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T H E S I S

for the Degree of M.D., EDINBURGH UNIVERSITY,

Presented By

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on

THE EXAMINATION of the GASTRIC CONTENTS as an
Aid to the DIAGNOSIS of CARCINOMA of the
STOMACH.

September 1927.



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I N T R O D U C T I O N .

To emphasise the tragic importance of gastric carcinoma to the community one need only mention that there are about 10,000 deaths annually from cancer of the stomach in the British Isles alone ^(HOFFMAN), and it is commonly supposed that malignant disease is on the increase. Further, we cannot look upon gastric cancer as a disease entirely limited to middle age or to old age. It is the experience of many to deal from time to time with cases of cancer of the stomach in patients between the ages of twenty five and forty, which is commonly supposed to be too early for the "cancer age"; and that ~~it~~ may even occur much earlier is shown by the fact that ⁽¹⁾ SULLIVAN of New York mentions four cases in infants under six weeks, one in a child of eighteen months, six below the age of ten and thirteen below the age of twenty.

The medical profession, up till now, have failed to solve the problem of the etiology of /

of malignant disease; and our only remedy is still the surgeon's knife, unless the disease be located in certain sites where radium may be used with advantage. In the case of cancer of the stomach it cannot be too often or too strenuously emphasised that it should be dealt with surgically at the earliest possible moment.

It is not so long ago that, in the orthodox teaching on the diagnosis of gastric carcinoma, emphasis was laid almost entirely on the palpable tumour, the coffee-ground vomiting, the cancerous cachexia and the enlarged supra-clavicular glands; and if, more by luck than good guidance, an early cancer was found at operation the abdomen was usually rapidly closed, since, except in the hands of a very few surgeons, gastrectomy was regarded as being outside the bounds of justifiable interference.

A great advance has been made in the last few years, and the results of early operative removal have been most encouraging; but surgical technique /

technique has completely outpaced the results of diagnostic endeavour; and to-day, in the absence of prevention, the early diagnosis of gastric carcinoma is the real problem on which all attention should be concentrated.

Part of the difficulty in the early diagnosis of this disease lies with the public, who, though many are perfectly willing to be overhauled once or twice a year by their dentist to prevent advanced dental disease, do not consider similar precautions necessary in regard to cancer, and the doctor is generally only called in when their symptoms are pronounced and, in consequence, their disease in an advanced stage. None the less there can be little doubt that we, as a profession, are as much to blame as the ~~elity~~⁽²⁾, for as OSLER has said "if we hear that a woman of a certain age complains of a bloody discharge from the uterus, the possibility of malignant disease is at once thought of; but how many of us consider a like grave possibility when a patient of the same age complains of stomach symptoms, perhaps with a moderately/

moderately sudden onset?"

The researches of the **PENNSYLVANIA**
(3)
CANCER COMMISSION shed a strong light on the reasons for the unfortunate cancer condition. They gathered statistics concerning 400 cases of cancer, and found that in 68% of the cases over a year on the average had elapsed after the patients had consulted their family physicians before they were referred to a surgeon, as it takes about this time or less for the extension of the disease into the enighbouring glands, which may then be felt as lumps by the examining doctor, and a certain diagnosis made. This then is the chief reason why physicians delay in such cases - to make a certain diagnosis - and so the cause of the awful result is easily seen, for the symptoms and purely bedside signs of early cancer of the stomach must be doubtful, if the disease is to be permanently and successfully removed.

How then is the goal of early diagnosis
(4)
 to be reached? **OSLER** says "that the practitioner should recognise the fact that there are many cases/

cases of cancer of the stomach in which a positive diagnosis cannot be reached for weeks or months by any known means at our command except exploration." WILLIAM MAYO (5) in 1904 insisted on the same thing. WHEELER (5) says that he has taught for many years that "if there is no gain in weight in a gastric case after efficient medical treatment malignant disease should be suspected and exploration is more than justified." (5) HORDER recommends "laparotomy in a gastric case, irrespective of age, whenever there is failure to gain weight or to maintain weight after the end of the third week of efficient medical treatment." Innumerable other authorities are of the same opinion.

