The physiological determination of meal size in pigs

By T. RICHARD HOUPT, *New York State College of Veterinary Medicine, Cornell University, Ithaca, New York* 14853, *USA*

As a meal is being eaten, rapid inhibitory signals to the central nervous system (CNS) determine what the size of that meal will be. These signals are initiated by food in the alimentary canal, and inhibition of further eating results when sufficient food has been ingested to correct the nutritional deficit. The match between size of meal and nutritional deficit is, however, only a rough approximation. Control of meal size in pigs will be the primary subject of this paper; however, similar studies on ruminants and equids will be considered briefly.

Ruminants

In the ruminant the reticulo-rumen shields the lower tract from the immediate changes associated with eating a meal, and so it is not surprising that controls are initiated predominantly in the reticulo-rumen. The volume or bulk of the feed, causing distention of the reticulo-rumen (Grovum & Phillips, 1978; Grovum, 1979); certain of the volatile fatty acids stimulating reticulo-rumen sensory receptors (Baile & Mayer, 1967) or hepatic receptors after absorption (Anil & Forbes, 1980); and rumen hyperosmolality (Phillips *et al.* 1981) are probably the prime stimuli initiating inhibiting signals to the CNS during a meal to cause cessation of that meal. The subject has been comprehensively reviewed by Baile & Forbes (1974). Inhibitory signals from gastrointestinal (GI) sites beyond the reticulo-rumen seem unlikely to participate in the immediate determination of meal size, although such intestinal signals as cholecystokinin (CCK) do depress food intake in sheep in a dose-related manner (Grovum, 1981).

Equids

The control of food intake in equines appears to be somewhat different. Studies with sham-fed ponies indicate that oropharyngeal signals play a major and immediate role in meal-size determination (Ralston & Baile, 1983*a*,*b*) while gastrointestinal factors such as distention are relatively weak or slow (Ralston & Baile, 1982, 1983*a*,*b*).

Pigs

Pigs eat discrete meals which are mostly taken during the day and there is a close association of water drinking with meal eating (Auffray & Marcilloux, 1980; Bigelow, 1984). That pigs do vary intake to match nutrient deficit is indicated by the compensatory increase in intake that occurs when the diet is diluted with indigestible material (Owen & Ridgman, 1968) and by their ability to decrease voluntary oral intake within 1 d to compensate precisely for nutrients given

intragastrically (Pekas, 1983). However, the relative importance of inhibitory signals during a meal coming from the oropharyngeal region as compared to those from the GI tract has not been adequately investigated in the pig, but it has been assumed that GI controls are important.

The controls of meal size appear early in the newborn pig. Intragastric preloads given by stomach tube into newborn, hungry piglets decrease the amount of milk sucked from the sow afterwards (Stephens, 1975; Houpt *et al.* 1977, 1983*a*,*b*). The preloads in order of increasing satiety effectiveness were: isotonic saline (9 g sodium chloride/l), cream, protein hydrolysate, maize oil, milk, 50 g glucose/l, 30 g NaCl/l and 50 g lactose/l. More than one stimulus may be effective: distention by isotonic saline, release of CCK by fats and proteins, hyperosmolality, and a glucose action.

Duodenal hyperosmolality

When glucose or NaCl solutions at various concentrations and in small volume were delivered in young weaned pigs directly into the duodenum via implanted catheters just before a meal, meal size was depressed in direct proportion to hyperosmolality (Fig. 1; Houpt *et al.* 1979). The duodenum has been found to be the most sensitive site to the satiety effects of preloads (Stephens, 1980; Houpt, 1982). The duration of the test meal was less than 10 min, and it seemed likely that the satiety effects were initiated in the intestine. This appeared to be confirmed when it was found that infusion into the portal vein of the same solutions to simulate absorption failed to depress meal size (see also Stephens & Baldwin, 1974). Further, when a topical anaesthetic was included in the duodenal infusion, much of the satiety effect was lost. Finally, non-absorbable mannitol and sorbitol had much attenuated satiety effects as compared with equivalent glucose and NaCl infusions. The same hypertonic loads delivered automatically during spontaneous meals similarly reduced meal duration and size (Houpt *et al.* 1983*c*).

