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DUODENAL CONTROL OF GASTRIC EMPTYING IN THE MILK-FED CALF

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SUMMARY

1. It has been ascertained experimentally that an open duodenal cannula does not cause any marked variation in emptying of the abomasum when compared to the rate of emptying of the normal viscus or when the cannulae are closed.

2. Duodenal re-entrant cannulae provide a preparation whereby it is possible to infuse the duodenum via the distal cannula and to collect simultaneously the effluent fluid of the abomasum from the proximal arm of the cannula (Fig. 1).

3. With this preparation the duodenal infusate is not contaminated by the gastric effluent and thus the duodenal stimulus can be restricted to the single non-varying effect of the infusate.

4. In the milk-fed calf using this preparation the following facts have been established.

(*a*) On infusion into the duodenum, hypotonic and isotonic solutions of sodium chloride and sodium bicarbonate increase abomasal emptying; bicarbonate being the more effective stimulus.

(*b*) Potassium chloride, calcium chloride, glucose and hydrochloric acid inhibit gastric emptying when infused into the duodenum.

(*c*) Ammonium chloride, urea, lactose and acetic acid have little effect.

(*d*) Hypertonic solutions of all substances tested were inhibitory to gastric emptying when infused into the duodenum.

5. It has been demonstrated unequivocally that it is the effect of the infusate in the duodenum which controls gastric emptying for when the stomach is isolated from the duodenum, gastric emptying can be manipulated from the duodenum whatever the stomach contents may be.

6. Our results bring firm experimental confirmation of the views discussed by Hunt & Knox (1968) that gastric outflow is regulated by mechanisms initiated from receptors situated in the duodenum.

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INTRODUCTION

Extensive studies have firmly established the close functional alliance of stomach and duodenum. Alvarez (1935) and many others have suggested that an important part of the mechanism that regulates gastric outflow through the pylorus is the duodenum. He suggested also that the main factor which regulates the rate of exit of the gastric chyme is its degree of acceptability by the duodenum. Thomas (1957), reviewing the mechanisms and regulation of gastric emptying and secretion, states that the effector systems of gastric muscle contraction and gastric secretion are under multifactorial control through facilitatory and inhibitory mechanisms activated reflexly and neurohormonally from receptors situated mainly in the gut itself.

Hunt (1956), following careful evaluation in man of gastric emptying, introduced a hypothesis that at least one component of the control of gastric emptying was activated by a duodenal osmoreceptor responding to the osmotic pressure generated by various molecules and ions of the gastric chyme. Bell & Razig (1973*a*, *b*) showed a close similarity between the physiology of the abomasum of the milk-fed calf and the simple stomach, and produced experimental evidence that similar duodenal receptors are implicated in controlling gastric emptying in both the simple and compound stomach.

Sircus (1958) investigated the effect on gastric secretion of various substances introduced directly into the duodenum and reported that two separate inhibitory mechanisms appear to originate in the duodenum, one activated by change in pH and the other by change in osmolarity. He suggested that the pH sensitive mechanism exerts its effect through neural pathways and the osmolar sensitive mechanism through a humoral pathway.

The main aim of the present study was to acquire information on the mechanisms of gastric (abomasal) emptying when simple substances were infused directly into the duodenum in a manner whereby the gastric effluent was diverted from the duodenum yet its volume could still be measured. Some of the experimental results have been presented briefly to the Physiological Society (Bell & Mostaghni, 1972).

METHODS

The general management of the calves was as described by Bell & Razig (1973*a*). The 'test meal' technique and the use of the abomasal cannula have also been described (Bell & Razig, 1973*a*). Both single and re-entrant duodenal cannulae were placed as close to the pylorus as was reasonable using a method similar to that described by Markowitz (1954) (Fig. 1).

Experimental procedures. On the day of an experiment the morning feed was withheld, but since the duration of a test meal was restricted to 45 min the only interference in the normal routine of the animal was that the morning feed was delayed for 1 hr. In experiments using re-entrant cannulae the proximal duodenal cannula was used for the collection of abomasal effluent and the distal cannula for the instillation of test solutions (Fig. 1). Duodenal infusion was effected by gravity from a funnel connected by a tube attached to a small rubber bung which was inserted either into the single duodenal cannula or into the distal cannula of the re-entrant pair. The rate of infusion of fluid from the funnel was controlled by a clamp. Following the introduction of 950 ml. test meal into the abomasum, infusion into the duodenum was started immediately, the solution being maintained at 39° C and the infusion rate at 10 ml./min.

Analytical procedures. Measurement of any change in the volume of the test meal was made by the phenol red marker technique already described (Bell & Razig, 1973*a*).

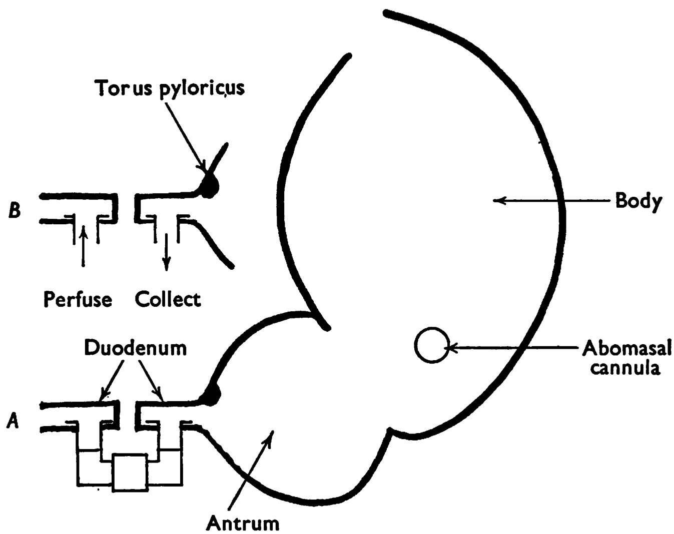

Fig. 1. Diagram of the abomasum and proximal duodenum of the calf to show the disposition of the cannulae. In *A* the cannulae are arranged for the normal transference of gastric chyme or test meal to the duodenum. In *B* the cannulae are arranged for the infusion of the duodenum and for the collection of gastric effluent.

