therefore similar to the responses stimulated by OP-CCK and related peptides in the rat[7] and dog[8].

The actions of VIP and secretin on pancreatic secretion in the rat are shown in Figure 2. It is apparent that porcine secretin evoked dose-related increases in the flow of pancreatic juice at doses which were approximately 50 times less than those active in turkeys. In contrast VIP, in doses 20 times greater than those administered to the turkey, evoked only small increases in the flow of juice, although these were significantly greater than do basal levels ($P < 0.05$). However it is obvious from Figure 2 that the responses to VIP in the rat were not dose-related so that a precise estimate of the relative potency of secretin and VIP in this species cannot be made.

The action of peptides on the rate of flow and protein secretion from the turkey pancreas

Peptide	Rate of flow (µl/g gland. 10 min)	Rate of protein secretion (mg/g gland. 10 min)
Basal secretion	12.1 ± 2.0	0.31 ± 0.02
Porcine secretin (5 µg/kg)	23.1 ± 5.8[a]	0.76 ± 0.25[a]
OP-CCK (0.5 µg/kg)	28.7 ± 7.2[a]	6.5 ± 1.6[a]
Porcine/bovine glucagon (200 µg/kg)	9.9 ± 1.8	0.30 ± 0.17

The peptides were administered i.v., in random order, to each of 5 turkeys. The response was taken as the rate of flow and protein secretion which occurred in the 10 min period immediately after the injections. At least 30 min was allowed to elapse between injections. Values are means ± S.E.M., [a]denotes values significantly different from basal ($p < 0.01$).

It is clear from these results that VIP was a strong stimulant of the flow of pancreatic juice in the turkey, but not in the rat or cat[2]. The strong action of VIP on the avian pancreas indicates that in one respect at least this peptide resembles avian secretin more closely than either porcine secretin or glucagon. Although there have been several discussions recently about the evolutionary significance of similarities in the aminoacid sequences of mammalian secretin, glucagon, VIP and various other peptides[9–11], relatively little is understood of the phylogenetic relationships between these molecules. The results presented here raise the possibility that VIP and avian secretin may have inherited from a common ancestor features which are not present in modern mammalian secretin and glucagon[12].

Zusammenfassung. Das vasodilatierende intestinale Peptid vom Schwein hat beim Truthahn, nicht aber bei der Ratte, eine starke pankreassekretionfördernde Wirkung. Somit besteht beim Vogelsekretin Verwandtschaft bezüglich Wirkung und unterscheidet sich dadurch vom Schweinesekretin oder vom Glucagon.

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Starvation and Gastrin Storage in the Pyloric Antral Mucosa of Male Rabbits

The second gastrointestinal hormone, gastrin, was discovered by Edkins[1] and it has since engaged the attention of many workers. So far, the natural form of forms in which gastrin exist in the pyloric mucosa and in circulation are unknown. The mode of synthesis, the factors controlling the rate of synthesis, and even the storage of gastrin in the pyloric mucosa are still not known. This work was done to determine the effect of starvation on gastrin storage and activity in the pyloric mucosa of male rabbits.

Materials and methods. Thirty-six 6 – $6^1/_2$-month-old male rabbits weighing between 2.3 – 2.5 kg were used for the experiments. 9 of the rabbits were taken out during feeding, weighed and then killed, while feeding was discontinued for the remaining 27 rabbits. Blood was collected from each of the killed rabbits and the blood glucose content was determined separately by the glucose oxidase method using *O*-dianisidine[2]. The stomachs and the livers of the rabbits were immediately removed. The livers were weighed, while the stomachs were cut open, washed clean with water, and the pyloric antrum cut out. The pyloric mucosa was scraped off carefully from the underlying musculature. The pyloric mucosae from the 9 stomachs were divided into 3 batches, each containing pyloric mucosae from 3 stomachs. These were then separately weighed and subjected to the gastrin extraction procedure described by Blair, Harper, Lake, Reed and Scratcherd[3].

12 h after last contact with food but with free supply of water, 9 other rabbits were weighed, killed and the blood, livers and stomachs treated as in the first group. 36 h after last contact with food but with free supply of water, 9 other rabbits were treated as in the first 2 groups. 72 h after last contact with food but also with free supply of water, the remaining 9 rabbits were weighed killed and treated as in the first 3 groups of rabbits. The extracts obtained from the 4 groups of male rabbits were dried and the quantity of powdered extract per gramme wet weight of the different pyloric mucosa was determined. Solutions of known concentrations of the extracts were prepared using normal saline (0.15 *M*) as solvent.

Assay of the mucosal extracts. The continuous stomach perfusion technique described by Ghosh and Schild[4] was modified for the assay. Male Wistar strain rats weighing between 180–210 g were used. The rats were anaesthetised with urethane in 25% w/v solution given i.p. at 0.6 ml/100 g body weight. The operative procedures on the rats were similar to those described by Ghosh and Schild[4] but the femoral vein was cannulated

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Some of the results obtained in the 4 types of male rabbits used.

