

# GASTRIC SECRETION IN INFANTS AND CHILDREN

BY

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A simple, rapid and satisfactory method of investigating the gastric secretion in infants and children is of undoubted value in their clinical investigation. The difficulties experienced by the use of the ordinary methods in children necessitates a new approach. With the usual method of passing a gastric tube followed by a test meal, the psychical and physical disturbances which ensue must have an adverse effect upon the functions in question. The swallowing of considerable amounts of saliva and mucus introduces difficulties. The gastric fluid removed after a test meal consists of an intimate mixture in which there is no pure gastric juice. The juice has undergone considerable change, such as dilution, buffering and partial neutralization. The variations in the type of meal used, both qualitatively and quantitatively, the frequency of vomiting during the test, and the length of time usually required for its completion all tend to lessen the value of the method.

Our aim therefore has been to elaborate a technique which eliminates swallowing a meal and at the same time causes no disturbance to the child. In order to dispense with the neutralizing and buffering effects of the milk meal, a dilute aqueous solution of ethyl alcohol has been used, following the suggestion of Chesney<sup>1</sup>.

In all the experiments used for this investigation, the conditions were kept as constant as possible. The collections were made in the morning after a night's fasting, except in the case of infants where there was an interval of about six hours. A special tube was devised, consisting of a small narrow perforated light metal tip connected to very narrow rubber tubing, the width allowing the tube to be passed easily through the nose of even the smallest child. The nasal route has several particular advantages, causing much less general disturbance, no vomiting, and no increased salivation, because the soft rubber does not irritate the tongue or pharyngeal wall, and also allows the child to breathe easily and eliminates damage to the tube by the teeth. The metal tip aids in guiding the tube into the oesophagus and provides a means of moving the aspirating end around in the stomach in order to obtain all the fluid therein. The resting juice is completely aspirated with a syringe; 20 to 40 c.cm. of neutral 7 per cent. ethyl alcohol in distilled water at body temperature is introduced slowly into the stomach through the tube. The child is quite unconscious of the admission of the fluid and remains undisturbed. No swallowing occurs and salivation is at a minimum. At intervals of ten

or fifteen minutes over a period of one hour, 10 c.cm. are removed, the stomach being completely emptied at the final aspiration. Normally the fluid obtained is clear and watery.

Information obtainable from these specimens includes the presence or absence of suspended matter, and the acidity. No absolute values for the volumetric gastric secretion can be obtained by this method because there is no control of the volume of alcohol-water which has left the stomach either by absorption or passage onwards. However, in cases where only a knowledge of a qualitative acid secretion is desired the information is yielded. In a large series of infants and children no instance occurred where the alcohol-water failed to excite a flow of acid gastric juice, but in some cases the secretion apparently ceased after thirty minutes.

Owing to the confusion which has appeared in medical literature concerning the terms achlorhydria and achylia gastrica, it appeared imperative that in all cases where an apparent failure of acid gastric secretion occurred after the ordinary meal stimulus, or if anacidity was found, a convenient or separate test should be carried out by the use of histamine as detailed below, the gastric tube being left in situ.

#### **Investigations with histamine.**

This substance, a decarboxylation product of histidine, was introduced for use in man by Carnot in 1922, who observed an active secretion of acid gastric juice following injection. Since this date various investigators have used the substance in experimental studies on gastric secretion in adults; the work having been facilitated by the preparation of histamine in a pure state. Pharmacologically it is practically ineffective when given by mouth, but by subcutaneous injection it causes a transitory circulatory effect by capillary dilatation as seen by cutaneous flushing. With a dose sufficient to produce a maximal flow of gastric juice no adverse symptoms are produced. In a very large series of patients, the specially pure product of Imido-Roche of Paris has given excellent results. The stimulation of gastric secretion would appear to be a specific effect of the substance. Evidence has recently been obtained to show that no stimulation occurs in the case of the other digestive secretions.