RESULTS

Evaluation of the validity of the measurement of the flow from the abomasum

The establishment of duodenal re-entrant cannulae provided a preparation whereby it was possible to infuse the duodenum via the distal cannula and to collect simultaneously the effluent fluid of the abomasum from the proximal arm of the cannula. With this preparation the abomasal effluent did not pass to the duodenum so that the duodenal infusate was not contaminated by the gastric effluent and thus the duodenal stimulus was restricted to the single non-varying effect of the infusate.

Since Thomas, Crider & Mogan (1934) claimed that in the dog an open duodenal cannula increased the rate of emptying in the stomach, it was important to ascertain in our preparation of the calf whether an open duodenal cannula affected the rate of emptying of the abomasum.

The following preliminary experiments were therefore devised to examine the rate of emptying of the abomasum.

(*a*) The measurement of the amount of water test meal leaving the abomasum across the still connected duodenal cannulae to the duodenum using phenol red as a marker.

(*b*) The comparison of the volume of water test meal leaving the abomasum, measured by the phenol red marker technique, with the volume of test meal collected from the open proximal duodenal cannula.

(*c*) The comparison of the volume of water test meal leaving the abomasum measured by the phenol red marker and the direct collection of the fluid leaving the proximal duodenal cannula, while at the same time infusing distilled water at 39° C and at a rate of 10 ml./min into the distal duodenal cannula.

The results obtained from these experiments carried out in six calves are shown in Table 1.

TABLE 1. Summary of results obtained from six calves to show the effect on gastric evacuation of a test meal (950 ml. H_2O) through closed duodenal re-entrant cannulae compared with the collection of this effluent from the proximal duodenal cannula (see Fig. 1 and note that *a*, *b* and *c* also relate to text)

Arrangement of stomach output cannulae	Per cent water test meal remaining: Phenol red estimation	Per cent water test meal remaining: Duodenal cannula output
a Duodenal cannula closed (6)*	47·5 ± 5·3†	—
b Duodenal cannula open (6)	47·7 ± 3·3	44·6 ± 3·2
c Duodenal cannula open, distilled water infused into duodenum (6)	47·1 ± 5·1	45·9 ± 3·9

* No. of calves tested † S.D.

It can be seen that the rate of emptying of a standard water test meal from the abomasum of the calf was generally the same whether the duodenal cannulae were connected or open and that infusion of distilled water into the duodenum via the distal cannula at a standard pressure and rate did not affect abomasal emptying. The volume of test meal remaining in the abomasum after 45 min was somewhat less than 50 per cent under the experimental conditions listed above.

It was concluded, therefore, that infusion of the duodenum through the distal arm of a pair of duodenal re-entrant cannulae and the collection of the gastric effluent from the proximal cannula was a valid technique, especially when control and experimental data were compared in a single animal.

As will be seen below infusion of the duodenum from a single duodenal cannula is probably not valid for the higher concentrations of some solutions.

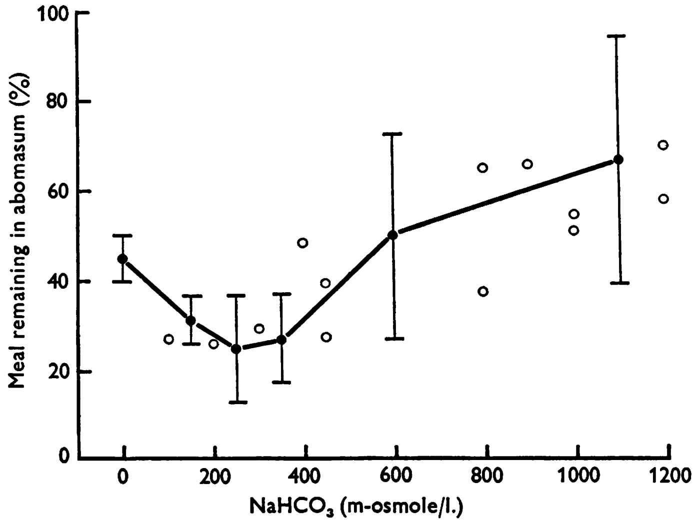

Fig. 2. Rate of emptying of water meal from abomasum following infusion of sodium bicarbonate into the duodenum. The arrangement of the duodenal cannulae is as shown in Fig. 1*B*, the abomasum being effectively isolated from the duodenum.

The curve illustrates the degree of emptying of the abomasum following perfusion of the distal duodenum with rising concentration of sodium bicarbonate solutions. The values given for abomasal emptying are the mean value ± S.D. for six calves (filled circles). The open circles are from further individual experiments from the six calves.

The maximal effect of gastric (abomasal) emptying is brought about when sodium bicarbonate 200–300 m-osmole/l. (i.e. a near isotonic solution) is infused into the duodenum; higher concentrations of sodium bicarbonate reverse this effect and inhibit emptying.

The effect on abomasal emptying of infusing sodium bicarbonate or sodium chloride solutions into the duodenum

In all experiments the serial test meal technique elaborated by Hunt (1956) and adapted for the abomasum of the milk-fed calf by Bell & Razig (1973*a*) was used. Both sodium bicarbonate and sodium chloride solutions of rising concentrations were tested.

