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THE OSMOTIC EFFECTS OF SOME SIMPLE MOLECULES AND IONS ON GASTRIC EMPTYING

BY J. N. HUNT AND J. D. PATHAK
Department of Physiology, The Medical School, Guy's Hospital, London, S.E. 1, and Department of Physiology, The Medical College, Baroda, India

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The idea that the rate of emptying of the stomach is strongly influenced by the osmotic pressure of the gastric contents stems from the experiments of Carnot & Chassevant (1905). They found that in dogs with duodenal fistulae saline nearly isosmotic with plasma left the stomach more rapidly than saline solutions which were more concentrated or more dilute. The influence of the concentration of salt on gastric emptying appears to be much the same in man as it is in dogs. Shay & Gershon-Cohen (1934) in their radiographic studies noted that tap water left the stomach more slowly than isotonic saline. They also concluded that in order to slow emptying—presumably relative to the emptying of tap water—'hypertonic' solutions of salts and glucose were necessary, whereas hydrochloric acid slowed emptying in solutions less concentrated than plasma in terms of milli-osmoles per litre.

The present experiments, extending those described by Hunt in 1956, are a study of the working of the receptors concerned in the slowing of gastric emptying that appear to be sensitive to the osmotic properties of the luminal contents of the duodenum and small intestine (Shay & Gershon-Cohen, 1934). The results of some experiments with acids which probably work differently (Sircus, 1958) are also described for comparison.

METHODS

After washing out the stomach with 250 ml. of tap water at about 8 a.m., test meals of 750 ml. of distilled water at 37° C containing various concentrations of solutes were given to four fasting volunteer medical students and the experimenters. The test meals contained, in addition to the solutes introduced as experimental variables, phenol red about 60 mg/l., which served as a marker and had no material influence on gastric emptying (Hunt, 1956). The meal was given down a tube into the stomach in about 75 sec. The tube was usually left down until the gastric contents were recovered some 10–30 min later, and the stomach was then washed out with 250 ml. tap water. The amount of phenol red recovered in this wash-out divided by the concentration of phenol red in the previously recovered major portion of gastric contents gave the volume of gastric contents not aspirated previously, usually about 20 ml. The volume of the original meal remaining in the stomach at the time of the recovery was calculated from the amount of phenol red recovered. In arranging these experiments the interval between giving the meal and recovering it was usually adjusted for each subject so that the volume of meal recovered was at least 100 ml. out of the original 750 ml. given. Strict adherence to the routine procedure was necessary to obtain reproducibility.

The data reported here were collected during five years: because of a realization that the data initially obtained were inadequate in range or number for a new purpose, an interval of years separates some of the experiments within a single series in the same subject. Although the subjects studied are fewer than we would wish, the large number of meals given, over a thousand, and their scatter in time do provide some safeguard against the results being relevant only to special circumstances. The intensive study of a few subjects was necessary to reduce the variability due to differences between subjects, so allowing quantitative comparisons of the action of solutes and mixtures of solutes. In some subjects who gave very variable results the experiments were ended shortly and these results are not considered.

RESULTS

The results record the relations between the volume of a test meal recovered from the stomach at a fixed time after its instillation and the milliosmolar (m-OSM) concentration of solutes in the instilled meal. For the most part these relationships were linear, so that straight lines could be fitted to the data by the method of least squares. Where the relationship was not linear over the whole range, for example in Fig. 4, the lines were calculated only for that part of the range which appeared on inspection to be linear. Such lines are shown as full; curved lines, shown interrupted are fitted by eye.

The influence of some monovalent and divalent anions and cations on the volume of meal remaining in the stomach after a fixed interval

Figure 1 shows the relationship between the concentration of either hydrochloric acid or potassium chloride and the volume of test meal recovered after 20 min in subject J.N.H. It may be seen that hydrochloric acid was about three times more effective per osmole than potassium chloride in increasing the volume of test meal recovered from the stomach. Similar data for other electrolytes are given in Table 1. As the concentrations were raised, so the amount of the original test meal recovered from the stomach after a fixed interval increased. Hydrochloric acid was the most effective per osmole, ammonium chloride the least effective.

In previous work (Hunt, 1956; Pathak, 1959) it was noted that the threshold concentration for the slowing of gastric emptying by hydrochloric acid was about 20 m-OSM, and in the present work that for potassium chloride seemed to be at least 40 m-OSM. Accordingly the regression equations shown in Table 1 for solutions of hydrochloric acid and for solutions of potassium chloride include only data for test meals containing concentrations of acid of 20 m-OSM or more, and concentrations of potassium chloride of 40 m-OSM or more. Reference to the intercepts (*a*) of the regression lines for meals containing hydrochloric acid or potassium chloride and the axis for volume, in part 1 of Table 1, shows that in W.D.L.P. and J.N.H. the mean values for the volume of meals of water remaining at 20 min are less than those shown in part 2. This finding is consistent with the view that there is a threshold concentration for the slowing action of hydrochloric acid and of potassium chloride. It may also be seen in Fig. 1 that potassiun chloride was equally effective in slowing gastric emptying with and without 40 m-osM hydrochloric acid.

