SOME ASPECTS OF GASTRIC FUNCTION IN THE NEWBORN

BY

SEYMOUR MASON

From the Children's Department, St. Bartholomew's Hospital, London

(RECEIVED FOR PUBLICATION JANUARY 23, 1962)

Gastric digestion of protein is dependent on the hydrogen ion concentration of the stomach contents. Human gastric juice will digest casein optimally in the *p*H ranges 1·8 to 2·2 and 3·5 to 3·6. Between and above these ranges hydrolytic activity rapidly declines and is minimal between *p*H 2·5 and 3·2 (Taylor, 1959). Pepsin is the main enzyme concerned, but others, i.e. parapepsins, have been demonstrated (Ryle and Porter, 1959).

At any given time the *p*H of the stomach contents will be the result of several factors. Under physiological conditions these will include free hydrochloric acid, ingested food, swallowed saliva and regurgitated duodenal contents. Other factors, such as gastric mucus, may also play a part.

During infancy gastric acidity is low, especially so in the newborn period (Miller, 1941). This low acidity together with the high buffering capacity of milk seems an unlikely combination for the production of a medium of a sufficiently low *p*H to digest protein.

The present study is concerned essentially with the *p*H changes in the newborn infant's stomach during the whole interval between feeds under as near physiological conditions as possible. In a number of cases the presence or absence of hydrolysed protein has been determined.

Methods

Studies were made on 25 healthy, full-term infants aged between 5 and 13 days. All were fed at the breast and were gaining weight satisfactorily. They were fed at approximately four-hour intervals, the first feed of the day being at 5.30 a.m. Immediately before the 9.30 a.m. feed a plastic gastric tube was passed and a specimen of stomach contents withdrawn. The tube was removed, and the baby then fed normally from the breast. After the feed the gastric tube was again passed and was kept in the stomach until just before the next feed. Samples of gastric contents were removed at intervals.

In the great majority of cases the babies slept soundly once the tube was inserted. In only one case, the author's child, was it necessary to abandon the experiment after three hours because the infant appeared unduly disturbed!

After the withdrawal of each sample the tube was filled with its own volume (usually about 1·5 ml.) of sterile distilled water and flushed through with an equal volume of air before spigotting.

The ease with which specimens could be obtained, and the gross appearances of each were noted. The *p*H was estimated immediately using narrow-range paper indicators. Where estimations of protein hydrolysis were to be made the specimens were kept under refrigerated conditions until required.

Samples obtained from nine babies at 90 and 180 minutes after the beginning of the feed were examined for the presence of hydrolysed protein. In four cases this was done by a formol titration, and in five cases a qualitative biuret test was performed after precipitating any remaining soluble whole protein with 20% zinc sulphate. In three of the cases the specimens were also incubated at 37° C. for 30 minutes at a *p*H of 2·0 both with and without the addition of pepsin, and determinations were again made.

Results

From 25 babies 192 specimens were obtained.

General Appearances. Visible bile was present in only eight specimens taken from three babies (see Table 1). In one case bile was present in the first and last specimens and in the other two it appeared between 120 and 165 minutes after the start of the feed. The presence of bile in these specimens did not materially affect the general trend of *p*H changes, and it is unlikely that the tube had entered the duodenum.

In three cases no adequate specimen could be obtained before the feed in spite of varying the position of the tube and of the baby. In one case no material was obtained after 150 minutes, although a specimen was quite easily obtained before the feed. In five cases adequate specimens were unobtainable after 180 minutes and three of these were the babies from whom no material was obtainable before the feed.