TABLE 2. The effect of infusing sodium bicarbonate solutions into the duodenum on emptying of a test meal from the abomasum. The solutions were warmed to 39° C and infused at 10 ml./min into the duodenum via the distal cannula and the abomasal output collected from the proximal cannula of the re-entrant cannulae

Calf	$NaHCO_3$ infused into the duodenum (m-osmole/l)	Per cent meal remaining after 45 min	Ratio of retention meal/water	pH of abomasal contents: At 0 time	pH of abomasal contents: After 45 min
15	0 (water)	42·5	1·00	2·7	1·9
	300	29·5	0·69	2·6	1·9
	600	34·0	0·80	2·6	2·0
	900	79·8	1·87	2·6	2·0
	1100	94·6	2·22	2·7	2·2
17	0	40·3	1·00	3·0	1·7
	150	31·5	0·78	3·1	1·8
	250	30·5	0·75	2·9	1·7
	400	48·6	1·20	2·8	1·7
	600	82·8	2·05	3·0	2·1
	900	6·60	1·63	2·9	2·2
	1100	68·1	1·68	3·0	2·3
18	0	52·9	1·00	3·3	2·1
	100	26·1	0·49	2·7	1·7
	200	25·8	0·48	3·0	1·8
	350	26·3	0·49	2·9	1·8
	550	99·1	0·17	2·8	1·8
	700	15·3	0·29	2·8	2·1
	1100	40·4	0·76	2·8	2·1
23	0	42·0	1·00	3·1	1·9
	150	23·9	0·56	3·2	2·0
	250	17·9	0·42	3·1	1·9
	350	25·3	0·60	3·1	1·9
	450	39·2	0·93	3·0	2·0
	600	47·8	1·13	3·0	2·0
	800	65·3	1·55	3·2	2·2
	1000	51·0	1·21	3·2	2·2
	1200	69·9	1·66	3·1	2·2
24	0	47·7	1·00	3·2	1·8
	150	34·0	0·71	3·2	1·8
	250	14·7	0·30	3·1	1·8
	350	16·7	0·35	3·3	2·1
	450	27·6	0·57	3·3	2·1
	600	35·3	0·74	3·1	2·1
	800	37·3	0·78	3·0	2·1
	1000	55·0	1·15	3·0	2·2
	1200	57·8	1·21	3·0	2·3

Sodium bicarbonate. The experiments described in this section were made on six calves and the results are shown in Fig. 2. It can be seen that abomasal emptying varies with the concentration of sodium bicarbonate solutions infused into the duodenum.

The pattern of induced emptying can be divided into three phases.

(*a*) Hypotonic solutions of sodium bicarbonate cause rapid emptying of the stomach contents.

(*b*) The maximal effect varies between calves but is greatest when near isotonic solutions are used.

(*c*) When hypertonic solutions are infused into the duodenum, inhibition of emptying occurs and increases with rising concentration.

The details of the emptying of serial test meals when water was used as the test meal together with phenol red as a volume marker during infusion of sodium bicarbonate solutions through the duodenum are given in Table 2.

A sodium bicarbonate solution of about 250 m-osmole/l., when infused into the duodenum, was the best stimulus to activate emptying of the stomach, although values ranging from 200 to 500 m-osmole/l. were very

TABLE 3. The effect of infusing sodium chloride solutions into the duodenum on emptying of a test meal from the abomasum

Calf	NaCl infused into the duodenum (m-osmole/l.)	Per cent meal remaining after 45 min	Ratio of retention meal/water	pH of abomasal contents: At 0 time	pH of abomasal contents: After 45 min
15	0 (water)	42·5	1·00	2·7	1·9
	300	28·2	0·66	2·6	1·9
	600	37·5	0·88	2·7	2·1
	900	56·9	1·33	2·7	2·2
	1100	56·6	1·33	2·6	2·2
17	0	40·3	1·00	3·0	1·7
	100	39·2	0·97	2·8	1·7
	200	28·0	0·69	2·8	1·8
	300	32·2	0·79	2·6	1·9
	500	37·0	0·91	2·6	1·9
	700	86·2	2·13	3·0	2·5
	900	87·0	2·15	2·9	2·5
	1100	100·0	2·48	3·3	3·0
18	0	52·9	1·00	3·3	2·1
	150	37·5	0·70	3·3	2·1
	250	35·5	0·67	2·9	1·9
	350	39·8	0·75	3·0	2·0
	600	54·1	1·02	2·9	2·1
	850	83·5	1·57	3·3	2·3
	1100	93·3	1·76	3·3	2·6

effective. When the infused sodium bicarbonate concentration was raised to 600 m-osmole/l. somewhat variable results occurred between different subjects. In calves 15, 18 and 24 this level of hypertonicity was still effective in activating emptying of the abomasum. On the other hand in calf 17 sodium bicarbonate was less effective than in other animals for, although 250 m-osmole/l. was the best stimulus, 400 m-osmole/l. did not increase gastric emptying compared with the water control.

The pH of the abomasal contents at the beginning of the test meal was near pH 3·0 and at the end of the meal it was somewhat more acid being about pH 2·0.

Using a single duodenal cannula to show the effect of sodium bicarbonate on abomasal emptying the results were almost identical with the dual cannulae preparation up to 600 m-osmole/l. but above this concentration the effect was to produce a marked increase in emptying. Since this secondary phase was associated with a sharp rise in the pH of the gastric contents it was assumed that reflux of some of the duodenal infusate had occurred. In consequence the now alkaline test meal affected the duodenal infusate directly by diluting the inhibitory effect of gastric acid.