Type of male rabbit	Crude gastrin extract in mg/gm pyloric mucosa	Gastrin activity expressed as synthetic human gastrin I equivalent in ng/mg crude extract	Blood glucose level in mg/100 ml blood	Weight of liver in g/kg body wt.
9 Unstarved rabbits	13.26 ± 0.92	56.12 ± 0.94	40.25 ± 2.65	32.85 ± 2.03
9 rabbits starved for 12 h but supplied water	16.52 ± 0.83	56.05 ± 0.83	38.75 ± 2.54	32.51 ± 1.92
9 rabbits starved for 36 h but supplied water	13.75 ± 0.75	55.52 ± 0.75	36.24 ± 2.15	28.25 ± 2.21
9 rabbits starved for 72 h but supplied water	11.46 ± 0.94	55.85 ± 0.68	30.65 ± 3.02	21.35 ± 1.78

for injection of solutions. The stomachs of the rats were perfused with normal saline (0.15 M) warmed to the rat's body temperature and the flow rate of the perfusate into the stomach was adjusted to give an effluent volume of 1 ± 0.1 ml/min. The effluent was collected at 10 min intervals and titrated to pH 8.8 with the Automatic Titrator (Radiometer Copenhagen) using a centinormal sodium hydroxide as the base. The above pH enabled the calculation of the total titratable acid in the collected effluent.

Doses graded from 62.5 µg to 1000 µg of the saline solutions of the pyloric extracts from the 4 sets of male rabbits and 15.75 ng to 63.0 ng of synthetic human gastrin I (SHGI) were injected i.v. through the femoral vein into the anaesthetised male rats. The mean rates of acid secretion in µEq/10 min to the injected doses of the stimulants were calculated according to the method of LAI[5]. Injected doses of the 4 types of pyloric extracts caused increased acid secretion. The log dose-response curves showed linear relationship for the 500 µg and 1000 µg of the saline solution of the pyloric mucosal extracts and 31.5 ng and 63.0 ng of the synthetic human gastrin I. These doses were then used for the 2+2 (4 dose) assay procedure.

The histamine contents of the crude pyloric extracts were determined using the isolated guinea-pig terminal ileum by the method of superfusion[6].

Results. The results are summarized in the Table. The crude gastrin extract per gramme wet weight of pyloric mucosa was highest in the 12 h starved rabbits, and the differences were significant when compared with values obtained in the rabbits killed during feeding, and those subjected to 36 h starvation, $P < 0.05 > 0.02$. The differences in the crude antral mucosal gastrin contents in the 12 h and 72 h starved rabbits gave $P < 0.01 > 0.002$.

There was no significant difference in the gastrin activity of the 4 types of pyloric extracts, $P > 0.10$. The mean histamine content of the 4 types of the crude gastrin extracts was 28.5 ± 1.25 ng/mg crude gastrin. The least secretorily active dose of histamine on the prepared rat stomach was found to be 8 µg histamine dihydrochloride. The minimum dose of the saline solution of the rabbit crude pyloric gastrin extract that elicited acid secretory response was 62.5 µg, which contained 1.78 ng histamine or $^1/_{5000}$ of the minimum dose of histamine dihydrochloride that elicited acid secretory response on the rat preparation. The blood glucose level in the rabbits killed during feeding gave the highest value. The differences in the values for both the 36 h and 72 h starved rabbits when compared with blood glucose value for the unstarved rabbits were significant $P < 0.01 > 0.002$ and $P < 0.001$ respectively.

The weight of the liver decreased as the length of starvation increased. The differences in liver weight in the unstarved and 36 h starved rabbits and also in the unstarved and 72 h starved rabbits were significant, $P < 0.001$. There was no significant difference in the liver weights of the unstarved and the 12 h starved rabbits.

Discussion. The above results raise a number of interesting questions. The lower value of crude gastrin content in the pyloric mucosa of rabbits killed during feeding may be due to increase gastrin release at that period caused by antral distension resulting from feeding. There is also the possibility that gastrin storage and probably synthesis occur best in the pyloric mucosa of rabbits about 12 h after the last contact with food, which in man would coincide with the post-absorptive phase. Also there is the possible suggestion that the rate of gastrin storage or synthesis, or both, decreases as the period of starvation increases to 36 h and 72 h, thereby diminishing the stored gastrin. No possible correlation could be made between the decreasing blood glucose level and the gastrin stored because even in rabbits starved for 12 h, which contained the highest crude gastrin content, the blood glucose level was less than in the unstarved rabbits. The gastrin activity of the 4 types of the crude extracts were not significantly different, indicating that the potency of the gastrin extract was not affected by starvation up to 72 h.

Résumé. Parmi les lapins mâles privés de nourriture pendant une période de 72 h au maximum, la quantité de gastrine brutte par gramme fut la plus élevée chez les sujets soumis à ce test pendant 12 h et la moins élevée chez ceux qui l'ont subit pendant 72 h au maximum. L'activité gastrique de l'extrait brut n'était pas affectée par la privation de nourriture et aucune corrélation ne put être établie entre le taux de la glucose sanguine et la gastrine accumulée chez les lapins affamés.

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