TABLE 1

RESULTS OF *p*H ESTIMATIONS OF 192 SPECIMENS OF GASTRIC CONTENTS FROM 25 BABIES

Case No.	*p*H															Remarks
	Pre-feed	Minutes After Beginning of Feed														
		30	45	60	75	90	105	120	135	150	165	180	195	210	225	
1	2·0			5·1		5·5		5·1		4·5		3·9		2·0		Formol titration
2	3·9			5·2				5·1						3·9		
3	3·9	6·1				5·1				3·9					3·9	
4	3·1*		6·7	6·7	6·7	6·7	6·1		6·1	5·8	5·2	5·1		4·5	4·5*	
5	6·1		6·7	6·7	6·4	6·4	5·8		6·1	5·5		5·1		2·8		Formol titration
6	3·9		7·1	6·8	6·1	5·8		5·2		5·1		4·5				Abandoned at 180 minutes
7	2·8	6·4		7·1	6·1		5·1		4·5		3·1		3·1			
8	2·5			6·4		6·1		5·5		3·9		3·9		2·0		Formol titration
9	3·9	6·4	6·7		6·4	5·8	5·5	5·1		4·5		3·9		3·1	2·0	Biuret
10	3·9	6·7	6·7		6·4	5·1	4·8		4·5*	5·1*		3·9		3·9		Biuret
11	2·5	7·1	6·7	6·1	5·5		5·1	5·1		2·5						Further specimens unobtainable
12		7·1	6·8	6·1		5·1	5·1		4·5	4·2		3·9				Further specimens unobtainable; biuret
13	3·9		6·1		6·1		5·8			5·1				3·9		
14	3·9		6·8	5·5	5·2		5·1		4·8		4·5		3·9		2·5	
15	2·5		5·5		5·8		5·5			5·2		5·1				Further specimens unobtainable; biuret
16	4·5	5·5			5·1				4·5					2·5		
17	4·5		7·1	7·1	7·1		6·8	6·4*	6·1*	5·8*	5·5*		5·1		4·8	
18	2·5	5·2		5·1	5·1		5·1		5·2		5·1		4·2		3·9	
19		6·8			7·1		6·7				4·5					Further specimens unobtainable
20		6·8		6·8		5·1		4·5		4·5	3·6					Further specimens unobtainable
21	3·9		6·8		6·1			5·5				4·5		3·9		
22	2·0			5·1		5·1		4·8		3·9		3·9†				Further specimens unobtainable; biuret
23	2·8		5·5	5·8	5·2		4·8		4·5			3·9			2·5	
24	3·9	6·7		6·1	5·8		5·2	5·2		4·5		3·9		2·8		
25	4·5	6·1	5·8		6·1	6·1		5·1		4·5			4·2		3·9	
Maximum ..	6·1	7·1	7·1	7·1	7·1	6·7	6·8	6·4	6·1	5·8	5·5	5·1	5·1	4·5	4·5	
Minimum ..	2·0	5·2	5·5	5·1	5·1	5·1	4·8	4·5	4·5	2·5	3·1	3·9	3·1	2·0	2·0	
Mean ..	3·5	6·4	6·5	6·3	6·0	5·7	5·5	5·2	5·1	4·6	4·5	4·3	4·1	3·2	3·5	

* Bile-stained. † Biuret positive.

These observations reflect the variability of the rate of gastric emptying in different babies and from time to time in the same baby. In the majority of cases some food still remained in the stomach immediately before a feed and sometimes, judging by the ease with which a specimen was obtained, the amount seemed considerable. In most instances, however, the amount was quite small.

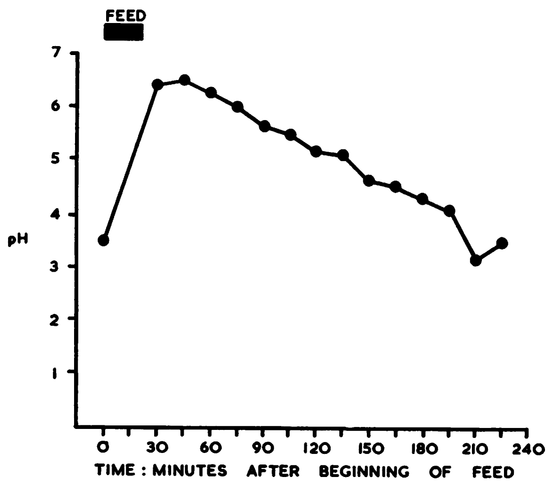

FIGURE.—Curve showing mean values of *p*H of the stomach contents of 25 newborn infants during the interval between feeds.

Casein curds were present in every specimen examined even when the amount of material was minimal. The first post-feed specimens in this series were collected 30 minutes after the beginning of the feed, and precipitation of breast milk caseinogen, therefore, occurs within this period of time.

There appears to be no connexion between gastric emptying and crying for food. The six babies whose stomachs were empty after 180 minutes were all sleeping peacefully and continued so until the next feed was due. The one baby in whom the procedure was abandoned at 180 minutes because of undue restlessness appeared to have a reasonably full stomach at that time.