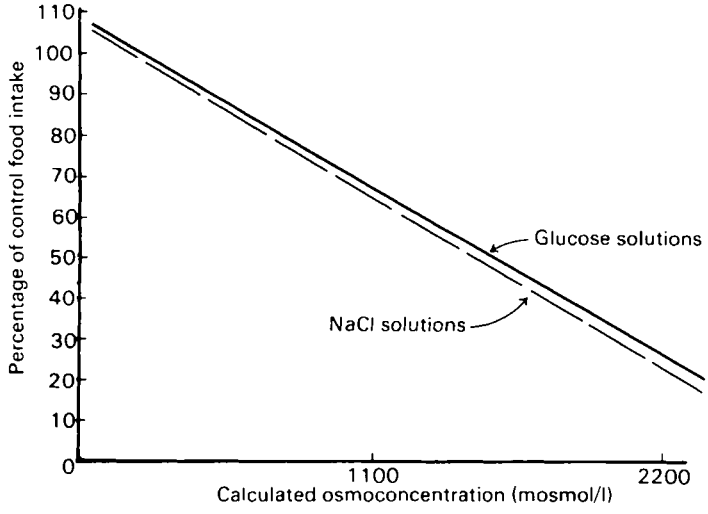

Fig. 1. Calculated osmolality of glucose and sodium chloride in duodenal preloads *v.* food intake in 10-min test periods (from Houpt *et al.* 1979).

https://doi.org/10.1079/PNS19850052 Published online by Cambridge University Press

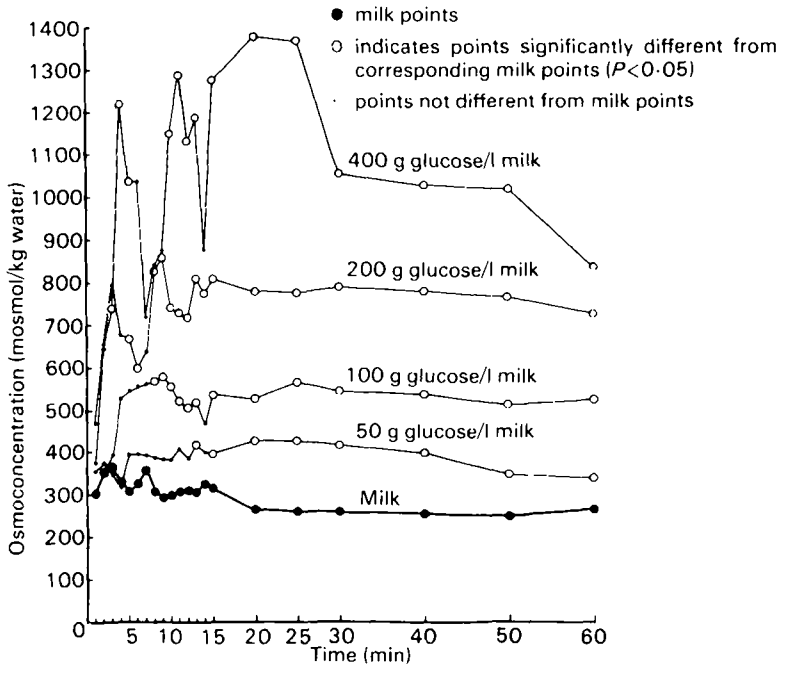

Fig. 2. Duodenal osmolality after ingestion at zero time of milk or glucose-in-milk solutions (from Houpt *et al.* 1983*d*).