Until the present investigation was carried out, histamine had been used on adults only. Polland<sup>2</sup> observed that variations in the height of chloride concentration in the gastric secretion after histamine represented individual differences. It is unknown whether chloride always leaves the secretory cells at a constant rate, but the juice as poured into the stomach shows differences in various people. The general character, however, of the curve of secretion volume is similar in all persons, there being a rapid rise in volume during thirty minutes immediately following histamine, and a continued fall thereafter until at sixty minutes the previous resting rate is regained. In pure specimens the curves of the titratable acidity and total chloride run practically parallel. The former may therefore be utilized as a fairly accurate measure of the chloride-secreting power of the stomach following histamine stimulation.

Polland's observations indicate that provided that pure gastric juice is examined, the titratable acidity at the height of secretion furnishes an index of the acid secreting power of the stomach glands, as it falls short of the actual chloride secretion by a constant amount. Careful observations show that all the gastric secreting functions show a co-ordinated response to histamine. Increase in titratable acidity results in a greater output of chloride than of base. Nitrogen is also actively secreted. The non-protein nitrogen secreted is proportional to the concentration in the blood, but like the total chloride content, it is always below the blood level.

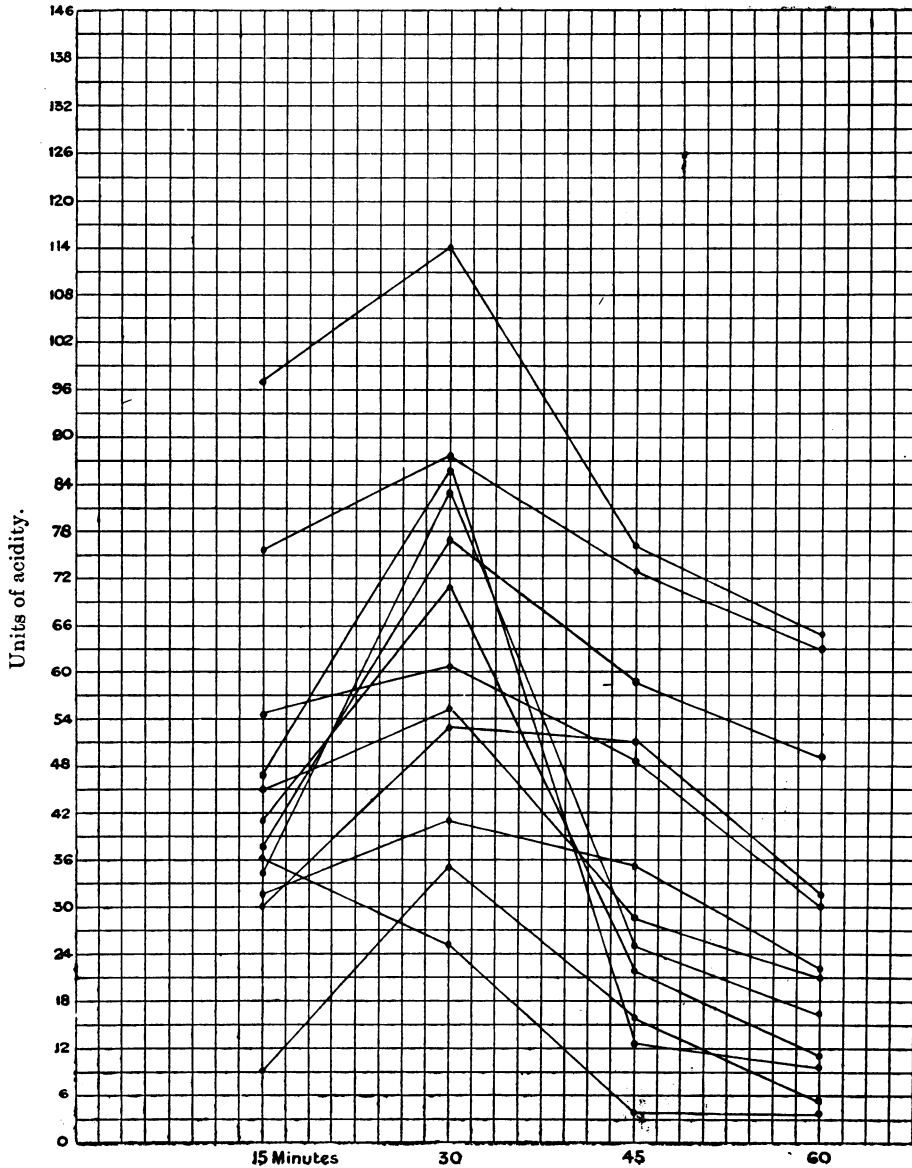
Active secretion of peptic enzyme also follows the injection of histamine. Cassel<sup>3</sup> has adequately demonstrated the power of histamine juice to digest protein. This worker has successfully carried out experiments which show that the juice rapidly converts inactive beef-steak into an active form which stimulates the production of a reticulocyte response in pernicious anæmia. There appears to be little doubt, therefore, that the gastric secretion following histamine injection is physiological in nature and represents the maximal functional level of the gastric secretory power in the individual concerned. Histamine injection in pernicious anæmia fails to produce any acid gastric secretion. By this means the true achylia gastrica is confirmed. Many conditions have been described as associated with achylia gastrica. These ideas have been dispelled since the active functional power following histamine has been determined. Atropine has no inhibitory effect upon the gastric action of histamine. Bloomfield and Polland<sup>4</sup> have further shown that repeated examination in the same person after a similar dose of histamine produced secretion curves in almost complete agreement. It is obvious, therefore, that the method may be applied for the study of the secreting powers of the stomach in children provided an accurate knowledge of the suitable dose of histamine for the child's weight and age is known. Careful experimentation has furnished an optimum dosage for the different age-groups studied in this paper.