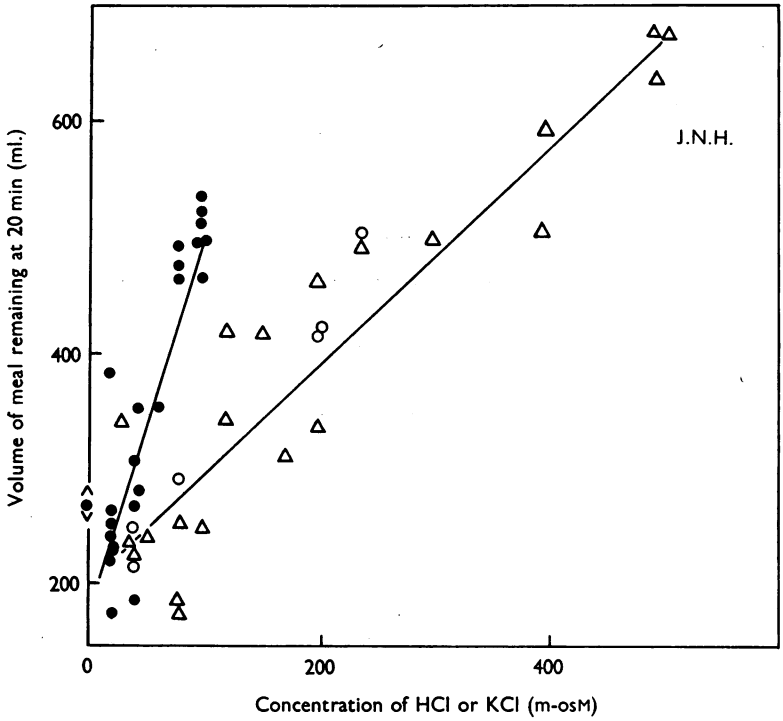

Fig. 1. A comparison of the influence of HCl (●) and of KCl (△) on the volume of test meals remaining in the stomach after 20 min.. ○ = KCl + 40 m-osmoles HCl.

Table 1 also shows data for solutions containing ammonium chloride, which was less effective per osmole in slowing gastric emptying than either ammonium sulphate or calcium chloride. Putting these data together the conclusion seems warranted that calcium and sulphate were effective, whereas ammonium and chloride were relatively ineffective, in slowing emptying.

The influence of sodium salts on the volume of meal recovered after a fixed interval

All the solutes so far considered except ammonium chloride increased the volume of meal recovered as the concentration of solute in the meal was raised. Sodium salts had a different action, as may be seen from Figs. 2 and 4 for example. As the concentrations of sodium chloride, sulphate or bicarbonate (Hunt, 1956) were raised, the volumes recovered from the stomach after a fixed interval of time fell until the concentration in the meal at the time of instillation reached about 250 m-osm with the chloride or bicarbonate, and about 50 m-osm with the sulphate. Data similar to those shown in Fig. 2 for J.N.H. were obtained for J.D.P. At higher concentrations all these salts of sodium increased the volume of the gastric contents recovered as the concentration in the test meal was raised.

TABLE 1. The influence of solutions of hydrochloric acid, sulphuric acid, potassium chloride, ammonium chloride, ammonium sulphate and calcium chloride on the volume of test meals remaining in the stomach after twenty minutes

Subject ...	J.D.P.				W.D.L.P.				J.N.H.			
Range of concentrations (m-osm)	n*	a	b	s.e. of b	n	a	b	s.e. of b	n	a	b	s.e. of b
HCl 20–100	14	375	2·66	±0·67	13	163	4·17	±0·65	22	180	3·07	±0·38
KCl 40–500	16	295	1·25	±0·20	30	265	0·95	±0·13	22	200	0·93	±0·25
	Mean volumes (ml.) of water remaining at 20 min											
Water	10	252 (s.e. ± 18)			11	319 (s.e. ± 15·3)			19	280 (s.e. ± 12·5)		
	Regression lines fitted to data including those for meals of water											
NH_4Cl 0–200	19	260	0·44	±0·16	21	323	0·20	±0·14	26	279	0·005	±0·18
$(NH_4)_2SO_4$ 0–300	19	230	0·91	±0·13	15	318	0·90	±0·18	23	273	0·64	±0·18
$CaCl_2$ 0–300	32	295	0·81	±0·14	18	327	0·86	±0·14	35	260	0·44	±0·14
H_2SO_4 0–100	14	264	4·80	±0·84	14	321	2·89	±0·50	23	242	2·60	±0·37

* y = volume of meal remaining (ml.) at 20 min; x = concentration of solute (m-osm); n = number of observations; a corresponds to the volume of meal remaining with zero concentration of solute, that is, the intercept of the regression line and the ordinate; b corresponds to the slopes of the lines as shown in Fig. 1; and $y = a+bx$.