Now, while there can be no doubt that the exploratory laparotomy is infinitely preferable to waiting for the obvious physical signs of cancer to manifest themselves and must occasionally be practiced, and that the safety with which the mere opening of the abdomen is now attended gives sanction to the proceeding, yet one cannot help feeling/

feeling that the physician is not justified in abandoning his birthright in internal diagnosis. One agrees with RUSSELL⁽⁶⁾ when he says "that the exploratory laparotomy tends indeed to be so widely applied and advocated that it threatens to be the bane of internal diagnosis. It has its own place but when it becomes the screen for ill-informed opinion, or ignorance of methods, it would be difficult to apply too damnatory criticism to it." And it seems to me that not only for the sake of the physician's reputation, but also for the maintenance of public confidence in surgery, every effort ought to be made to secure increasing accuracy in abdominal diagnosis, and the consequent cutting down of the exploratory operation to a minimum.

It is to this accuracy in the diagnosis of gastric carcinoma that the following thesis is directed, for though it is apparent that the bed side examination or X-ray examination can rarely reveal with certainty the existence of early gastric carcinoma, it yet seems to me that it has still to/

still to be proved that early cancer of the stomach cannot be demonstrated with certainty in the great majority of cases by simple laboratory methods.

I had not long undertaken my duties as House Physician at Chalmers Hospital before I realised that, in the course of my work, I should be called upon to examine the gastric contents of many cases, since, though there are only a limited number of general medical beds in the hospital, it has proved fortunate from my point of view, that patients presenting gastric symptoms form such a large proportion of general medical cases. None the less in my six months tenure of office, it would have proved impossible for me to have investigated more than a few cases of gastric carcinoma and cases showing achlorhydria, had not several house physicians at the Royal Infirmary been good enough to allow me to investigate all such cases or suspected cases in their wards. Through the kindness of Mr. Dowden and his house surgeon Dr. Amman the surgical side of this hospital has also been made available/

available to me, and one or two doctors have been good enough to allow me to investigate, with a view to diagnosis, a few of their private cases.

In closing I am greatly indebted to my chief Dr. Hewat for the interest which he has shown in my work, and the facilities which he has given me for carrying it out in the hospital.

B I B L I O G R A P H Y .

1. **HOFFMAN.** The mortality from Cancer Throughout the World. 1915
2. **OSLER & MACRAE,** Cancer of the Stomach 1900
3. **WINSLOW,** The Prevention of Disease. 165 1916
4. **OSLER,** The Principles and Practice of Medicine. 8th Edit. 534 1918
5. **WHEELER,** B.M.J.ii. November 1925
6. **RUSSELL,** The Stomach and Abdomen. 1921

H I S T O R I C A L .
RESUMÉ of LITERATURE.

The physiology of the human stomach has acquired so vast a literature since BEAUMONT'S day that it is manifestly impossible even to acquaint oneself with all its history, much less to assimilate and to analyse the countless observations and experiments upon which our knowledge has been based. The morbid processes of digestion have also an extensive literature of their own. In this section I have, therefore, endeavoured to confine myself to the literature which has a practical bearing on gastric secretion, and the examination of the gastric contents.

In recent years a great deal of work has been directed towards this subject and a great mass of data has accumulated. But, in spite of the advances which have been made, we are still without any clear picture of many of the phenomena concerned, and much recent work, has, in many cases, only served to throw into disrepute facts, which for many years were held to be definitely established. No one after a study of the literature can fail to be impressed with the great divergence of view which is there expressed.

The/

The following section comprises:-

- (1) A brief account of the histology of the gastric glands.
- (2) Older views on gastric secretion.
- (3) The evolution of the test meal.
- (4) Modern views on gastric secretion.
- (5) Methods used for the discovery and estimation of free and combined hydrochloric acid in the stomach contents.
- (6) Views on the significance of achlorhydria.
- (7) The Chemistry of lactic acid and the tests for its presence in the gastric contents.
- (8) Views on gastric analysis in carcinoma of the stomach.

THE HISTOLOGY of the GASTRIC GLANDS.