***p*H Results.** The results of the *p*H estimations are shown in Table 1 and the arithmetical mean of these results is plotted (Fig.).

The method used for the estimations of the *p*H in this series has been shown to give results which correlate well with those obtained with the Beckman glass electrode meter in the *p*H range 1 to 6 (Sippy and Fitzsimons, 1959).

The entry of milk into the infant's stomach occasions a sharp rise in the *p*H. The peak value is maintained for about 60 minutes following which there is a gradual fall. In only a relatively few instances does the *p*H come within or near the optimal ranges for the digestion of casein and then not until well after 120 minutes from the beginning of the feed.

In the greater majority of cases very little food is present in the stomach when the *p*H has fallen to these low levels.

Estimations of Protein Hydrolysis. Examination of 17 specimens from nine babies was carried out for evidence of protein digestion. Eight of these specimens were collected at 90 minutes after the start of the feed and their *p*H ranged between 5·1 and 6·4. No hydrolysed protein was detected in these specimens.

The nine specimens collected at 180 minutes after the start of the feed had a *p*H range of 3·9 to 5·1. In one specimen a small amount of hydrolysed protein was found at a *p*H of 3·9. None was detected in the other eight.

Incubation for 30 minutes at 37° C. of three of these 90-minute specimens with the *p*H adjusted to 2·0 still produced no evidence of protein digestion. The addition of pepsin, however, produced considerable protein hydrolysis at this level.

The three specimens collected at 180 minutes, and treated similarly, included that in which a small amount of digested protein had been found. In the latter instance adjusting the *p*H to 2·0 produced no greater amount of hydrolysis as judged by the intensity of the biuret colour change. In the other two specimens no hydrolysed protein was found at *p*H 2·0, but in all three the addition of pepsin at this level again led to a very marked colour change.

These results suggest that either (1) little or no proteolytic enzyme is secreted in the newborn infant's stomach, or (2) such amount as is produced is completely or almost completely inactivated at the high levels of *p*H that are normally attained or (3) none is secreted until about the fourth hour after a feed.

Discussion

Breast milk protein is precipitated within 30 minutes of its entry into the stomach of the newborn baby. In this series this occurred in the *p*H range 5·2 to 7·1. The formation of the casein curd is often regarded as a somewhat unphysiological phenomenon. Wolman (1946), however, considers coagulation of milk protein to be a first step in its dissociation, precipitated paracasein being molecularly less complex than its soluble precursor. He also suggests (Wolman, 1943) that the thick curd formed in some animals' stomachs can only pass slowly into the gut and more adequate gastric digestion is thus facilitated. Marriott and Davidson (1923) have suggested that the formation of insoluble protein prevents its absorption through the intestinal wall. It may well be that soluble whole protein can be absorbed through the stomach wall, and if caseinogen is not to be digested in the stomach its early precipitation is obviously essential.

While considerable variations obviously exist in the rate and extent of gastric emptying, Henderson (1942), by a radiological study of the situation in the newborn, has been able to establish some constancy of pattern. He showed that the pylorus relaxes during feeding, and much of an ingested meal passes directly into the duodenum. For the first hour following this, the stomach is relatively quiescent, but during the second hour vigorous peristalsis drives a large part of the gastric contents through the pylorus. There then follows a further period of relative quiescence, and any food remaining in the stomach changes little in amount until the next feed is given.

If these findings are correlated with the results of the present study it will be seen that the major part of a newborn infant's feed leaves the stomach without any possibility of protein digestion having occurred.

Some of the material entering the duodenum will be pure milk with little or no admixture of gastric secretions. Much of the material, having been in the stomach for up to two hours, will be at a *p*H just on the acid side of neutral. Whether this acidity is sufficient and will be maintained for a sufficient length of time to enable the infant to absorb adequate soluble iron and calcium salts in the duodenum and upper ileum to keep it in positive balance as regards these elements is doubtful. It is more probable that in the newborn infant the absorption of calcium, and possibly of iron, is dependent on the formation of soluble amino-acid complexes (McCance, Widdowson and Lehmann, 1942).