The influence of glucose and sodium chloride together on the volume of test meal recovered after a fixed interval

Glucose added to test meals increased the volume of the test meal recovered as the concentration was raised (Hunt, 1956) like the solutes referred to in Table 1. Figure 3 gives data on the effect of various concentrations of glucose, on the relation between the concentration of sodium chloride and the volume of meal recovered after 30 min. It may be seen:

(1) That 382 m-osm glucose in the meal apparently made the volume recovered independent of the concentration of sodium chloride in the meal, that is, the highest line on the figure is horizontal;

(2) That increase in the concentration of glucose increased the volume recovered from the stomach in the presence of various concentrations of sodium chloride;

(3) That the minimum volume recovered occurred with about 50 m-OSM sodium chloride in the meal instead of 250 m-OSM sodium chloride in the absence of glucose.

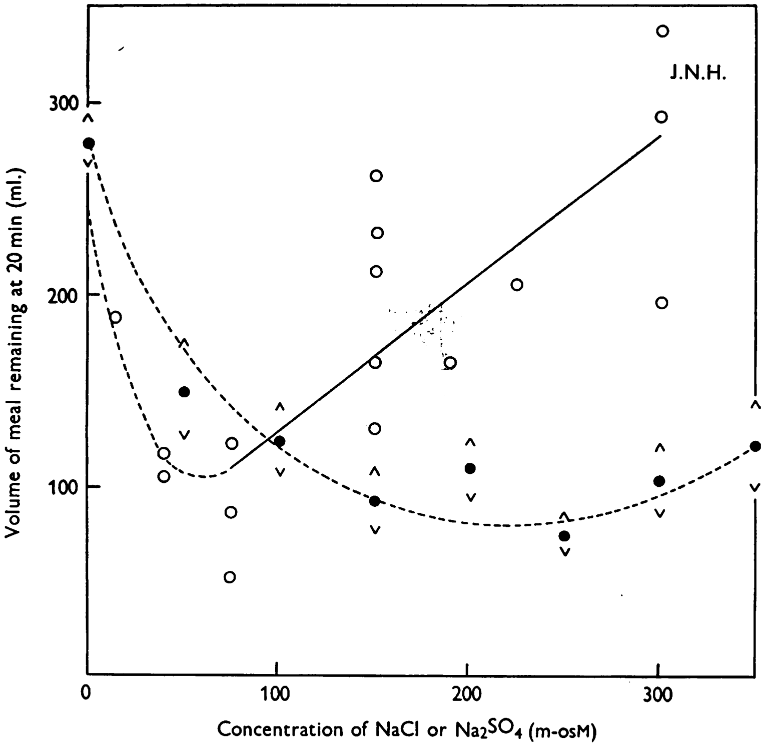

Fig. 2. A comparison of the influence of NaCl (●) and of Na_2SO_4 (○) on the volume of test meals remaining in the stomach after 20 min (J.N.H.). In all Figs. S.E. of means indicated by $\overset{\wedge}{\vee}$.

Figure 4 shows some data from experiments designed to put the conclusions from Fig. 3 on a more secure basis. In this instance the recoveries were made after 20 min and the effect of 126 m-OSM glucose and sodium chloride was compared with that of sodium chloride without glucose. The figure shows:

(1) That the concentration of sodium chloride giving a minimal recovery, that is, maximal rate of emptying, is less with 126 m-OSM glucose than it is with sodium chloride alone;

(2) That the increase in the volume recovered per osmole increase in concentration of sodium chloride in the meal is less in the presence of glucose;

(3) That at high concentrations of sodium chloride the volume recovered

with the meals containing glucose was *less* than with the meals containing sodium chloride alone.

Altogether 306 test meals of this type were given to three subjects. In the other two the results were similar to those shown in Fig. 4, except that in one the lowering of the concentration of sodium chloride giving the maximal recovery in the presence of glucose was not shown.

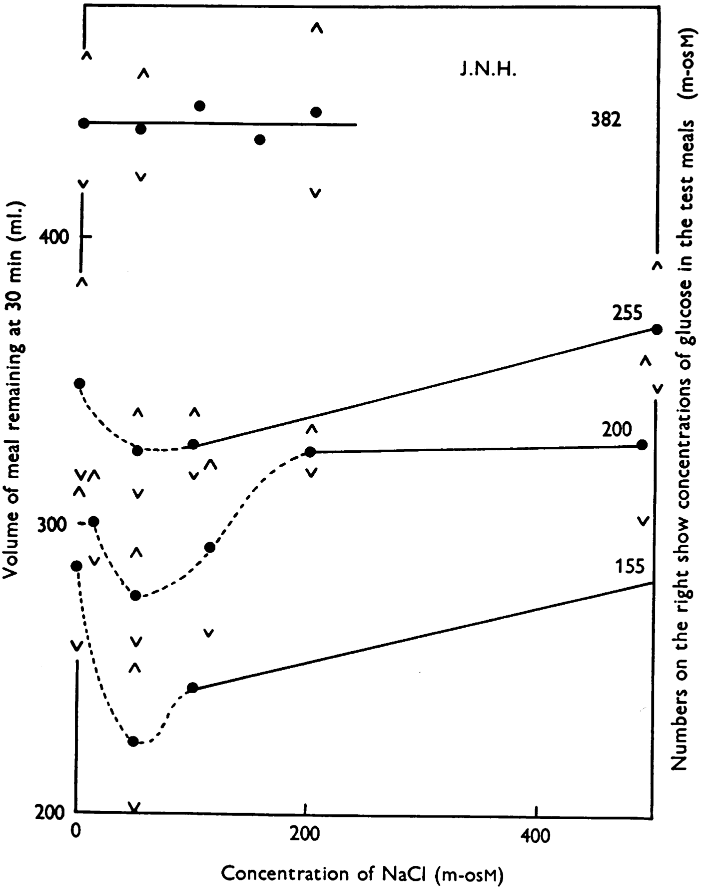

Fig. 3. The influence of different concentrations of glucose on the volume of saline solutions remaining in the stomach after 30 min (J.N.H.).