The mucous membrane lining the stomach is a relatively thick one, the thickness being largely due to the length of the long tubular gastric glands (1) (SCHAFER). At the dome of the fundus the mucous membrane is thinned out and the glands are fewer, (2) due, it is suggested by LIM, to the fact that food does not lie in contact with this part of the stomach which is filled by the "air ball" seen in the X-ray photographs.

The superficial epithelium consists of columnar goblet cells which secrete mucus. It is suggested/

suggested by BENNET⁽³⁾ that it is possible that these cells may modify the gastric juice by absorption or diffusion.

The glands are simple tubules except in the region of the pyloric antrum and cardiac orifice, where they are more racemose in character.

There are three types of cells found in relation to these glands. HEIDENHAIN⁽⁴⁾ described only two types, namely, parietal and central, according to their relationship to the lumen of the gland.

The parietal types are the oxyntic cells, which secrete acid, and which are found everywhere in the stomach, except in the region of the pyloric antrum where they are absent. The central type of HAIDENHAIN⁽⁵⁾ has been further differentiated by BENSLEY

into superficial cells and deep cells, according to the positions they occupy in the gland in relation to the lumen of the stomach. The superficial cells

are identical with the cells forming the glands in the pyloric part of the stomach, and both LIM⁽⁶⁾ and

Bensley have suggested that their sole function is the secretion of mucous.
 and BENSLEY have all the characteristics of zymogen secreting cells, and are responsible for the pepsin of the gastric juice.

EARLIER VIEWS on GASTRIC SECRETION.

For a long time it was thought that the special reflex which brought about the gastric secretion had for its afferent nerves the lingual and glossopharyngeal. That is, it was thought that the presence of food in the mouth set up impulses in these nerves which served as afferent nerves for both the salivary and gastric glands. In 1890 **PAWLOW**⁽⁷⁾ disproved this theory by his classical experiments on dogs with oesophageal and gastric fistulae, in which he proved to his own satisfaction that the vagus was the secretory nerve to the stomach, and that psychic excitation was sufficient to produce a very large secretion of gastric juice. It was seen, however, that in normal feeding the quelling of the pangs of hunger and a feeling of satisfaction set in long before the end of the digestive period. Thus, during a great part of the time when secretion was going on, there could have been no psychic stimuli passing down the vagi at all. Formerly it was thought that this continued secretion after the impulses along the vagus had stopped, was due to food in the stomach stimulating the gastric mucous membrane. **PAWLOW** shewed by his experiments on animals, that this/

this, indeed, was the case, but that it did not take place in the simple way that the older observers had thought, since indigestible foreign bodies in the stomach did not apparently influence its secretory behaviour. This was also demonstrated by BEAUMONT⁽⁸⁾ in his fistulous case in man.

The work of EDKINS⁽⁹⁾ led him to believe that the actual cause of this secondary secretion was a gastric hormone - secretin - caused by the action of the first products of digestion on the pyloric mucous membrane. This secretin on passing into the blood stream, had a specific action upon the gastric glands causing them to secrete the secondary gastric juice.

The cause of the intermittent relaxation of the pyloric sphincter during digestion has been the subject of much investigation and speculation. CANNON⁽¹⁰⁾, who did a great deal of work on this subject, argued that the fundamental factor regulating sphincter action was the hydrochloric acid of the gastric contents. The general theory of this "acid control of the pylorus" was dependent on the principle that acid in the stomach caused a relaxation of the sphincter when the concentration of acid was sufficiently great, while, on the contrary, acid in the duodenum/

duodenum caused a contraction; so that an automatic "see-saw" mechanism continued to operate until the whole of the gastric contents reached the intestine.

Lastly it was held by **PAWLOW** and generally believed that gastric secretion was an intermittent process requiring stimulation by food or psychic factors before secretion was normally produced; and that no gastric secretion took place in the fasting state.

The views of **PAWLOW** and the earlier observers have in recent years been considerably modified principally due to the evolution of the Test Meal by means of which it has become possible to repeat on the human subject a number of the experiments which **PAWLOW** had to perform on animals.

THE EVOLUTION of the TEST MEAL.

As early as 1780 **SPALLANZANI**⁽¹¹⁾ was investigating gastric juice. He usually obtained this by causing vomiting; but in some cases he caused sponges or food in perforated capsules to be swallowed and these were recovered for examination, either by pulling them up by means of threads attached to them or by forced vomiting.