The object of the present investigation following the use of histamine was to determine if possible the volume and acidity of the pure gastric secretion occurring in infants and children. Obviously, by other methods, such as the use of test meals or even of alcohol-water mixture, this information has been impossible to obtain. By the use of histamine no diluent action or other disturbing factor is introduced. By experience of the action of histamine during duodenal drainage experiments it has been learned that the secretion of the stomach following injection remains within the stomach during the period under investigation :—namely, the sixty minutes immediately following. Hence volumetric estimation of the gastric secretion is rendered fairly accurate by the method.

**Dosage.**—The optimum quantity of histamine (Roche) to be used has been determined by a large number of experiments. Careful use of a range of doses in the same patient, in several instances, has shown that there is a certain optimum quantity of histamine which will produce a maximum acidic concentration in the individual. A greater dose will produce a larger volume.

but the acidity remains approximately the same as with the smaller optimum dose. In the different age groups studied, fortunately the optimum dose has been found to coincide with the amount which produces signs of general

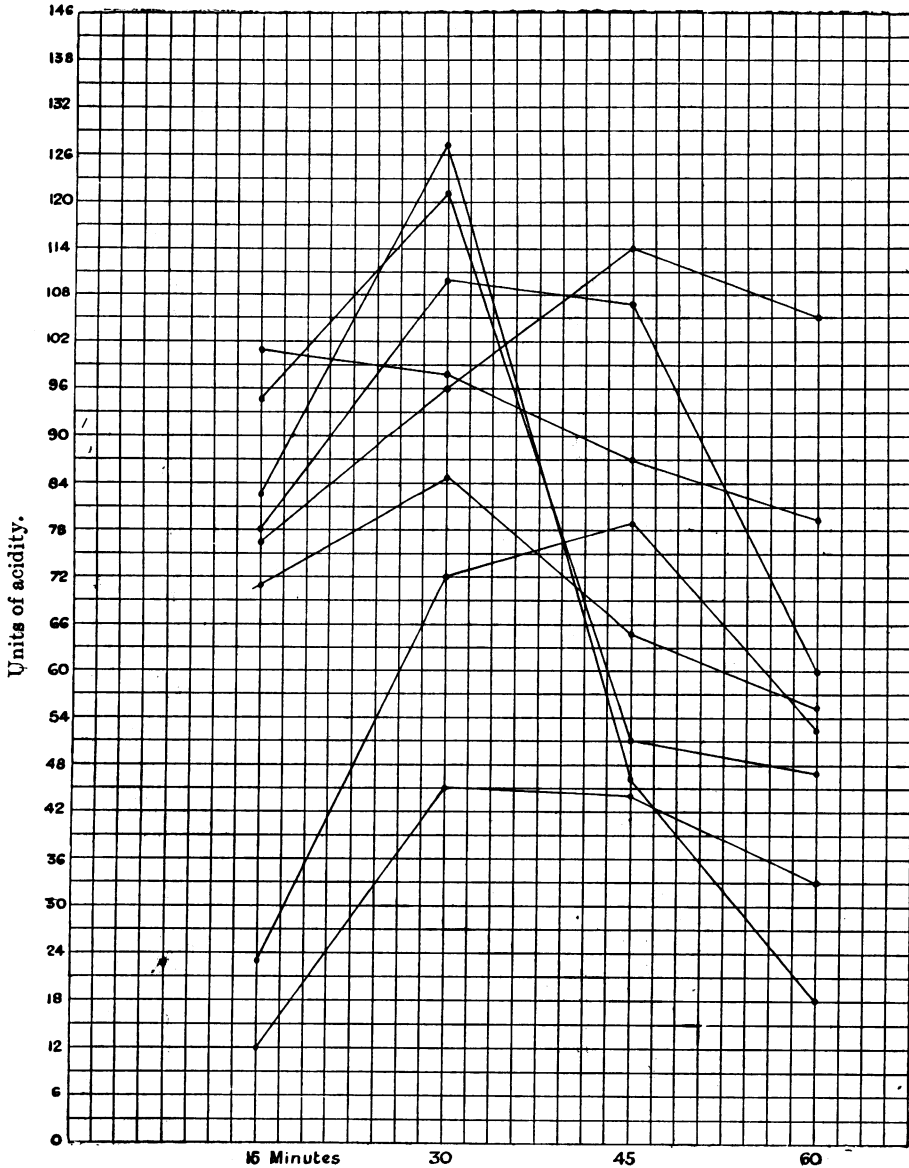
CHART A.  
INFANTS AGED  $\frac{1}{2}$  TO  $1\frac{1}{2}$  YEARS. GASTRIC ACIDITY.



histamine effect without any adverse reactions. The reactive indications are a moderate generalized cutaneous hyperæmia and a slight acceleration of the pulse rate, without headache or signs of collapse. No rule could be adopted for calculation of the adequate dose according to the child's weight

but trial has shown that up to 2 years of age 0.15 mgrm., from 4 to 6 years 0.2 mgrm., and from 10 to 12 years 0.3 mgrm. have been correct for individuals within the average.

