tractility, but their destruction or amine-depletion would remove a potentially important compensatory mechanism for augmentation of the myocardial force development and velocity of contraction in the failing heart[10,11]. In conclusion, preservation of the inbuilt intrinsic nervous apparatus of the heart should be taken into consideration in association with the problem of myocardial preservation.

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Intravenous injections of cholecystokinin and caerulein suppress food intake in domestic fowls

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Summary. As with various mammals, cholecystokinin (CCK) and caerulein have short-term, dose-related, inhibitory effects on feeding when injected i.v. in domestic fowls. It is estimated that in meals lasting more than about 6 min there could be time for ingested food to reach the duodenum and for the release of CCK to act as a satiety signal.

Cholecystokinin (CCK) is a polypeptide hormone which is released in the duodenum and jejunum upon entry of ingesta[2,3]. It causes contraction of the gall bladder, inhibits gastric emptying, stimulates pancreatic enzyme secretion and is also found in the brain[3,4]. It has a dose-related inhibitory effect on feeding when injected in various mammals[5-9] and has been proposed as a short-term physiological satiety signal[4]. There is evidence that it occurs in the brain and gut of birds[10,11], and porcine CCK stimulates pancreas activity in turkeys[12], but Snapir and Glick[13] were unable to demonstrate a significant reduction in intake in domestic fowls following i.p. injections of CCK and caerulein, a decapeptide chemically similar and with similar properties to CCK. However, they tested only 1 dose of CCK (20 Ivy dog units/kg b.wt) and 2 of caerulein (1 and 2 µg/kg), their samples were small and it is possible that i.p. injections are less effective with birds than mammals. We now report that CCK and caerulein suppress feeding in a dose-related manner when injected i.v. in domestic fowls.

Methods. For the CCK experiment 10 immature medium-hybrid hens (Rhode Island Red × Light Sussex) were housed and tested in individual cages on a 14-h photoperiod (07.00–21.00 h) and were given access to a commercial pelleted diet for 6 h/day (10.00–16.00 h), having been trained to this schedule for a week before testing started. They were tested for 5 weeks from 12 to 17 weeks of age, when their mean body weights increased from 1.46 ± 0.02 (SE) to 1.89 ± 0.04 kg. CCK has a half-life of only 2 or 3 min[14] and its effects are short-lived[5,7], so food consumption was measured in the periods 10.00–10.15 h and 10.15–16.00 h every day from Monday to Friday. At 10.00 h on Tuesdays and Thursdays each bird was injected by wing vein, immediately before receiving its food, with either 1, 5, 10, 20 or 40 Ivy dog units (IDU)/kg of the synthetic C-terminal octapeptide of CCK (Squibb Institute for Medical Research, New Jersey; assuming that 1 mg CCK = 3000 IDU[9]) dissolved in 0.9% NaCl solution (10 IDU/ml), or an equivalent volume of the 0.9% saline. Injected volumes varied from 0.15 to 8 ml. Every bird received each of the 10 injections once, in random order, according to a Latin square arrangement. Half the birds received CCK on Tuesday and the corresponding dose of saline on Thursday of the same week, and the other half were injected in the reverse order. With each bird and dose, food consumption from 10.00–10.15 h and 10.15–16.00 h on CCK and saline injection days was compared with the corresponding control intake, taken as the mean from Monday, Wednesday and Friday of that week. To test the significance of effects, error variances were estimated by performing analyses of variance between and within weeks.

For the caerulein experiment the above procedure was repeated with 10 immature hens of a different, light-hybrid (White Leghorn), strain. They were tested from 15 to 20 weeks of age and weighed from 1.25 ± 0.02 to 1.52 ± 0.03 kg. The 5 doses of caerulein (Sigma, London) injected were 0.1, 0.5, 1,2 and 4 µg/kg, dissolved in 0.9% saline (1 µg/ml), as before. Injected volumes of caerulein and saline varied from 0.13 to 6 ml.