Little scientific advance was made, however, in the direction of test meals till 1879, when **VON LEUBE**⁽¹²⁾ employed a tube for securing gastric contents. Stomach tubes had, of course, been used in ancient times/

times for therapeutic purposes, but VON LEUBE seems to have been the first to use the tube in order to procure specimens for analysis.

Following LEUBE'S technique EWALD (13) devised means of establishing the use of the tube in a more standard test, employing a known constant stimulus and examining the response at a definite constant time after the stimulus had been employed. EWALD'S method is largely employed at the present time. The examination is conducted early in the morning, the patient having fasted from the night before. The test meal, consisting of a pint of tea and a small piece of toast is given and an hour later an ordinary large stomach tube is passed, and as much as possible is syphoned from the stomach. The volume is measured and the analysis proceeded with.

The form of the test breakfast itself has since been the subject of many changes, but EWALD'S test meal is still very frequently employed. Indeed BOAS' test breakfast is the only other in general use. This is made by boiling two Tablespoonfuls of fine breakfast oatmeal in a quart of water until the total bulk is reduced to one pint; the mixture is then strained through coarse muslin. The resultant meal is more readily aspirated than is the tea and toast meal, its white colour enables the detection of bile/

bile and blood to be made easily, and there is less possibility of lactic acid being formed from oatmeal than from bread; these advantages outweigh the less palatable character of the meal.

It is interesting to note that the earlier observers were impressed with a desire to be able to follow through the "digestive cycle" more completely. LEUBE, himself, attempted a form of fractional test meal by removing portions of the meal at frequent intervals; but the size of the tube employed rendered this process so uncomfortable as to make it inapplicable for general use. EWALD, too, attempted a similar procedure, with unpromising results. With the advent of a small bore, flexible rubber tube, fractional analysis was placed on its present practical basis.

It appears that, as early as 1893, GROSS⁽¹⁴⁾ had reported on the use of a soft Nelaton catheter for this purpose; but it was not till 1914 that REHFUSS⁽¹⁵⁾ described a method of obtaining a continued record of the digestive functions of the stomach by the use of his modification of EINHORN'S duodenal tube, through which samples of a test meal were withdrawn at intervals, until the stomach was found to be empty. Analyses of each of the samples was then made, the free hydrochloric acid and total acidity estimated in each case, and the results plotted as/

as a curve.

This fractional method has many obvious advantages over the old one hour method. These may be summarised as follows:-

- (i) It permits of accurate measurement of the fasting juice and a study of its mucus, bile and cell content, together with estimation of its free and total acidity.
- (ii) It provides in a graphic form an indication of the chemical processes at each stage of gastric digestion, and by recording the times at which bile regurgitation occurs, it gives an indication of the occurrence of pyloric relaxation and duodenal reflux.
- (iii) It detects late rises in acidity and such phenomena as continued secretion.

From the point of view of this thesis, this third advantage is one of the most important which the fractional method has over the one hour method. In my series of fractional test meals I have found it to be not at all uncommon for free Hcl to be completely absent from the gastric contents an hour after a meal, & yet to be present in small quantities, & very occasionally in large quantities, at some later period of digestion. The same thing was observed at the New Lodge Clinic ⁽¹⁶⁾ where, out of 325 consecutive fractional test/

test meals free Hcc. was absent in 34 (10.5%) cases; it was absent from the 1 hour fraction in 30 (9.2%) additional cases, in 22 of which it was also absent from the resting juice and from the $\frac{3}{4}$ hour fraction, although free acid was present at other times during the test meal, 15 times in normal amount and once in actual excess. In the additional 9.2% of cases, the old fashioned one hour test meal would have led to a diagnosis of achlorhydria, whereas the fractional method showed that free acid was present in either subnormal, normal or even excessive quantity, but that its first appearance was delayed. Thus achlorhydria is much less frequently found by the new method than the old method would have led one to suppose.

- (iv). It determines with considerable accuracy the emptying rate of the stomach for a standard meal.
- (v). By combining chloride estimations with those for free and total acidity, it furnishes information relative to the factors causing neutralization, and so indirectly again to the functions of the pylorus.
- (vi). In pathological cases the odour of the samples, the presence of food residue in the fasting specimen, of blood or pus in this or subsequent specimens, and other physical characters may also be observed.