These results supported the concept of a duodenal osmoreceptive control system; however, only if a rise of duodenal osmolality occurs in the time-span of a meal, could such a control system play a role in meal size determination. To test this, duodenal content was sampled, using implanted catheters, during and after ingestion of liquid nutritive 'meals' and of a gruel of milk and pelleted feed (Houpt *et al.* 1983*d*). Duodenal osmolality rose rapidly to about half the osmolality of the ingested fluid (Fig. 2). When the gruel was given, duodenal osmolality rose rapidly to 500–600 mosmol/kg water but, even when solutes were added to the gruel to raise its osmolality, duodenal osmolality failed to rise proportionately (Fig. 3). In all cases the elevated osmolality persisted long beyond the end of the meal.

CCK as an inhibitory signal. It has been hypothesized that CCK released from intestinal mucosa during a meal acts as an inhibitory signal to the CNS resulting in termination of the ongoing meal (Gibbs *et al.* 1973). CCK levels do rise in the blood of pigs after feeding (Go *et al.* 1971; Englert, 1973), and injection of either CCK of porcine origin (CCK-33) or the synthetic octapeptide (CCK-8) in doses calculated to raise plasma concentration to postprandial levels can depress meal size. Single injections given intravenously to young pigs just before 10-min test meals reduced the size of those meals in a dose-related fashion (Anika *et al.* 1981). Such effects of CCK are short-lived (Baldwin *et al.* 1983; Houpt, 1983) and after about 5 min normal feeding usually resumes. This is presumably a result of the short half-life of CCK in vivo (Rayford *et al.* 1976). Continuous infusions of CCK at lower dose rates better simulate the natural release of CCK during a meal.

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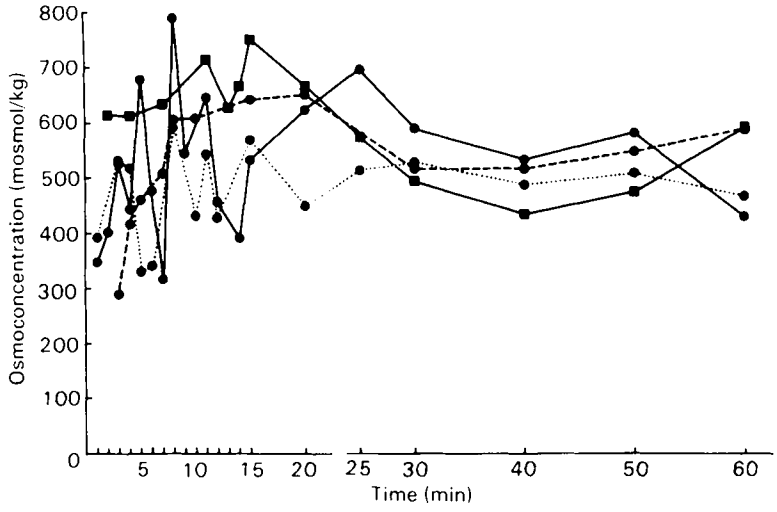

Fig. 3. Effects of ingestion of dry feed mixed with milk, plus glucose added to milk, on duodenal osmolality. (●·····●), Feed + milk; (■——■), feed + milk + 100 g glucose/l; (●——●), feed + milk + 200 g glucose/l; (●– – –●), feed + milk + 400 g glucose/l. Meal began at zero time and ended between 15 and 20 min. Osmolality at zero time was presumably slightly less than 300 mosmol/kg water in this fasted pig (from Houpt *et al.* 1983*d*).

Anika *et al.* (1981) found that although a single injection of 40 Ivy dog units (IDU) CCK-33/kg body-weight (about 1·3 μg CCK-33/kg) were necessary to depress the size of a 10-min test meal to 40% of control values in pigs fasted for 4 h, only 2 IDU/kg per min were needed to depress meal size similarly when given as a continuous infusion during the entire meal.

