to 5.5. The pH of the solutions of KOENIG, GROAT and WINDLE was 4.2. The dorsal part of the lateral funiculus was cut on the left side in the first lumbar segment in 4 cats. This cut interrupted spinal afferents to the lateral cervical nucleus[6] and fibres in the dorsal spinocerebellar tract[7]. After 6 days' survival, the animals were perfused with one of the solutions. The central nervous system (including the upper cervical region and the cerebellum), and also the lesion of the 4 cats were immediately dissected and 3 of

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