Of the possible fallacies which have to be considered the following are important:-

- (1) The action of the tube as a foreign body in the stomach.

As we have already seen both BEAUMONT⁽⁸⁾ and PAWLOW⁽⁷⁾ proved that inert foreign bodies in the stomach did not in any way influence its secretory behaviour.

- (2) The stimulation of excessive salivation which might possibly tend to dilute and, to a less extent, neutralise the free acid.

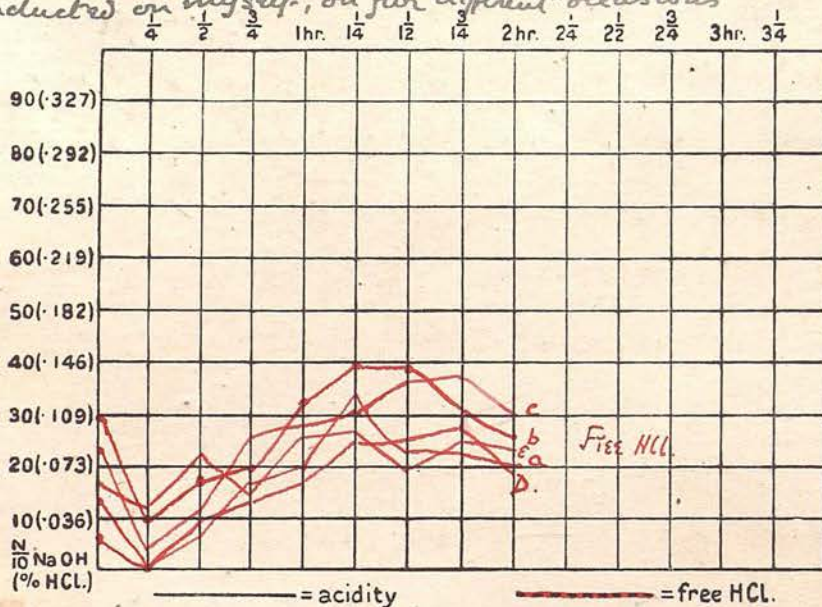
BENNET & RYLE⁽¹⁷⁾ found that in a very few cases the presence of the tube caused such a vigorous reflex salivation that an artificial hypo-acidity was actually induced. The number of such cases of excessive salivation is, however, so small as to make this objection of little importance.

- (3) Diminution of the psychic secretion by the circumstances of the test and the unappetising character of the meal.

The importance of the psychic secretion is uncertain. As will be seen later, many modern observers believe that PAWLOW laid far too great emphasis on the secretion induced in a hungry animal by seeing and smelling food.

- (4) /

The fractional examination of the gastric contents
conducted on myself, on five different occasions



DOWN BROS., LTD., LONDON.

Gastric Analysis.

a = First Examination. b = second etc.

- (4) Emotional inhibition or exaggeration of secretion during the test.

BENNET & VENABLES⁽¹⁸⁾ greatly modified the acid curve with the standard meal, and lengthened the emptying-time of healthy individuals by suggesting nausea or anxiety to them while under the influence of hypnosis. The emotional stresses of a test meal, however, are rarely very significant. In my own case I certainly found this objection to be of little significance. I have carried out a fractional examination of my own gastric juice on five different occasions. On the first occasion I had more difficulty in swallowing the tube and more emotional upset than I have seen in the vast majority of patients. On subsequent occasions, the process became gradually easier to me, till on the fifth occasion, I swallowed it as easily as a pill, and while the tube was in the stomach continued at my work with complete comfort; and yet an examination of the chart will show no great variation between the curves of the various examinations.

- (5) Duodenal regurgitation from retching.

Retching after the tube is properly in the stomach is very rare. I have only observed it in one case out of the ^{seventy-five} ten cases I have examined by the fractional method.

(6)/

(6) Variations from day to day in the curve
of a given subject.

BELL & MACADAM⁽¹⁹⁾ performed the interesting experiment of examining the same man on no less than twenty consecutive days. They found the rate of emptying remarkably constant and the general conformation of the curves similar.