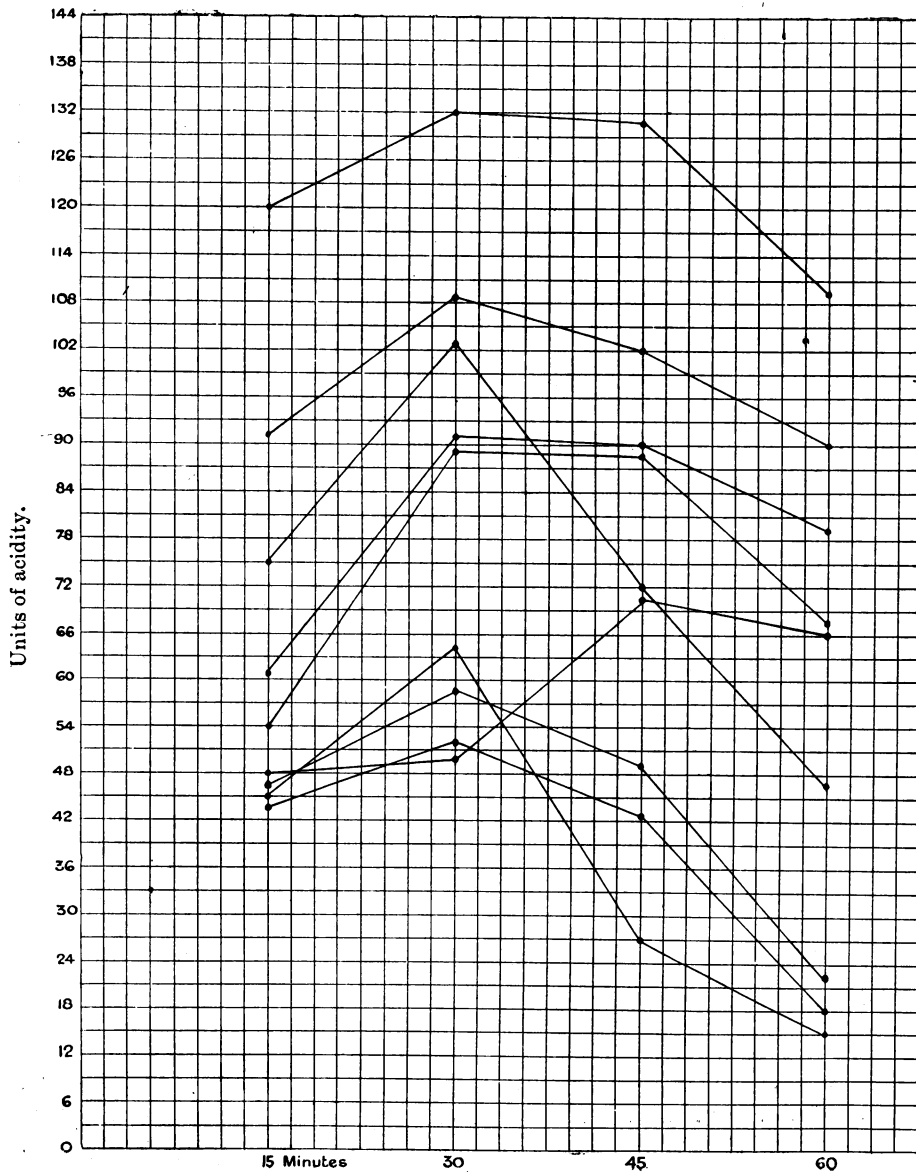
CHART B.  
CHILDREN AGED 4 TO 6 YEARS. GASTRIC ACIDITY.



**Procedure.**—The patient is kept lying down and quiet. Usually the experiment is carried out in the morning immediately following the night's fast. In the case of infants an interval is allowed of four or five hours after the last feed, which should be glucose water instead of milk. Under these

conditions the gastric secretion obtained is devoid of food substances. The tube as previously described is inserted, and the patient allowed to settle down for about a quarter of an hour. Any gastric contents are removed. Histamine is then injected subcutaneously in the dose adequate for the age and size of the patient.