The relation between the concentration of sodium chloride and the volume of meal recovered was further studied with an experiment of the type illustrated in Fig. 3 in J.D.P. and J.N.H., with recoveries at 20 min after instillation. The slopes of the lines relating concentration of sodium chloride to volume recovered, over the range where the relationship seemed linear, are given in Table 2. The slopes became less as the concentration of glucose was raised, as may be seen from Fig. 5, in which the slopes of the lines from Table 2 have been plotted against the relevant concentration of glucose. By extrapolation the concentration of glucose abolishing the effect of the concentration of sodium chloride on the volume of meal recovered was found to be 254 m-osm for J.N.H. and 270 m-osm for J.D.P. When these values are adjusted for the osmotic coefficient of glucose they become 274 and 290, that is slightly less than isosmolar with plasma.

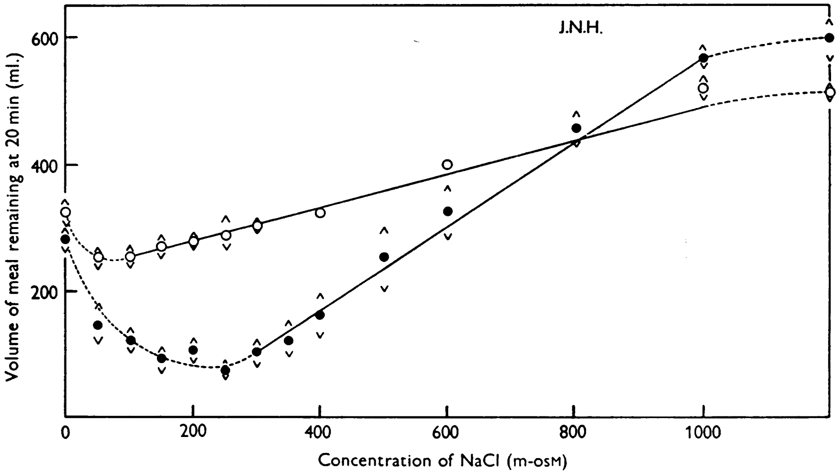

Fig. 4. The influence of the concentration of NaCl alone (●) and of NaCl in the presence of glucose 126 m-osm (○) on the volume of test meals remaining in the stomach after 20 min (J.N.H.).

Table 2. The influence of the concentration of glucose on the relationship between the volume of meal remaining in the stomach after twenty minutes and the concentration of sodium chloride in the test meal

Concentration of glucose (m-osm)	Range of concentrations of NaCl (m-osm)	J.D.P.				Range of concentrations of NaCl (m-osm)	J.N.H.			
		n	a	b	s.e. of b		n	a	b	s.e. of b
0	160–780	16	114	0·42	±0·07	350–1000	15	−105	0·68	±0·06
100	200–800	5	120	0·39	±0·09	150–800	7	124	0·385	±0·04
127	—	—	—	—	—	100–600	30	227	0·26	±0·055
155	190–810	8	265	0·16	±0·07	200–810	8	298	0·22	±0·06
200	200–800	12	370	0·17	±0·05	100–1000	10	377	0·18	±0·085
255	—	—	—	—	—	0–1000	10	505	0·036	±0·012

* y = volume of meal remaining at 20 min (ml.); x = concentration of sodium chloride (m-osm); n = number of observations; a corresponds to the volume of meal remaining with zero concentration of sodium chloride, that is the intercept of the regression line and the ordinate; b corresponds to the slopes of the lines similar to those shown in Fig. 3; $y = a+bx$.

An interesting feature of this failure of the mechanism determining gastric emptying to respond to sodium chloride in the presence of glucose can be appreciated by looking at Fig. 4. The volume of meal recovered with 1200 m-osm sodium chloride was *less* in the presence of 126 m-osm glucose than it was without the glucose, although in the absence of sodium chloride glucose *increased* the amount recovered. It seemed desirable to make a direct contrast between the influence of a constant concentration of glucose upon the response to a changing concentration of sodium chloride, and the influence of a constant concentration of sodium chloride upon the response to a changing concentration of glucose, although the general form of the relationship at concentrations of sodium chloride up to 200 m-osm is apparent from Fig. 3. Eight test meals of 30 min duration, containing varying amounts of glucose and 500 m-osm sodium chloride, were given to J.N.H.: the slope of the line relating concentration of glucose to volume of meal recovered was 1·27, s.e. ± 0·27. There is thus no doubt that sodium chloride even at a m-osm concentration greater than that of the plasma did not abolish the slowing action of glucose on gastric emptying, whereas a solution of glucose isosmotic with plasma did abolish the slowing action of sodium chloride.