My own curves, taken at varying intervals of days or weeks, show great similarity. See Chart.^(P20A)

McCRACKEN⁽²⁰⁾ in a series of consecutive tests on seventy-five cases, considered the variations to be greater than is commonly supposed, but yet insufficient to affect seriously the diagnostic significance of the results obtained.

One may, therefore, say that the variations obtained from the same individual on different occasions have, as a rule, been slight. Where they appear more considerable, the general conformation of the curve is maintained and the rate of emptying is very constant. Subjects with low curves or achlorhydria, on the first occasion show low curves or achlorhydria subsequently; subjects with high curves show high curves on subsequent occasions.

(7)

- (7) Variations in acidity at different levels of the stomach

(21) GORHAM and (22) KOPELOFF have criticised

the fractional test meal on the ground that acidities at different levels in the stomach are sufficiently divergent to render the ordinary conclusions unreliable.

It need hardly be pointed out, however, that an essential part of the technique is to keep the tube at the same level throughout the test. (22) WHITE in his experiments paid special attention to the position and movements of the tube tip by means of X-ray screening during the course of the test. He found that in 95% of his cases, the tip of the tube "lay like a sinker on the lowest part of the greater curvature of the stomach, and did not move a half inch in position during the withdrawal of samples". The tip, he concludes, is not moved much by peristaltic waves, and does not shift to different portions of the stomach.

- (8) Variations with sex and age.

In regard to sex variations, FOWLER & (24) ZENTMIRE examining the resting juice in healthy women, obtained results completely similar to those (25) obtained in men by FOWLER, REHFUSS & HAWKE (22) KOPELOFF found the acidities in normal females to run/

run on the average, at a slightly higher level than those in normal males.

(26)
 HANEBOG holds that there is a tendency to diminished secretion with advancing years.

On the whole, however, the sex and age variations may be said to be negligible. In summary, we may conclude that the practical utility of the fractional method is much greater than that of the one hour method. It must be clearly understood, however, that fractional analysis is a clinical test and can never by any stretch of imagination be regarded as an accurate chemical procedure. Its findings merely portray in a general way the results of the numerous processes influencing the chemistry of the gastric contents from moment to moment.

The modifications of EINHORN'S duodenal tube which REHFUSS devised to adapt it to gastric work, consisted in alterations in the tip of the instrument. The perforations in the tip of EINHORN'S tube were large enough to permit of the aspiration of the duodenal contents, but easily became choked in withdrawing the contents of the stomach. To overcome this difficulty, REHFUSS used a tip with large slots in it, the diameter of the slots being equal to/

to the calibre of the tube. He also used a heavier metallic tip, as he found that this made it easier for the patient to swallow the tube and ensured it lying in the lowest part of the stomach.

More recently RYLE has still further altered the tube. He uses a narrow rubber tube with a blind end into which is inserted an oval lead weight. At a distance of about 2 mm. from the tip it is perforated by several holes of about 2 mm. diameter.

The advantages claimed for this tube are that it is more easily swallowed and withdrawn; the perforations being in the elastic wall of the tube, are less easily blocked than they would be in a rigid metal tip, and if they do become choked, they are easily cleared by air pressure; the end cannot become detached; there is no likelihood of strong suction on an empty stomach producing trauma of the gastric mucosa.

At this stage, it may be well to consider the effect of fractional analysis in relation to the study of gastric motility. While fractional analysis alone may hold no definite advantage over X-ray methods in this sphere, yet there is ample scope for a test which provides for the study of gastric motility and gastric secretion at the same time.

In/

In this connection it is interesting to record the results of motility tests performed in a large series of patients seen at the Mayo Clinic ⁽²⁷⁾. **The motility was tested both by X-ray examination** after bismuth given six hours previously, and by gastric analysis about twelve hours ~~after the~~ ingestion of raisins or charcoal. In this series of cases it was found that X-ray examination recorded 70% more retentions than were shown by the test meal. ⁽²⁸⁾ **RUSSELL** on the other hand, finds that a bismuth meal is got rid of by the stomach in a much shorter time than an ordinary meal of mixed foods, and holds that fractional analysis is the most accurate test of normal gastric motility.