There is little doubt that the newborn infant is capable of producing gastric proteolytic enzymes, and these have been demonstrated in the 16-week foetus (Keene and Hewer, 1929). It appears,

TABLE 2

SUMMARY OF PREVIOUS INVESTIGATIONS INTO *p*H OF CONTENTS OF INFANTS' STOMACHS

Authors	Number of Babies Investigated	Ages of Babies	Time After Feed When Observations Made (min.)	Test Feed	*p*H	
					Range	Mean
Hahn (1914)	37 (94 specimens)	<12 months	45–135	Cow's milk and water		5·0
Davidsohn (1921)	9	< 4 months	60	(*a*) 1 part cow's milk, 2 parts water	4·1–5·8	5·1
				(*b*) 2 parts cow's milk, 1 part water	3·1–5·6	4·9
Babbott, Johnston, Haskins and Shohl (1923)	43 (227 specimens)	3–19 months	60	Reconstituted dried milk	3·2–5·0	
Marriott and Davidson (1923)	40	<12 months	120	Breast milk		3·75
	12	<12 months	120	Undiluted cow's milk		5·1
	17	<12 months	120	Lactic acid milk		3·71
Griswold and Shohl (1925) ..	25	5 days	60	50 ml. of reconstituted dried milk	2·0–2·8	2·5
	25	10 days	60		2·1–3·0	2·5
Wills and Paterson (1926) ..	6	1–7 months	60–90	Breast milk	2·0–3·2	2·7
Klumpp and Neale (1930) ..	10	1–3 months	1 hour after feed entered duodenum	Cream	2·6–5·0	4·0
	13	3–12 months	1 hour after feed entered duodenum	Cream	2·7–5·8	4·3

however, that little or none is secreted in the newborn baby in response to the ingestion of breast milk. In this series only one of nine babies had digested protein in its stomach after three hours, and then only to a minor degree. It is most improbable that pepsin is only secreted in the fourth hour after a feed when the amount of food remaining in the stomach may be very little.

A number of investigations into the *p*H changes in infants' stomachs following feeds have been made by various workers. The only paper concerning the newborn appears to be that of Griswold and Shohl (1925). They found a *p*H range of 2·0 to 2·8 in the stomachs of 25 babies one hour after a feed of 50 ml. of a reconstituted dried milk. At this time they noted that very little food was remaining in the stomach and took this as an indication of the completeness of gastric digestion. In the present series such low *p*H levels only occurred towards the end of the four-hour interval between feeds when the amount of food remaining in the stomach was usually quite small. It is probable that with the small feed given by these workers the stomach emptied more rapidly than it would have done under more physiological conditions.

After the newborn period, acid secretion increases with the growth of the infant (Miller, 1942). Suitable conditions for the gastric hydrolysis of casein might be produced, therefore, in the stomachs of older babies. To balance the increased acidity, however, there is an increasing intake of milk. The results of previous investigations into the *p*H of gastric contents of older infants are summarized in Table 2. The variability of these figures is at least partly due to the different 'test feeds' used, the varying times after the feeds at which samples were taken and the different ages of the infants. As might be expected, the figures are somewhat lower than those found in the present series, but are generally well outside the optimal ranges for casein digestion. Berfenstam, Jagenburg and Mellander (1955), however, have detected traces of hydrolysed protein in the stomachs of older infants by estimations of the percentage of amino nitrogen to total nitrogen. Oddly enough they found a greater degree of digestion with cow's milk than with breast milk.

In older children conditions are still far from favourable for any advanced degree of gastric hydrolysis of cow's milk protein (Wolman, 1946), and a consideration of the work of Beazell (1941) and of Borgström, Dahlquist, Lundh and Sjövall (1957) indicates that even in adults optimal conditions are by no means invariably attained.

The stomach is thus little concerned in the digestion of milk protein throughout life, but least so in the newborn period when milk normally forms the only source of dietary protein.

At this time of life the hydrolysis of milk protein is almost entirely dependent on intestinal enzymes acting at high *p*H levels. In view of this one might wonder about the value of acidified milk as an aid to gastric digestion at this age or even in older infants. The use of this milk in early infancy is not without danger (Faber, 1923; Goldman, Karelitz, Seifter, Acs and Schell, 1961).

Summary

The *p*H changes in the gastric contents during the entire interval between feeds have been determined in 25 healthy, breast-fed, newborn infants.

In only a minority of cases did the *p*H fall to levels where any degree of casein hydrolysis could occur.