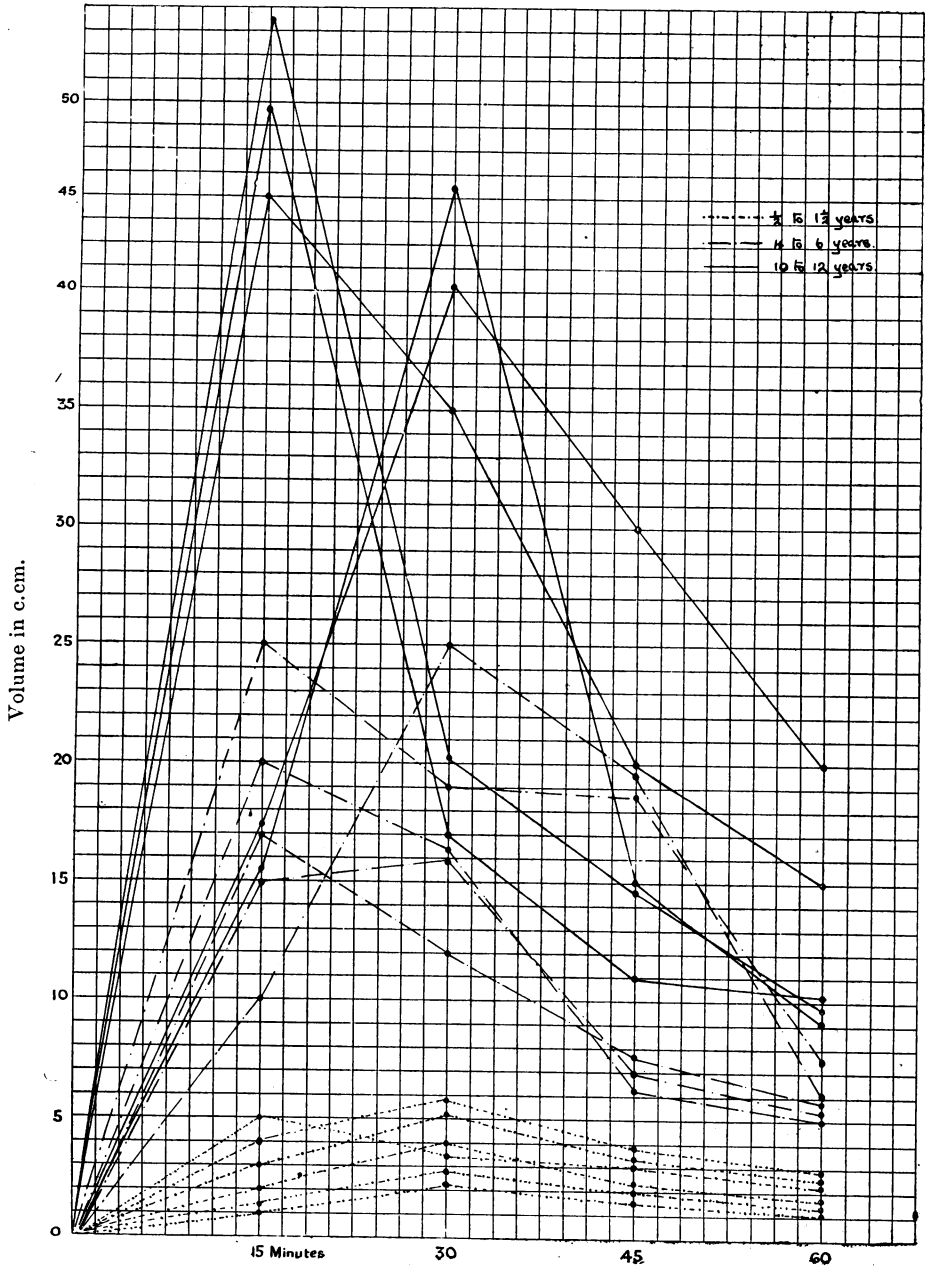
CHART C.  
CHILDREN AGED 10 TO 12 YEARS. GASTRIC ACIDITY.





Every fifteen minutes for one hour following injection the stomach contents are removed by suction with a syringe attached to the tube in situ. No disturbance whatever of the patient occurs and gentle movement of the patient on to the left and right sides alternately enables the metal tip to move

CHART D.  
VOLUME OF GASTRIC JUICE IN THE THREE AGE GROUPS.



within the stomach and so allows complete removal of all the secretion during the experiment. Since the gastric juice obtained is watery no difficulty is found in its removal. The fifteen-minute specimens are kept separately; each is examined for acidity and its volume also recorded. The pure specimens may be used for the determination of enzymes, base, and nitrogen, if desired. From the data obtained the chloride-secreting power of the stomach and the volumetric response to a fixed adequate stimulus is determined.