For the sake of completeness it is advisable to mention two other forms of gastric test.

One test which has been introduced recently ⁽²⁹⁾ by **DODDS**, depends upon an entirely different principle from any of the methods previously outlined. By taking samples of the alveolar air, at intervals immediately after a meal, **DODDS** was able to show that the tension of carbon dioxide in the alveolar air undergoes certain definite changes in response/

response to the amount of secretion poured out by the stomach and the lower portion of the alimentary tract. This test has the advantage of causing the patient no discomfort or inconvenience, and in pathological conditions DODDS finds that his results by this method are as characteristic as those obtained by means of gastric analysis. This test has not, as yet, been generally used, and it is thus impossible to estimate its general value.

The other test may also be put in the same category, nor does it seem to lend itself to general application. It depends in principle upon the estimation of the acidity of gastric contents by means of the H-ion concentration determined by the gas chain method. McLENDON⁽³⁰⁾ devised an electrode which could be introduced directly into the stomach, and in this way determined the H-ion concentration of the gastric contents in situ.

MODERN/

MODERN VIEWS on GASTRIC SECRETION.

⁽³¹⁾ CARLSON and ⁽³²⁾ KUNDE have shown that gastric secretion is a continuous process and that the stomach never stops secreting even after prolonged fasting. This statement is contrary to the view of PAWLOW, who, as we have seen, considered gastric secretion to be an intermittent process depending on stimuli of various kinds.

That this juice secreted in the apparently unstimulated stomach is true gastric juice, has been proved by BRESKIN and ⁽³³⁾ BYKOFF, but as contrasted with the copious, strongly acid and highly proteolytic juice which follows stimulation, it is scanty, viscid and contains a variable amount of free HCl, but always some total acid and ferment.

⁽³⁴⁾ CARLSON considers that PAWLOW placed too great emphasis on the secretion induced in the hungry animal by seeing and smelling food. ⁽²⁵⁾ HANEBOG also doubts the importance of psychic secretion in man. ⁽¹⁷⁾ BENNET & VENABLES failed to demonstrate it in a series of healthy students. None the less it cannot be taken as certain that PAWLOW'S observations on this subject have been disproved.

A good deal of work on the gastric hormone secretin, has recently been carried out by ⁽³⁵⁾ LIM and/

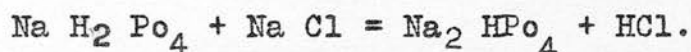
and his colleagues, ⁽³⁶⁾, also by KATSCH & KALK ⁽³⁷⁾
 and by IVY & OBERHELMAN ⁽³⁸⁾, the general result of
 all these researches appears to substantiate quite
 definitely EDKINS claim, that the pylorus does pro-
 duce a product which is an important factor in the
 production of gastric juice. On the other hand,
 secretin, according to these observers, is not pro-
 duced entirely by the pylorus, but may be produced,
 though to a much less extent, by the cardiac mucosa
 and duodenum.

It has been definitely established by
 BOLDYREFF ⁽³⁹⁾ that the regurgitation of alkaline juic-
 es from the intestine into the stomach, is part of
 the process of normal digestion, a process which the
 earlier observers had considered to be pathological.

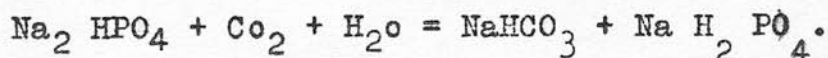
The theory of the "acid control of the py-
 lorus" put forward by CANNON, though simple and fas-
 cinating, has been found to be untenable. It has
 been shown that food can leave the stomach without
 any difficulty under conditions quite definitely
 excluding the presence of acid. For instance, in
 achylia gastrica, the sphincter appears to act quite
 satisfactorily, and SPENCER, MEYER, REHFUSS & HAWK, ⁽⁴⁰⁾
 have found the pylorus opening in the presence of
 strongly alkaline gastric contents. There has, how-
 ever, been no satisfactory explanation put forward
 as/

as to why the pylorus opens and shuts to take the place of CANNON'S theory. This question still remains a mystery, but on the whole, the most important factor appears to be the consistency of the food in the stomach.