Sodium chloride. The pattern of abomasal emptying of a standard water test meal obtained when sodium chloride solutions were used as duodenal infusate was qualitatively similar to that obtained with sodium bicarbonate solutions (Table 3).

In the three calves investigated sodium chloride solutions of 200–300 m-osmole/l. produced the greatest emptying of water from the abomasum.

In calves 15 and 17 sodium chloride solutions equivalent to 600 and 400 m-osmole were less effective than lower concentrations but still activated greater rates of emptying than the water control, but calf 18 showed slight inhibition of abomasal emptying when 600 m-osmole/l. was infused into the duodenum.

In all calves abomasal emptying was slowed when sodium chloride solutions above 600 m-osmole/l. were infused into the duodenum.

The effect of infusing the duodenum from a single cannula produced generally the same result as in the dual cannulae preparation; high saline concentrations were never associated with rapid emptying. The stomach contents never became markedly alkaline on sodium chloride infusion as they did with sodium bicarbonate which adds weight to the suggestion that the activation when strong sodium bicarbonate solutions were infused into the duodenum from a single cannula was secondary to reflux of infusate to the stomach associated with alkalinization of the test meal.

Comparison of the effect of sodium bicarbonate and sodium chloride. Earlier experiments utilizing the serial test meal technique had shown that sodium bicarbonate at equimolar concentration was more effective than sodium chloride in producing abomasal emptying (Bell & Razig, 1973*b*).

Further experiments were carried out on three calves to compare the duodenal effect of similar concentrations of sodium chloride and sodium bicarbonate on abomasal emptying. The effects of equiosmolar solutions of these two sodium salts on abomasal emptying are listed in Table 2 and Table 3. It can be seen that at all concentrations sodium bicarbonate is a better activator of abomasal emptying than similar osmolar solutions of sodium chloride. High concentrations of sodium chloride completely inhibit gastric emptying.

TABLE 4. The effect on abomasal emptying of infusing potassium chloride solutions into the duodenum

Calf	KCl infused into the duodenum (m-osmole/1.)	Per cent meal remaining after 45 min	Ratio of retention meal/water	pH of abomasal contents: At 0 time	pH of abomasal contents: After 45 min
17	0 (water)	40·3	1·00	3·00	1·7
	100	90·2	2·23	2·85	1·9
	200	93·6	2·32	2·85	2·0
	300	97·3	2·41	2·80	2·0
	450	97·6	2·42	2·80	2·1
22	0	51·2	1·00	3·6	2·1
	100	54·5	1·06	3·6	2·0
	250	69·0	1·34	3·0	2·2
	400	67·1	1·31	2·9	2·3
	600	100·0	1·95	3·0	2·5
23	0	42·0	1·00	3·1	1·9
	100	64·2	1·52	2·9	2·1
24	0	47·4	1·00	3·2	1·8
	100	52·6	1·10	3·1	1·9
	250	52·3	1·09	3·0	2·3
	450	79·0	1·65	3·3	2·7
	600	79·5	1·66	3·2	3·0
	700	87·3	1·83	3·1	3·0

The effect of some other substances infused into the duodenum on gastric emptying

Since Bell & Razig (1973*b*) have shown that other salts, sugars and acids inhibit gastric emptying as they do in man, these substances were re-examined using the improved technique of infusing the duodenum via re-entrant cannulae to assess the effect on emptying of a standard water test meal from the stomach.

For brevity the results are presented in tabular form with minimal comment since the present results in the main confirm those obtained in the earlier experiments using serial test meals (Bell & Razig, 1973*b*).

Potassium chloride. In all calves potassium salts at all concentrations tested produced inhibition of gastric emptying and as a rule the effect increased with rising concentration (Table 4).

Calcium chloride. The results are shown in Table 5 and can be seen to be similar to those obtained with potassium chloride causing inhibition of gastric emptying.

TABLE 5. The effect on abomasal emptying of infusing calcium chloride solutions into the duodenum

Calf	$CaCl_2$ infused into the duodenum (m-osmole/l.)	Percentage meal remaining after 45 min	Ratio of retention meal/water	pH of abomasal contents: At 0 time	pH of abomasal contents: After 45 min
22	0 (water)	51·2	1·00	3·6	2·1
	100	67·4	1·31	2·6	2·1
	250	77·7	1·51	2·6	2·3
	400	88·8	1·73	2·7	2·5
	600	100·0	1·95	2·9	2·7
23	0	42·0	1·00	3·1	1·9
	100	66·7	1·58	3·1	2·2
	250	72·1	1·71	3·1	2·3
	400	71·8	1·70	3·0	2·35
	600	87·8	2·09	3·1	2·7
26	0	41·6	1·00	3·5	1·9
	150	45·0	1·08	3·2	2·1
	250	56·7	1·36	3·1	2·2
	400	62·8	1·50	3·0	2·25
	600	100·0	2·40	3·1	2·5
	800	100·0	2·40	3·0	2·6

Ammonium chloride. The results given in Table 6 are clearly different to those obtained with potassium chloride and calcium chloride for hypotonic solutions: ammonium chloride in two calves caused a definite increase in abomasal emptying. Unlike sodium chloride, however, ammonium chloride at isotonic levels does not activate abomasal emptying nor does it produce strong inhibition of emptying in hypertonic concentrations.

Urea. In the three calves examined dilute solutions of urea enhanced abomasal emptying somewhat but the effect is not as profound as with sodium bicarbonate although it is quite definite (Table 7). The most marked inhibition occurs with solutions of urea near to the tonicity of blood plasma while higher concentrations cause only slight inhibition of emptying.

Glucose. Experiments were carried out on three calves and the results are shown in Table 8. Glucose solutions ranging from 100 to 1200 m-osmole/l. all inhibited gastric emptying of the test meal, but the higher concentrations, although having more marked effects, never produced complete inhibition.