At such times, usually during the fourth hour after a feed, there was little food remaining in the stomach.

Hydrolysed protein was found in the stomach of only one of nine babies three hours after the beginning of the feed, and then only to a minor degree.

The absorption of calcium and iron in milk-fed infants cannot be entirely dependent on the formation of soluble acid salts in the small bowel.

There appears to be little or no *theoretical* indication for the use of acidified milk as an aid to gastric digestion in infancy.

I am indebted to Dr. Charles Harris for his encouragement and valuable advice during the course of this work and for permission to study patients under his care. Dr. C. J. B. Fenton devised and carried out the experiments for the detection of hydrolysed protein, and I am extremely grateful for his advice and help. The unfailing co-operation of Miss M. Bigmore and Miss H. Gribble, Sisters, Martha Ward, is very much appreciated.

References

Babbott, F. L., Johnston, J. A., Haskins, C. H. and Shohl, A. T. (1923). Hydrogen-ion concentration of gastric contents of infants. *Amer. J. Dis. Child.*, **26**, 475.

Beazell, J. M. (1941). A re-examination of the role of the stomach in the digestion of carbohydrate and protein. *Amer. J. Physiol.*, **132**, 42.

Berfenstam, R., Jagenburg, R. and Mellander, O. (1955). Protein hydrolysis in the stomachs of premature and full term infants. *Acta paediat. (Uppsala)*, **44**, 348.

Borgström, B., Dahlquist, A., Lundh, G. and Sjövall, J. (1957). Studies of intestinal digestion and absorption in the human. *J. clin. Invest.*, **36**, 1521.

Davidsohn, H. (1921). Beitrag zur Physiologie und Pathologie der Magenverdauung beim Säugling. *Arch. Kinderheilk.*, **69**, 239.

Faber, H. K. (1923). Hydrochloric acid milk in infant feeding. *Amer. J. Dis. Child.*, **26**, 401.

Goldman, H. I., Karelitz, S., Seifter, E., Acs, H. and Schell, N. B. (1961). Acidosis in premature infants due to lactic acid. *Pediatrics*, **27**, 921.

Griswold, C. and Shohl, A. T. (1925). Gastric digestion in newborn infants. *Amer. J. Dis. Child.*, **30**, 541.

Hahn, M. (1914). Gastric digestion in infants. *ibid.*, **7**, 305.

Henderson, S. G. (1942). The gastrointestinal tract of the healthy newborn infant. *Amer. J. Roentgenol.*, **48**, 302.

Keene, M. F. L. and Hewer, E. E. (1929). Digestive enzymes of the human foetus. *Lancet*, **1**, 767.

Klumpp, T. G. and Neale, A. V. (1930). The gastric and duodenal contents of normal infants and children; duodenal enzyme activity and gastric and duodenal reactions (H-ion). *Amer. J. Dis. Child.*, **40**, 1215.

McCance, R. A., Widdowson, E. M. and Lehmann, H. (1942). The effect of protein intake on the absorption of calcium and magnesium. *Biochem. J.*, **36**, 686.

Marriott, W. McK. and Davidson, L. T. (1923). The acidity of the gastric contents of infants. *Amer. J. Dis. Child.*, **26**, 542.

Miller, R. A. (1941). Observations on the gastric acidity during the first month of life. *Arch. Dis. Childh.*, **16**, 22.

—— (1942). Gastric acidity during the first year of life. *ibid.*, **17**, 198.

Ryle, A. P. and Porter, R. R. (1959). Parapepsins: two proteolytic enzymes associated with porcine pepsin. *Biochem. J.*, **73**, 75.

Sippy, H. I. and Fitzsimons, E. J. (1959). Measurement of free acid in gastric juice by means of indicator paper. *J. Amer. med. Ass.*, **170**, 1157.

Taylor, W. H. (1959). Studies on gastric proteolysis. I. *Biochem. J.*, **71**, 73.

Wills, L. and Paterson, D. (1926). *A study of gastric acidity in infants. Arch. Dis. Childh.*, **1**, 232.

Wolman, I. J. (1943). Gastric digestive secretions in infancy and childhood: a review. *Amer. J. med. Sci.*, **206**, 770.

—— (1946). Gastric phase of milk digestion in childhood. *Amer. J. Dis. Child.*, **71**, 394.