Results and discussion. I.v. injections of CCK, caerulein and saline caused significant reductions in food intake in the period 10.00–10.15 h compared to that on control (non-injection) days (figure, table). The reductions due to CCK and caerulein were greater than those due to saline, and increased significantly with dose (table), whereas those due to the isotonic saline were not related to dose, and may have been a consequence of the actual handling and injection of the birds. The suppression of food intake due to injection of the peptides disappeared in the period 10.15–16.00 h, when there was a compensatory increase in feeding on CCK and caerulein injection days which was not related to dose. Intake from 10.15 to 16.00 h on saline injection days decreased significantly with dose in the case of the light-hybrids (caerulein), but not the medium-hybrids (CCK), and with both strains did not differ signifi-

Mean food intake (g) on control (non-injection) days, saline injection days and drug (CCK or caerulein) injection days, from 10 birds and 5 doses

		Control (days)	Saline (days)	Drug (days)	Significance of treatment/dose interaction Saline	Drug
CCK (medium-hybrids)	10.00–10.15 h	34.7[a]	30.3[b]	23.7[c]	NS	**
	10.15–16.00 h	75.3[a]	77.9[a]	83.7[b]	NS	NS
	10.00–16.00 h	110.0[a]	108.2[a]	107.4[a]	NS	NS
Caerulein (light-hybrids)	10.00–10.15 h	34.6[a]	29.5[b]	25.0[c]	NS	*
	10.15–16.00 h	52.0[a]	53.8[a]	56.9[b]	**	NS
	10.00–16.00 h	86.6[a]	83.3[b]	82.0[b]	*	NS

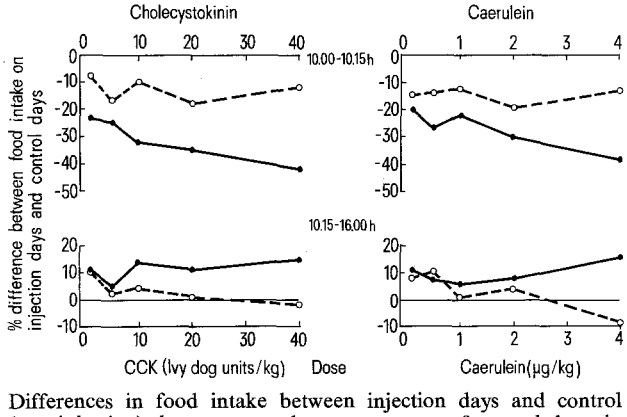
Significance of treatment and treatment/dose effects were obtained from analyses of variance between and within weeks. Treatment means having the same superscript do not differ significantly ($p > 0.05$). NS, not significant, $^*p < 0.05$, $^{**}p < 0.01$.

cantly from intake in the same period on control days. The compensatory increase in feeding from 10.15 to 16.00 h on injection days was sufficient to equal total intake on control days in the case of the medium-hybrids, but not the light-hybrids.

Thus, in 2 strains of domestic fowls, i.v. injections of CCK or caerulein caused dose-related reductions in food intake in the first 15 min of access to food after 18-h deprivation periods. The extent of these reductions was comparable to that obtained with similar doses of the peptides in rats, monkeys and rabbits[5–7,9], and their short-lived nature has been confirmed in another experiment with fowls, where it was found that inhibitory effects of injections of 5 and 20 IDU/kg CCK disappeared in 20–40 min (Savory, in prep.).

It has been argued that the action of CCK reflects satiety, and is not a side effect, because it elicits the complete behavioural sequence of satiety in rats[15], and treated animals drink normal amounts after water deprivation, do not appear ill, do not develop conditioned taste aversions with CCK and are not hyperthermic[5,9,16]. The spontaneous meals of fowls are usually briefer and more numerous than those of mammals[17,18], and fowls do not really show behaviour that is characteristic of satiety. They do, however, display obvious symptoms when they are unwell, and as none of these were seen following the peptide injections, it is possible that the suppression of feeding in the present experiments reflects satiety.

Concentrations of endogenous CCK have not been evaluated in birds, so it is not known whether the doses used here are within the physiological range. Nor is it known how CCK might act on satiety, whether via the CNS[19,20], the digestive system[6], or both. The frequencies of meal and interval lengths of birds are usually distributed in negative exponential form[17,21], which implies considerable randomness in meal occurrence, and evidence from low preprandial correlation coefficients suggests that they often terminate meals prematurely for reasons other than satiety. Also, food does not all pass directly to the intestine, but may be delayed in the crop or gizzard. Nevertheless, the fact that exogenous CCK can apparently cause the termination of meals only 3 or 4 min after injection in fowls (Savory, in preparation) indicates that in meals lasting more than about 6 min there could be time for ingested food to reach the duodenum[22] and for the release of CCK to act as a satiety signal.



Differences in food intake between injection days and control (non-injection) days, expressed as percentages of control days, in the first 15 min (10.00–10.15 h) and following 345 min (10.15–16.00 h) of a 6-h daily feeding schedule, with 5 doses of the synthetic octapeptide of CCK or caerulein (●——●), or equivalent volumes of 0.9% saline (○– – –○), injected by wing vein at 10.00 h.

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