TABLE 6. The effect on abomasal emptying of infusing ammonium chloride solutions into the duodenum

Calf	NH_4Cl infused into the duodenum (m-osmole/l.)	Per cent meal remaining after 45 min	Ratio of retention meal/water	pH of abomasal contents: At 0 time	pH of abomasal contents: After 45 min
26	0 (water)	41·6	1·00	3·5	1·9
	100	38·6	0·92	3·2	1·9
	200	59·2	1·42	3·1	2·0
	350	57·3	1·37	3·0	2·1
	500	66·0	1·58	3·1	2·3
29	0	49·0	1·00	3·1	1·9
	100	29·5	0·60	3·0	1·8
	200	41·3	0·84	2·8	1·8
	350	62·2	1·26	3·0	2·0
	500	64·5	1·31	3·0	2·2
	700	87·0	1·77	2·9	2·5
31	0	43·3	1·00	2·9	1·8
	100	51·7	1·19	2·9	1·8
	200	45·5	1·05	2·6	1·9
	350	58·3	1·34	2·4	2·1
	500	58·2	1·34	2·4	2·1
	700	52·4	1·21	2·4	2·3

Lactose. In the main, infusion of lactose solutions into the duodenum produced slight inhibition of gastric emptying but in one calf lactose 100 m-osmole/l. caused a definite increase in abomasal emptying and in another animal a slight delay occurred at this concentration. Isotonic solutions of lactose were not inhibitory, and higher concentrations of this sugar were also mildly inhibitory (Table 9).

Hydrochloric acid and acetic acid. As can be seen from Tables 10 and 11, the general effect of both acids on infusion of the duodenum was to inhibit gastric emptying. This was true for all dilutions of hydrochloric acid and for the higher dilutions of acetic acid. Lower dilutions of acetic acid, however, produced contrary results; for example, 10 m-equiv/l. increased abomasal emptying somewhat in both calves.

To test the interrelation of the gastric contents and the duodenal infusate upon abomasal emptying

In the experiments reported above the effect of various duodenal infusates on a standard water test meal placed in the abomasum has been examined and it has been shown that when used as a duodenal infusate, some substances inhibit but others activate gastric evacuation.

TABLE 7. The effect on abomasal emptying of infusing urea solutions into the duodenum

Calf	Urea infused into the duodenum (m-osmole/l.)	Per cent meal remaining after 45 min	Ratio of retention meal/water	pH of abomasal contents At 0 time	pH of abomasal contents After 45 min
26	0 (water)	41·6	1·00	3·5	1·9
	100	32·3	0·77	3·4	2·0
	200	50·0	1·20	3·2	2·1
	300	38·5	0·92	3·0	2·0
	500	44·9	1·07	3·1	2·1
	700	52·0	1·25	3·1	2·2
	900	53·0	1·27	3·1	2·3
	1200	55·1	1·32	3·1	2·3
29	0	49·0	1·00	3·1	1·9
	100	34·5	0·70	3·0	1·9
	250	30·5	0·62	2·9	1·9
	500	28·5	0·58	3·0	1·8
	700	42·0	0·85	2·9	2·0
	900	58·9	1·20	2·9	2·1
	1200	57·1	1·16	3·0	2·2
31	0	43·3	1·00	2·9	1·8
	150	47·3	1·09	3·0	1·8
	250	27·9	0·64	3·5	1·8
	500	54·8	1·26	2·5	1·9
	800	57·6	1·33	2·8	2·0
	1200	55·3	1·27	2·8	2·1

The following experiments using re-entrant cannulae were undertaken to test whether the chemical composition of the gastric contents was at all important in influencing gastric evacuation and whether if there was an effect, the gastric effect was dominated by the duodenal infusate.

The effect of sodium chloride on inhibitory substances. With 3 % glucose solution as the test meal, a serial trial with two calves produced results very similar to those obtained when water was used as a test meal. The maximum stimulus for gastric emptying was about 300 m-osmole NaCl/l. There was no suggestion from these results of an additive effect of the glucose in the

TABLE 8. The effect on abomasal emptying of infusing glucose solutions into the duodenum

Calf	Glucose infused into the duodenum (m-osmole/l.)	Per cent meal remaining after 45 min	Ratio of retention meal/water	pH of abomasal contents: At 0 time	pH of abomasal contents: After 45 min
6	0 (water)	50·0	1·00	3·4	2·0
	250	60·0	1·20	3·7	2·2
	500	57·7	1·15	3·7	2·2
	750	56·8	1·13	3·6	2·0
	1000	66·1	1·32	3·3	2·2
	1250	80·3	1·60	2·9	2·5
7	0	55·8	1·00	3·0	2·0
	250	62·8	1·12	3·6	2·0
	500	64·8	1·16	3·2	2·0
	750	68·7	1·23	2·9	2·1
	1000	88·1	1·57	2·9	2·4
	1250	68·0	1·21	3·2	2·2
8	0	45·8	1·00	3·0	2·1
	250	45·2	0·98	2·7	2·1
	500	57·5	1·25	2·9	2·2
	750	50·9	1·11	2·8	2·1
	1250	61·8	1·34	2·9	2·3

TABLE 9. The effect on abomasal emptying of infusing lactose solutions into the duodenum