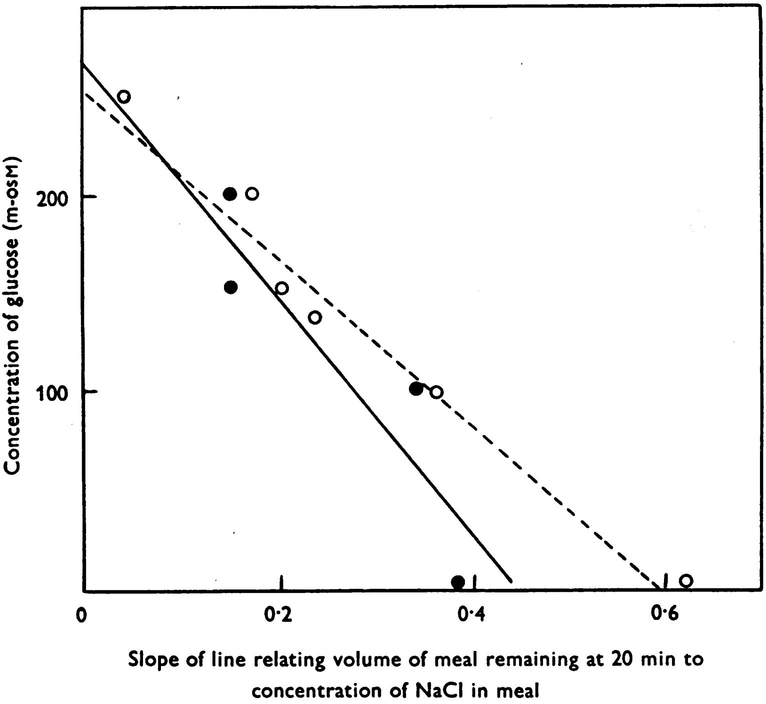

Fig. 5. The relation between the concentration of glucose in a test meal and the effect of NaCl on the volume of test meal remaining in the stomach after 20 min. ● J.D.P.; ○, J.N.H.

The influence of sodium chloride on gastric emptying in the presence of acid

Figure 6 shows the relationship based on 132 meals in three subjects between the concentration of sodium chloride in test meals and the volume

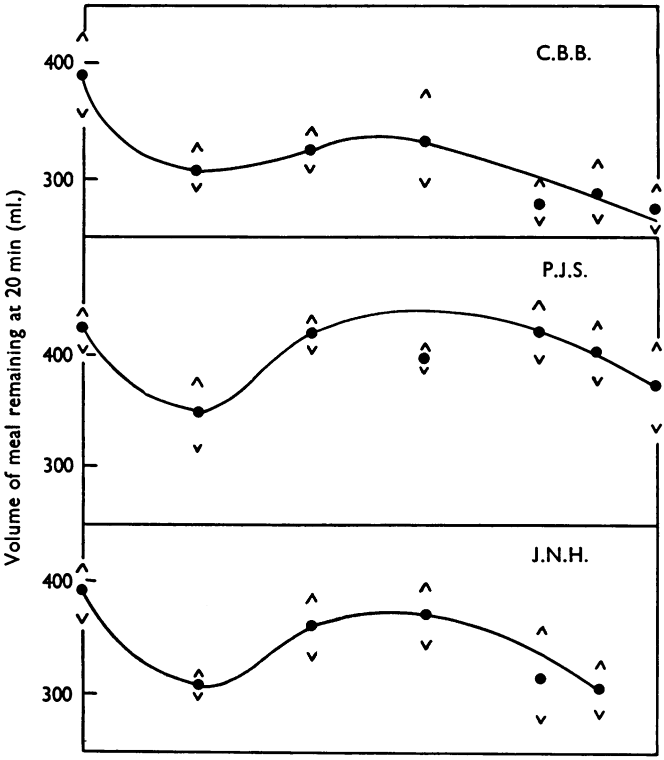

Fig. 6

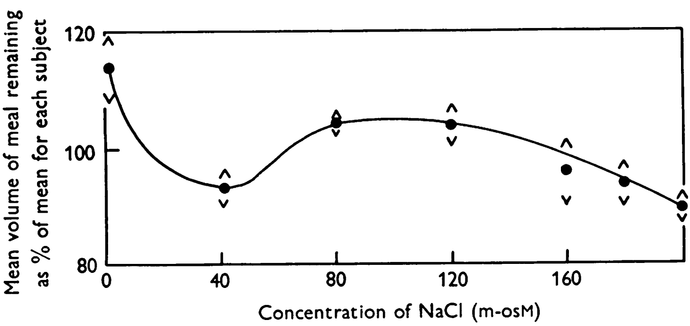

Fig. 6*a*

Fig. 6. The influence of sodium chloride in the presence of 40 m-osM HCl on the volume of test meals remaining in the stomach after 20 min (C.B.B., P.J.S. and J.N.H.); (6*a*) combined data of Fig. 6.

of meal recovered in the presence of 40 m-osM hydrochloric acid. These data were combined by expressing the volume of each recovery as a percentage of the mean volume of all recoveries for that subject. The means of these percentages for the three subjects are shown at the foot of Fig. 6. In the presence of 40 m-osM hydrochloric acid there was a lower recovery with the meal containing 40 m-osM sodium chloride than with immediately higher or lower concentrations of sodium chloride. With higher concentrations of sodium chloride the volume recovered fell as the concentration of sodium chloride was raised to 200 m-osM. It was not possible to explore the effects of higher concentrations of sodium chloride because they produced nausea.