**Results.**—The secretion of acid in the gastric juice of normal healthy children of three distinct age groups is shown in Charts A, B and C. Examination of a large series of cases in each group has been made, but only a number of these are included in the charts. It will be seen that each chart is similar in that in most cases the acidity reaches a maximum within thirty minutes after the histamine is given, and falls thereafter. A few exceptions to this occur, but the fall is always seen within an hour. In each age group there is a considerable range of maximal acidity, although the type of curve is similar in each case.

The volume of gastric juice secreted following the fixed adequate dose of histamine is shown in Chart D. As in the above series, three age groups were examined. Certain outstanding points are quite obvious. During the first year or so of life the total volume does not exceed 15 c.cm. in any case. A considerable rise in volume is obtained in the group aged from 4 to 6 years. Even a greater increase is shown in the eldest group aged from 10 to 12 years. In all the groups the larger volume is obtained during the first half-hour after histamine injection.

In carrying out a number of experiments it was immediately recognized that the physical characters of the pure gastric secretion obtained from the infant are distinctive. The juice is of viscid consistence, somewhat opalescent and odourless. The secretion removed from the older child is watery and clear with a characteristic odour.

#### DISCUSSION.

Certain comparisons can be made between the acid secretion in children obtained by this method and that obtained by Ryle<sup>5</sup> using the fractional test meal. Although the test meal introduces factors of dilution, buffering and so on, Ryle's series of 100 normal young adults shows the same outstanding fact, namely, the variability of the maximal acid concentration in a group of healthy individuals of similar age. This variation is apparent in all age groups. The results obtained here in children are confirmatory of those obtained by Ryle in adults. It would therefore appear that high or low gastric acidity is a quality inherent in the individual even in very early life. As in Ryle's series, it is probable that a large percentage of cases falls into a medium range and the extreme ranges are in the minority.

What is the significance of the very small volume obtained in the infant and the relatively greater volume in the older child? In several instances, where a tube has been inserted in the duodenum to check the absence of loss of gastric juice from the stomach, 120 c.cm. have been obtained, and in two cases 140 c.cm. were removed in the course of an hour from children aged



about 10 years. It would appear that the larger volume obtained cannot be due simply to the naturally larger stomach in the older child. A more plausible hypothesis would be that the volumetric secretion is a reflection of the nature of the diet at the different ages. It is suggested that the small volume of viscid fluid in the infant is a concentrated medium to allow of adequate dilution by the relatively large fluid volume of the milk diet; while on the other hand, in the child advanced beyond the milk feeding age, the copious secretion is possibly a provision for the more solid foodstuffs and the adequate formation of the chyme. The small total quantity of acid present in the infant's secretion is rapidly diluted and buffered by the milk foods. This explains the higher acidity in the chyme of the child than in the infant. It is unusual for the reaction of the chyme in an infant to be more acid than pH 4.0 or 3.5. Some unpublished recent experimental work by Esslemont<sup>6</sup> shows that even where the acidity in the infant's stomach is higher than this, the duration of a range of acidity compatible with peptic digestion is only maintained for a short period of time, rarely more than fifteen minutes or half-an-hour. It would therefore appear that the gastric secretion in an infant, being so small in volume and so heavily diluted after feeds, cannot allow of any significant degree of protein digestion in the infant's stomach. Further recent experimental work of the writer has shown that this is compensated for by a high tryptic power of the pancreatic secretion in the infant.

#### Conclusions.

(1) An easy and accurate method of obtaining the gastric contents in the child is described.

(2) A 7% alcohol-water mixture is an adequate stimulus of gastric secretion in the child and may be used as a test for achlorhydria.

(3) The only adequate test for achylia gastrica is the absence of acid gastric secretion after the subcutaneous injection of histamine.

(4) The maximum acidity of the pure gastric juice varies considerably in any one age group in infants and children. This is similar to Ryle's results in adults using the fractional test meal.

(5) The volume of gastric secretion in infants during the milk feeding period is very small; after this period of life the quantity is very greatly increased.

(6) It is suggested that the gastric secretion in the infant does not play so important a part in normal digestion as it does in the older child.

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