Calf	Lactose infused into the duodenum (m-osmole/l.)	Per cent meal remaining after 45 min	Ratio of retention meal/water	pH of abomasal contents: At 0 time	pH of abomasal contents: After 45 min
26	0 (water)	41·6	1·00	3·5	1·9
	100	50·2	1·20	3·2	1·9
	200	60·6	1·45	3·4	1·9
	300	57·0	1·37	3·3	2·0
	500	52·7	1·26	3·1	2·1
29	0	49·0	1·00	3·1	1·9
	100	46·6	0·95	3·0	1·8
	200	49·0	1·00	2·6	1·9
	300	69·2	1·41	2·7	2·0
	400	82·1	1·67	2·8	2·2
31	0	43·3	1·00	2·9	1·8
	100	25·3	0·58	3·0	1·8
	200	47·4	1·09	2·8	2·0
	350	55·1	1·12	2·8	2·1
	550	54·0	1·10	2·7	2·2

TABLE 10. The effect on abomasal emptying of infusing hydrochloric acid into the duodenum

Calf	HCl infused into the duodenum (m-equiv/l.)	Per cent meal remaining after 45 min	Ratio of retention meal/water	pH of abomasal contents: At 0 time	pH of abomasal contents: After 45 min
4	0 (water)	31·4	1·00	4·0	1·8
	10	27·0	0·85	4·3	1·8
	20	57·3	1·82	3·9	1·9
	30	84·0	2·67	3·6	1·8
	50	88·0	2·80	3·9	1·6
	60	80·0	2·54	4·3	1·6
7	0	55·8	1·00	4·0	2·0
	10	72·6	1·30	3·7	2·4
	20	78·8	1·41	3·6	2·0
	35	74·6	1·33	3·9	2·2
	50	79·2	1·41	3·6	2·5
	60	100·0	1·79	4·1	2·1
8	0	45·8	1·00	4·0	2·1
	10	94·3	2·05	2·9	2·2
	20	68·4	1·49	2·7	1·9
	30	84·7	1·84	2·6	2·0
	40	72·5	1·58	2·8	1·9
	60	98·3	2·14	2·7	1·9

TABLE 11. The effect on abomasal emptying of infusing acetic acid into the duodenum

Calf	Acetic acid infused into the duodenum (m-equiv/l.)	Per cent meal remaining after 45 min	Ratio of retention meal/water	pH abomasal contents: At 0 time	pH abomasal contents: After 45 min
29	0 (water)	49·0	1·00	3·1	1·9
	10	34·0	0·69	2·6	1·9
	20	44·2	0·90	2·5	2·0
	40	61·3	1·25	2·4	2·1
	60	79·3	1·61	2·4	2·3
51	0	43·3	1·00	2·9	1·8
	10	37·9	0·87	2·8	1·9
	20	53·4	1·23	2·8	1·9
	35	62·0	1·43	2·9	2·1
	50	79·6	1·83	2·6	2·3

stomach and the saline perfusion of the duodenum to enhance gastric emptying above the threshold for each single substance.

To test this point further the effect of a standard optimal sodium chloride stimulus was used as the duodenal infusate but the concentration of the glucose test meal in the abomasum was varied. The results are given in Fig. 3 where it can be seen that the emptying of all concentrations of glucose test meals from the stomach is enhanced when isotonic sodium chloride is infused into the abomasum.

The effect of sodium bicarbonate on inhibitory substances. Very similar results to those of sodium chloride were obtained when sodium bicarbonate 300 m-osmole/l. was infused into the duodenum with glucose test meals instilled into the abomasum.

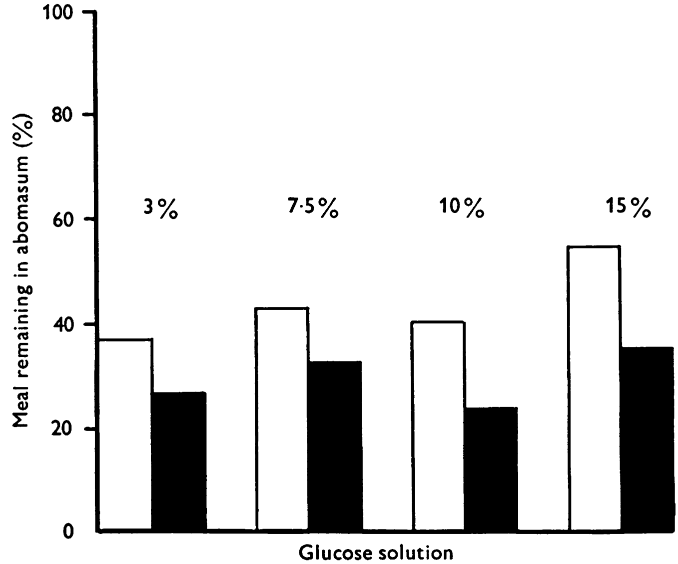

Fig. 3. The effect of infusing the duodenum with sodium bicarbonate 300 m-osmole/l. on test meals of varying concentrations of glucose. The open columns are the controls for the different glucose meals and the closed columns the rate of emptying of the same solution when the duodenum is infused with isotonic sodium bicarbonate. In all cases the isotonic sodium bicarbonate as duodenal infusate increased the rate of gastric emptying.