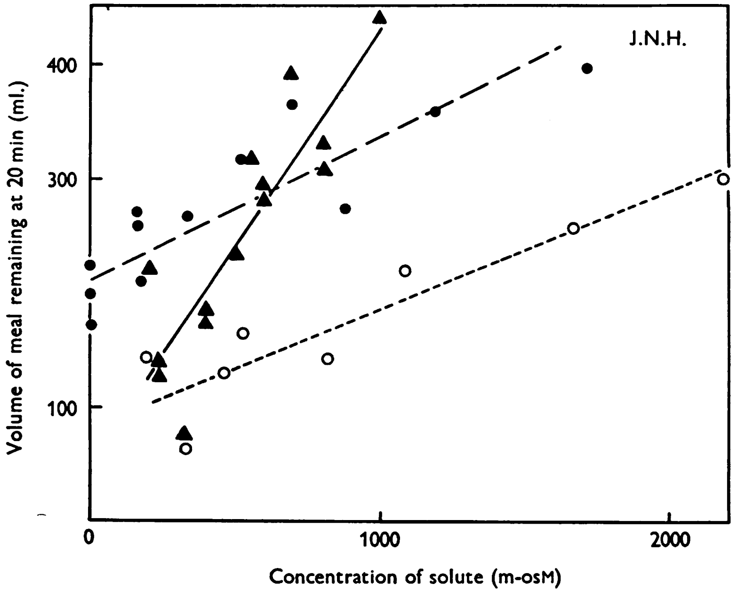

Fig. 7. The influence of ethanol (●), urea (▲) and glycerol (○) on the volume of test meals remaining in the stomach after 20 min (J.N.H.).

The influence of urea, ethanol and glycerol on the volume of test meal recovered after a fixed interval

Figure 7 shows data obtained in J.N.H. from test meals containing urea or glycerol. The response to test meals containing these solutes was similar to the response to meals containing sodium salts. There was a minimal recovery with 100–200 m-osM solutions. At higher concentrations these solutes gave progressively larger recoveries. Figure 7 also shows that with meals containing ethanol no minimal recovery was detected, the volume recovered increasing progressively as the concentration of ethanol in the meal was increased from zero.

DISCUSSION

The present experiments have confirmed the conclusions of earlier workers (Apperly, 1926; McSwiney & Spurrell, 1933; Shay, 1944) that there is a relationship between the concentration of a solute in a test meal and the rate of gastric emptying of the meal, and that this relationship varies with the solute concerned. The problem here is to describe the working of the receptor mechanism in this regulation of gastric emptying.

The rate of emptying of the stomach might be thought to depend upon the degree of distension of the duodenum or jejunum by the gastric effluent. If the original meal contained some solute which was very little absorbed, the volume of the contents of the sensitive segment might remain large as a result of the osmotic action of the solute, and gastric emptying would be slowed. Hypotheses of this kind appear to be made untenable by the equal action per osmole of calcium chloride and sulphates (Ingraham & Vissher, 1938), which are relatively little absorbed from the intestine, and glucose which is very readily absorbed. In addition, it has been found that when two meals are given in succession the second, passing into a full intestine, leaves the stomach more rapidly than the first (Hunt & Macdonald, 1954). Further, with meals of 750 ml. the 'half-life' of the emptying process is constant over the period during which the main part of the meal empties, but the fullness of the intestine must vary considerably during this time (Hunt & Macdonald, 1954). Taken together these facts suggest that some mechanism other than the fullness of the duodenum or small intestine controls gastric emptying under these conditions.

In the discussion which follows, the stimulus to the receptor mechanism has to be assumed to be adequately described by specifying the composition of the test meal. The experiments are designed to minimize the importance of any alimentary contributions to the environment of the receptor by washing out the stomach before the meal is given, by using a large volume of meal and by considering data mainly obtained from meals of short duration. At the time of the recovery the meal was usually diluted by about 10% as judged from the change in concentration of phenol red. There was no evidence that the highly concentrated solutions were more diluted in the stomach (Hunt, Macdonald & Spurrell, 1951), the greatest dilution occurring with meals which emptied rapidly, because of the smaller volume of the meal diluted by secretion and because secretion was less inhibited. At the time of the recovery the concentration in the gastric contents of acid derived from secretion was almost always less than 10 m-equiv/l., which is below the known threshold for effects on gastric emptying: and, finally, some of the receptors responding to solutes in the gastric contents probably lie just beyond the pylorus (Shay & Gershon-

Cohen, 1934), so that dilution by pancreatic secretion or bile might not influence the solution in contact with them. Considering all these points together, it may be concluded that although assessing the stimulus to the receptors from the composition of the instilled meal introduces an error it can be accepted for the moment. None of the test meals used in the experiments reported here produced nausea. Even had they done so it would not invalidate the results, since the work is concerned with the relationship between stimulus, receptors and response and not with the pathways mediating the response. It appears that the receptors of low threshold initiating the sensation of nausea lie in the walls of the duodenum (references cited by Hunt, 1956).