Depression of meal size could be an abnormal action of CCK. The higher doses of CCK, however, did not cause an aversion to a novel taste temporally associated with the CCK injection, an aversion that would have developed if the CCK had caused discomfort (Anika *et al.* 1981). Recently Baldwin *et al.* (1982, 1983) have shown a similar dose-related, but brief, satiety effect of a single intravenous injection of CCK-8 into pigs fasted for 17 h and feeding operantly. However, there was also a brief period of inhibition of operant water drinking and even of operantly obtained heat by pigs in a cool environment. They suggest that the CCK-satiety effect is due to a general depression. However, CCK may have a specific satiety effect but concomitantly cause a general sedation, as expressed by the drowsiness typically seen after a full meal, as well as after a meal shortened by CCK infusion. The question remains unresolved.

An attempt to determine the site of action of CCK in inhibiting eating was made by comparing the satiety effects of CCK-8 when infused into various tissues with the effects of intrajugular vein infusion (Houpt, 1983). Pigs, fasted for 4 or 5 h, were presented with dry pelleted feed and, simultaneously, an infusion of CCK-8 was begun via small implanted catheters at the rate of 2 IDU/kg per min (67 ng CCK/kg per min) and continued during a 10 min test meal. When infused into the jugular vein, this dose rate reliably reduced the duration and size of an ongoing

meal to 65% of that of control values. The usual behavioural sequence for sated pigs following the meal was: gentle exploratory actions with the snout, nudging and licking the wooden cabinet where the infusions were made, and, often, lethargy and even lying down and dozing. Feeding would often resume about 5 min after the CCK infusion ended, presumably because the injected CCK had been metabolized. Continuous infusions were made at the following sites: carotid artery with the catheter directed toward the brain; portal vein directed toward the liver; gastric branch of the splenic artery directed toward the stomach; aorta with tip caudad to the cranial mesenteric artery ('long catheter') or craniad to the coeliac artery ('short catheter'); intraperitoneal with tip on surface of duodenum or ileum. The same procedure of CCK infusion and feeding was followed and the effects on meal size via each route were compared with control meals when isotonic saline was infused.

When infused via the jugular vein, carotid artery or aortic artery cranial to the coeliac and cranial mesenteric arteries, CCK was equally effective in decreasing meal size (Fig. 4). This indicates that the site of satiety action is unlikely to be on the brain directly, but rather that the CCK infused into the carotid artery quickly reaches the jugular vein after passing through the short carotid circulatory bed. The equal effectiveness of the short aortic catheter route indicated that the site of action was in the circulatory bed of the abdominal aorta. Infusion into the long

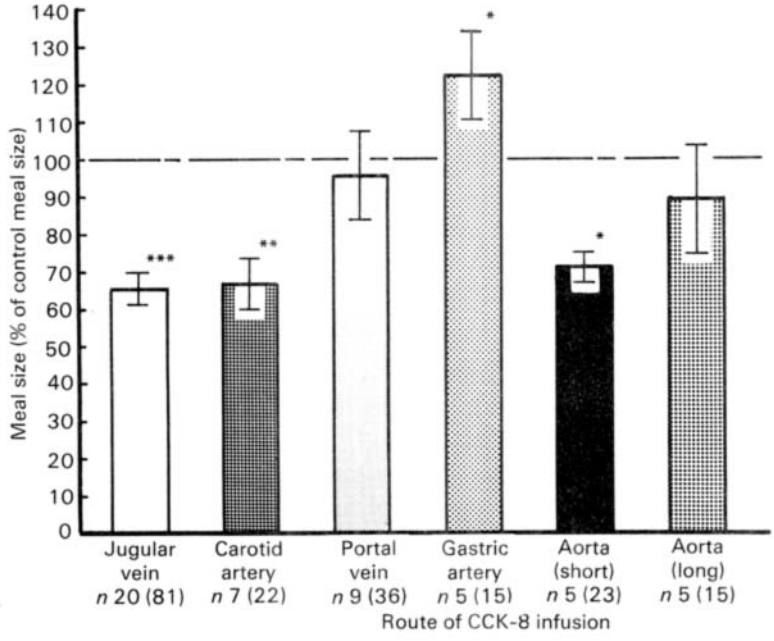

Fig. 4. Effects on meal size of cholecystokinin (CCK-8) infused continuously at 67 ng/kg per min during a 10 min feeding period. Meal size is expressed as a percentage of mean meal size on adjacent control days when saline (9 g sodium chloride/l) was infused. Mean values are given, with standard errors represented by vertical bars. Means for meal size were significantly different from paired control meals: $^{*}P<0.05$, $^{**}P<0.01$, $^{***}P<0.001$. No. of pigs used are indicated with total numbers of measurements in parentheses (from Houpt, 1983).