To test the activating effect of isotonic sodium bicarbonate solution on gastric emptying more rigorously, substances known to inhibit abomasal emptying were used as the test meal. The re-entrant cannulae preparation used for these tests ensured that the duodenal infusate was uncontaminated by the gastric effluent. Each individual meal was first tested without duodenal perfusion to provide a control against the effect of duodenal perfusion with sodium bicarbonate on the different test meals. It can be seen that in each control about 50 per cent of the volume of the test meal is emptied. With potassium chloride and calcium chloride the slightly higher retention values may be due to a minor inhibitory effect mediated through the mucosa of the small area of duodenum retained to implant the proximal cannula (Fig. 4). When similar control test meals were introduced into the abomasum, but now the duodenum was simultaneously infused for the 45 min test period with $NaHCO_3$ 250 m-osmole/l., the degree of abomasal emptying was very greatly enhanced, less than 20% of the test meal remaining in the stomach; the substances which would have normally been retained when used as a normal test meal were all evacuated as was the water meal control. This effect on gastric emptying shows that irrespective of the gastric contents emptying occurs at the same rate, and depends upon

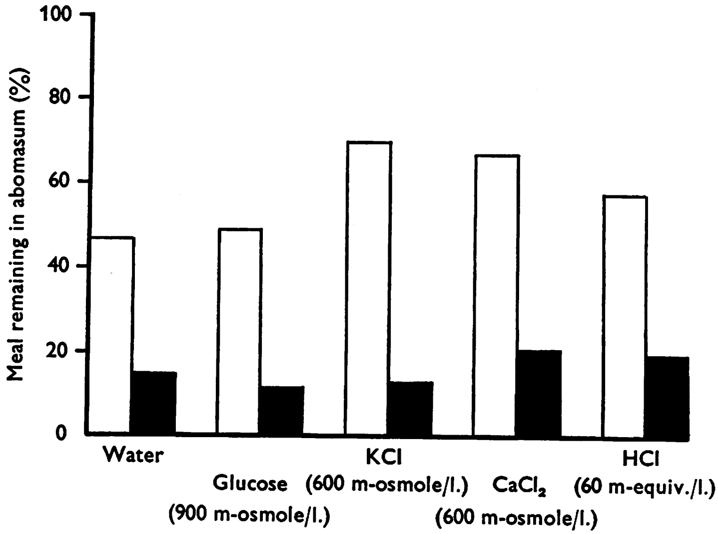

Fig. 4. The effect on emptying from the abomasum of various substances with and without infusion of the duodenum with isotonic sodium bicarbonate solution. The open column is the control for each substance and the closed column the rate of emptying of the same solution when the duodenum is infused with isotonic sodium bicarbonate solution. The increased rate of gastric emptying associated with bicarbonate infusion of the duodenum is obvious.

the duodenal activator which therefore must be the controlling factor of gastric motility and consequently gastric emptying. Isotonic sodium chloride produced exactly the same result as isotonic sodium bicarbonate in these experiments.

The effect of inhibitory substances on sodium bicarbonate and chloride. To test this very striking effect further, similar experiments were performed but substances known to activate gastric emptying were used as test meals and inhibitory substances used as duodenal infusates. It can be seen in Fig. 5 that the control test meals of water and isotonic solutions of sodium bicarbonate and sodium chloride were emptied from the proximal duodenal cannula so that only 30–40 % of the meal remained. When, however, the duodenum was infused with an inhibitor of gastric evacuation such as KCl 600 m-osmole/l., the isotonic sodium bicarbonate and sodium chloride test meals were almost wholly retained within the abomasum. Almost identical results were obtained when 600 m-osmole calcium chloride/l. or 10 m-equiv HCl/l. were used to infuse the duodenum.

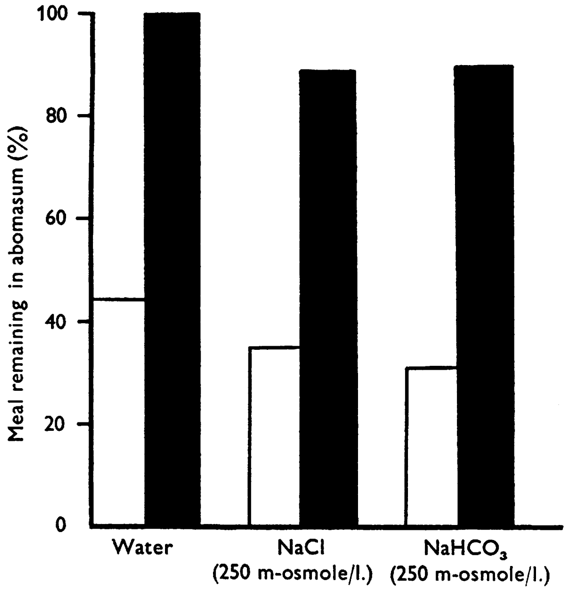

Fig. 5. As in Fig. 4, but here the duodenum is infused with potassium chloride 600 m-osmole/l.

The isotonic sodium chloride and sodium bicarbonate solutions as well as water are almost wholly retained when the duodenum is infused with the inhibiting substance (potassium chloride).

DISCUSSION

Earlier work in sheep on the rate of passage of chyme from the abomasum to the duodenum has indicated that open duodenal cannulae hardly affect gastric emptying (Harris & Phillipson, 1962). We were able to confirm this quite clearly in the calf and this finding validates the experimental arrangement used in most of our experiments. Our results are inconsistent with the views of Thomas *et al.* (1934), based on experiments in the dog, that an open duodenal cannula increases the rate of emptying from the stomach. The difference between dog and calf may be due to intraspecies variation in gastric emptying or a difference in the nature of the food since dogs eat more solid food than calves.

Our results confirm that substances such as sodium bicarbonate and sodium chloride activate gastric emptying through their action at the duodenal level. Using the calf preparation with re-entrant cannulae, solutions containing 200–300 m-osmole/l. of either of these salts when infused into the duodenum were shown to be very effective stimuli to gastric emptying, a result which explains the reports of Bell & Razig (1973*b*) that test meals of these solutions placed in the stomach are rapidly expelled. It has already been shown in many investigations that isotonic saline increases emptying of test meals (Carnot & Chassevant, 1905; McSwiney & Spurrell, 1933; Gianturco, 1934; Hunt, 1956). It should be noted that Singleton (1961) demonstrated that in adult goats 2% sodium chloride solution (*ca.* 600 m-osmole/l.) infused into the duodenum increased abomasal motility.