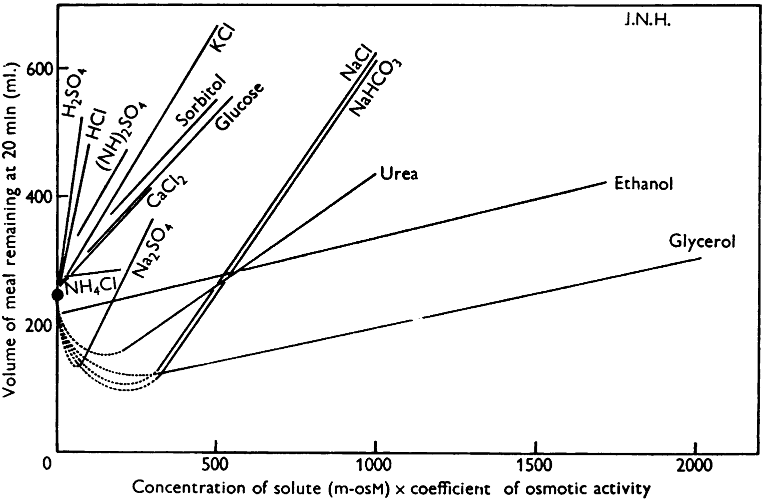

Fig. 8. The influence of the osmotic activity of various solutes on the volume of test-meal remaining in the stomach after 20 min (J.N.H.). Because Table 1 and Fig. 1, 2 and 4 include divergent data for eight meals of water obtained after the majority of the experiments in Fig. 8 were completed, the mean volume of meal of water recovered is not the same in Fig. 8 as in the other Figures. (On figure, for $(NH)_2SO_4$ read $(NH_4)_2SO_4$.)

It may be seen in Fig. 8 and Table 3 that the slopes of the lines relating the m-osM concentration of solute and the change in volume of meal recovered are approximately the same for ammonium sulphate, potassium chloride, sorbitol, glucose, calcium chloride and at high concentrations for sodium chloride, sodium sulphate and sodium bicarbonate. These compounds include combinations of monovalent and divalent anions and cations, and non-electrolytes, and it is difficult to envisage a separate receptor for each. On the other hand a single receptor responding to all more or less equally would presumably be sensitive to some common property: their osmotic activity is a candidate for consideration and there is no obvious alternative. Hydrochloric and sulphuric acids are much more potent than the solutes mentioned above, so that they probably work via a different mechanism as they do in controlling gastric secretion in the dog (Sircus, 1958). It will be assumed that the osmotic regulation of emptying depends upon a single type of receptor, although at the moment there are no grounds, apart from the principle of Occam's razor, *entia non sunt multiplicanda praeter necessitatem*, for supposing that this is so.

TABLE 3. Relative activity of solutes on the osmoreceptor mechanism in one subject

Solute	a*	b	S.E. of b	n	Range of concentrations (m-OSM)
H_2SO_4	242	2·60	±0·37	16	0–77
HCl	238	2·32	±0·11	43	0–100
HCl	180	3·07	±0·38	22	20–100
KCl	200	0·93	±0·25	21	40–500
KCl	257	0·75	±0·07	40	0–500
$(NH_4)_2SO_4$	279	0·64	±0·18	23	0–225
Glucose	260	0·57	±0·04	36	0–550
Sorbitol	281	0·50	±0·07	24	0–500
$CaCl_2$	260	0·44	±0·14	35	0–300
Ethanol	213	0·12	±0·02	12	0–1720
NH_4Cl	273	0·005	±0·18	26	0–200
Na_2SO_4	52	0·77	±0·26	13	75–300
$NaHCO_3$	−115	0·70	±0·11	12	320–1000
NaCl	−105	0·68	±0·06	15	350–1000
Urea	76	0·38	±0·10	14	200–1000
Glycerol	85	0·10	±0·02	8	330–2170

* y = volume (ml.) of 750 ml. meal remaining in the stomach 20 min after ingestion; x = concentration of solute (m-OSM); n = number of observations; $y = a + bx$; a corresponds to the volume (ml.) of meal remaining at zero concentration of solute, that is the intercept of the regression line with the ordinate.

So far the effects of solutes on gastric emptying can be described and explained in seven sections which may be more readily understood when they are considered in conjunction with Table 3 and Fig. 8.

(1) Glucose, sorbitol, sulphates, salts of potassium, calcium and at high concentrations only, sodium, have about equal effects per osmole in slowing gastric emptying. They are postulated to reduce the volume of sensitive component of an osmoreceptor responding to the contents of the alimentary lumen beyond the pylorus. These solutes are thought to penetrate the selective membrane of the osmoreceptor slowly if at all. A signal from the osmoreceptor which slows gastric emptying is postulated to occur with test meals of pure water and to increase when the flux of water into the sensitive component is reduced by the osmotic action of solutes in the lumen.