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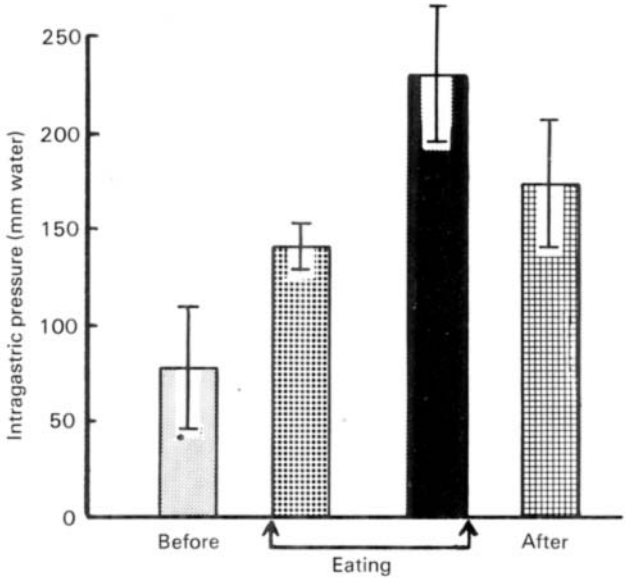

Fig. 5. Mean intragastric pressures for 1–2 min periods just before and just after eating began and just before and just after eating stopped in pigs (n 3, thirty measurements).

aortic catheter was less effective, indicating a site of action in the beds of the coeliac or cranial mesenteric arteries. The ineffectiveness of portal vein and gastric arterial infusions appeared to eliminate the liver and the main body of the stomach as sites, leaving the small intestine and perhaps the pylorus of the stomach. Numerous CCK receptor sites have been reported in the pylorus (Moran *et al.* 1984). However, when CCK was delivered to the serosal surface of the duodenum, there was no effect on meal size but, when put onto the surface of the ileum, there was a pronounced depression of meal size. There may be more than one site of CCK satiety action in the gut.

GI distention

The idea that GI distention, particularly of the stomach, is an important determinant of meal size is very old. Nevertheless, little work has been done to delineate the characteristics of this control system. In preliminary experiments using isolated segments of jejunum (Thiry fistulas), we have found that a rise of only a few centimetres of water pressure in the segment would inhibit eating behaviour with no signs of discomfort. On relief of this pressure, eating resumed (Houpt, 1982). Currently, we are studying the role of gastric distention during meals in pigs with catheters implanted with the tip in the stomach. This permits continuous measurement of intragastric pressure during eating as well as infusion of solutions to change the gastric pressure. In some experiments an inflatable cuff placed about the pyloric sphincter is being used to prevent gastric emptying during the meal. Preliminary results are shown in Fig. 5. When comparable end-of-meal pressures have been induced by infusion of saline solution, a cessation of eating

often results, but not always (T. R. Houpt, unpublished observations). The role of gastric distention may be complicated by interactions with other control systems.

Conclusion

Considerable work has been done to reveal what control mechanisms operate in pigs to determine meal size. However, even the mechanisms already investigated are not firmly established as operating during the normal meals, and the search for other satiety control systems that may also participate continues. Correlation of hormonal and metabolic changes with hunger or satiety offer clues (e.g. Anderson, 1974; Houpt *et al.* 1983*a*,*b*) for future investigation. Meanwhile, the osmoreceptive, CCK and GI-distention control systems are promising hypotheses worthy of study.

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Printed in Great Britain