It was stated by Hunt (1956) using the serial test meal technique that sodium bicarbonate is more effective than sodium chloride in inducing gastric emptying. A similar observation has been reported for the emptying of the abomasum of the milk-fed calf (Bell & Razig, 1973 *b*). Hunt (1956) suggested that both sodium salts exerted their action through a duodenal receptor mainly because of its permeability to sodium ions and solutions containing bicarbonate ions emptied more rapidly than those containing chloride ions. Our results strongly support Hunt's postulate for we have shown that both sodium salts affect gastric emptying at the duodenal level but that sodium bicarbonate is much more active than equivalent osmolar concentrations of sodium chloride.

The results reported here that increasing concentrations of calcium chloride infused into the duodenum inhibit abomasal emptying, is in close agreement with the findings in man (Hunt & Pathak, 1960), and in the calf (Bell & Razig, 1973*b*), that all concentrations of calcium chloride solutions used as a gastric test meal slow emptying of the viscus.

Bell & Razig (1973*b*) found that in the calf the same inhibition of gastric emptying by potassium chloride solutions described by Hunt (1956) for man, but noted that in the calf hypotonic solutions of potassium chloride (100 m-osmole/l.) slightly increased abomasal emptying. This latter effect has not been confirmed in our present study, thus Hunt's view that the cation does not penetrate the osmoreceptor remains an acceptable thesis.

Our results provide strong evidence in support of the view expressed by Hunt (1956) and Hunt & Pathak (1960) that an osmoreceptor in the duodenum is responsible for osmotic control of gastric emptying. Our experimental arrangement allowed duodenal infusion without any contamination from the gastric efflux and we used a standard water test meal introduced directly into the stomach. Under these circumstances sodium chloride, sodium bicarbonate and urea conform to the view expressed by Hunt & Knox (1968) that they are effective at the duodenal level because they can penetrate and activate an osmoreceptor in low concentrations and so cause rapid evacuation of the stomach. This effect we have shown, however, to be due strictly to increased action of gastric smooth muscle activated indirectly from the duodenum. The initiation of gastric emptying may result from distension of the viscus, but the subsequent exponential emptying, reported by Hunt (1956) and Bell & Razig (1973*b*), is maintained by duodenal activity. All salts are impermeable at high concentration so that the osmoreceptor, considered as a vesicle, is excited through deflation by non-penetrating cations and hypertonic solutions.

The inhibiting effect of hydrochloric acid on gastric emptying in man is well known (Hunt & Pathak, 1960) and has been noted also in the calf by Bell & Razig (1973*b*). A similar inhibitory effect of acid in the duodenum has been reported by Smith (1964) in the sheep and by Singleton (1951) in the adult goat.

Pathak (1959) reported, however, that weak concentrations of hydrochloric acid increased gastric emptying in man, as shown earlier in the cat by Hedblom & Cannon (1909); and Hunt & Knox (1969) confirmed that low concentrations of hydrochloric acid and lactic acid hasten gastric emptying in man. Gastric emptying of the stomach, isolated from the duodenum, was inhibited by all concentrations of hydrochloric acid that were infused into the duodenum. This confirms the view of Hunt & Knox (1968) that there are acid-receptors in the duodenum.

The results obtained on infusing the duodenum of the calf with ammonium chloride solutions were not equivocal there being some disparity between the three calves examined. Our results tend to confirm that at lower concentrations ammonium chloride has little effect, as reported by Hunt & Knox (1962) 'over a narrow margin of concentrations', but hypertonic solutions were slightly but clearly inhibitory. This result strengthens our view that the inhibitory effect of ammonium chloride on gastric emptying is mediated through a duodenal osmoreceptor and is not due to nausea as suggested by Hunt & Knox (1962).

Strong confirmatory evidence has been produced in the experiments reported here that it is from the duodenum that control of gastric muscle contractions is effected. This is clearly shown when, for example, a concentrated glucose solution is placed in the stomach it would normally be retained, but when the duodenum was infused simultaneously with isotonic sodium chloride or sodium bicarbonate solution the same glucose test meal was rapidly emptied from the stomach. Similarly other substances, such as hypertonic solutions of potassium chloride, calcium chloride and hydrochloric acid, when used as gastric test meals, cause marked retention, and are almost wholly evacuated from the stomach when the duodenum is infused with isotonic sodium bicarbonate or chloride (Figs. 3 and 4).

The reverse effects to those mentioned above on gastric emptying also hold for substances such as isotonic sodium bicarbonate or sodium chloride, which are normally readily evacuated from the stomach, are wholly retained when the duodenum is separately infused with substances such as potassium chloride, calcium chloride and hydrochloric acid which normally inhibit stomach motility (Fig. 5). The results emphasize the fact that duodenal control of gastric emptying may act by inhibiting the force of contraction of stomach smooth muscle and thus delay emptying.

This investigation has also demonstrated unequivocally that it is the duodenal infusate which controls gastric emptying, for when the stomach is isolated from the duodenum gastric emptying can be manipulated from the duodenum whatever the stomach contents might be. This result, therefore, strongly supports the views expressed by Hunt & Knox (1968) that duodenal receptor activity controls gastric emptying and confirms earlier views of Bell & Razig (1973*b*) that similar mechanisms control emptying of the abomasum.

The results reported here bring into question the physiological function of chemoreceptors recorded by axonography by Harding & Leek (1973). Our results give no clear indication of the means whereby the duodenum affects the smooth muscle of the stomach, but since the duodenum was transected, a transmural pathway is unlikely. We are presently investigating whether any nervous reflex pathway passes via the autonomic route or whether the effects are partially or wholly mediated through humoral channels.

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