(2) Ammonium, bicarbonate and chloride are postulated to penetrate the osmoreceptor freely by diffusion and to have no effect on gastric emptying except the inhibition by the water in which they are dissolved.

However, when any one of these ions is paired with any ion listed under 1, it is restrained from penetrating by the demands of electrical neutrality and has an action per osmole equal to any solute listed under 1. There is evidence to suggest that bicarbonate may penetrate more freely than chloride (Hunt, 1956).

(3) Ethanol and, at high concentrations, urea and glycerol, are postulated to penetrate the osmoreceptor more slowly than unrestrained chloride, bicarbonate or ammonium but more rapidly than the solutes listed under 1. As these non-electrolytes continue to have an action on the hypothetical osmoreceptor for up to 20 min, their steady-state distribution across the osmoreceptor membrane presumably sets up an osmotic gradient greater than that postulated for ammonium and bicarbonate, which reduces the flux of water into the receptor.

(4) At low concentrations sodium, urea and glycerol are postulated to be subject to either facilitated diffusion or active transport into the osmoreceptor, thus favouring the flux of water into the receptor and reducing the inhibitory action of the receptor which is postulated to occur with pure water.

(5) Solutions of glucose isosmotic with plasma are postulated to make the membrane of the osmoreceptor so permeable to sodium that it neither osmotically reduces the volume of the osmoreceptor at high concentrations nor increases it at low concentrations as a result of its supposed facilitated migration into the receptor.

(6) Strong acids and glucose are postulated to have different modes of action since hydrochloric acid and glucose have different effects on the response of the osmoreceptor to sodium chloride. Moreover, strong acids are about three times more effective per osmole than the next most powerful solutes in slowing gastric emptying. These views are in harmony with those of Sircus (1958) on the control of gastric secretion.

(7) The increased rate of emptying with low concentrations of sodium sulphate may possibly be the result of the presence of bicarbonate or chloride ion secreted from the pancreas. At higher concentrations of sulphate the effect of the chloride may be masked.

In devising further studies of the supposed osmoreceptor the red cell, which has been studied as an osmometer by Ponder (1940), may provide a useful model. Many of the properties postulated for the osmoreceptor have been demonstrated for red cells: for example, facilitated migration of glycerol (LeFevre, 1948) and sodium (Davson & Reiner, 1942); increased permeability to sodium on exposure to hypertonic solutions (Davson & Reiner, 1942); penetration by ammonium (Jacobs & Parpart, 1938); slower penetration by sulphate than by chloride (Davson, 1959, from data of Luckner, 1948) and restraint of penetration of chloride and bicarbonate by potassium, sodium or calcium (Ponder, 1953) are accepted. At high concentrations the red-cell membrane behaves as though it were impermeable to glucose (Widdas, 1954). It is interesting that the very indirect approach via studies of gastric emptying can lead to postulates so similar to the known facts about red cells.

SUMMARY

1. The influence on gastric emptying of several solutes in test meals was studied by plotting the volume of test meal remaining after a fixed interval against the osmolar concentration of the solute in the original meal.

2. On an osmolar basis hydrochloric acid and sulphuric acid were about three times as potent as potassium chloride in slowing gastric emptying.

3. Ammonium sulphate and calcium chloride were two to four times more potent than ammonium chloride in slowing gastric emptying.

4. At low concentrations the addition of sodium chloride and sodium sulphate to test meals increased the rate of gastric emptying. The osmolar concentration in the meal giving a maximal rate of emptying was less for sodium sulphate than for sodium chloride. At high concentrations sodium sulphate and sodium chloride were about equally potent in slowing gastric emptying.

5. Increasing the concentration of glucose in test meals containing sodium chloride progressively reduced the action of sodium chloride on gastric emptying. At concentrations of glucose nearly isosmotic with plasma sodium chloride lost all its influence on gastric emptying. In contradistinction, solutions of sodium chloride isosmotic with plasma did not abolish the inhibitory action of glucose on gastric emptying.

6. In the presence of 40 m-osm hydrochloric acid low concentrations of sodium chloride increased the rate of gastric emptying as they did in the presence of equipotent concentrations of dextrose. A complex relationship between concentration of sodium chloride and the rate of gastric emptying in the presence of acid was defined.

7. Urea and glycerol in test meals hastened gastric emptying at low concentrations but slowed it at high concentrations. Ethanol slowed gastric emptying as the concentration was increased.

8. The findings are explained on the assumption that there is an osmoreceptor mechanism in the intestine which inhibits gastric emptying. The majority of solutes are assumed not to penetrate the receptor, but sodium, urea and glycerol are thought to be subject to facilitated transport across the osmotic membrane at low concentrations and urea and glycerol to slow diffusion at high concentrations. Solutions of glucose isosmotic with plasma are thought to make the supposed osmoreceptor permeable

to sodium. The action of acids is thought to depend upon a separate mechanism.

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