There is now no doubt that the formation of a free acid from the alkaline blood and lymph, which proved a puzzling problem to the older observers, comes from the chlorides of the blood and lymph, and of the chemical theories advanced as to how this is done, MALY'S ⁽⁴¹⁾ is the most satisfactory. He considers that the acid originates by the interaction of sodium chloride and sodium dihydrogen phosphate, as is shown in the following equation:-



The sodium dihydrogen phosphate in the above equation is probably derived from the interaction of the disodium hydrogen phosphate and carbonic acid of the blood, thus:-



Other theories have tried to explain the formation of such a strong acid as hydrochloric by the law of "mass action". We know that by the action of large quantities of carbonic acid on salts of the mineral acids, the latter may be liberated in small quantities. We know further, that small quantities of acid

of acid ions may be continually formed in the organism by ionisation. But in every case we can only make use of these explanations, if we assume that the small quantities of acid are carried away as soon as they are formed, and thus give room for the formation of fresh acid. Even then it is impossible to explain the whole process. A specific action of the cells is no doubt exerted, for these reactions can hardly be considered to occur in the blood generally, but rather in the oxyntic cells, which possess the necessary selective powers in reference to the constituents of the blood, and the hydrochloric acid, as soon as it is formed, passes into the secretion of the gland in consequence of its high power of diffusion.

With regard to the percentage composition of the gastric juice, most observers are in substantial agreement.

The figures of HALLIBURTON ⁽⁴¹⁾ are quoted in the following Table.

Water/

Water	99.44%
Organic Substances (Chiefly pepsin)	0.32%
HCl	0.20%
Ca Cl_2	0.006%
Na Cl	0.14%
KCl	0.05%
Ca ₃ (PO ₄) ₂)	
Mg ₃ (PO ₄) ₂)	0.01%
F ₂ PO ₄)	

METHODS/

**METHODS USED for the DISCOVERY and ESTIMATION
of FREE and COMBINED HCl.**

Free hydrochloric acid is usually regarded as that part of the hydrochloric acid which is not combined with protein or any other potential base, and which is ionised to the same extent as it would be in simple aqueous solution.

A rough method of testing for its presence in gastric contents is to dip into it a piece of congo red paper, which turns blue in the presence of free hydrochloric acid. Congo red paper is prepared by soaking some filter paper in an aqueous solution of 0.1% congo red dye. The test is admitted by all to be a rough one, as very small quantities of free acid are not well demonstrated by it, and **MACLEAN** ⁽⁴²⁾ holds that lactic acid if present in large amount, may give a somewhat similar colour to that given by free hydrochloric acid.

The earliest indicator for the presence of free hydrochloric acid was that of GUNZBERG. It is made up of -

Phloroglucin	2 gm.
Vanillen	1 gm.
Absolute Alcohol	30 cc.

Two drops of this reagent are placed in a porcelain dish, and evaporated to dryness without scorching.

Two/

Two drops of filtered gastric contents are then added and evaporated to dryness as before. If free hydrochloric acid be present a bright pink colour appears. It is generally admitted that this is a certain test for the presence of free hydrochloric acid, for no other acids give this reaction. The test is also a delicate one. As the test involves evaporation, however, it is only convenient for the purpose of qualitative and not quantitative analysis, which latter requires titration. GUNZBERG'S method of titrating with soda or diluting with water until a reaction with a mixture of phloroglucin and vanillin is not obtained gives very reliable results, but the method is excessively tedious and difficult to apply.

The usual method of determining free acidity is to add TOPFER'S reagent (dimethylaminoazobenzene) to a measured sample and to titrate with standard soda until the pink tint disappears.

COLE & ADIE⁽⁴³⁾, however, do not find in TOPFER'S indicator a sufficiently accurate indication of free hydrochloric acid. They observe that its range of indication allows anomalous results to be given, for, though it at first indicates the neutralisation of free hydrochloric acid only, yet when the major part of the free HCl has been neutralised, it indicates some neutralisation of the protein salts of/

of HCl as well. They also say that it is unwarrantable to suppose that it does not react with organic acids. They recommend the use of the Thymol Blue indicator of CLARK & LUBS⁽⁴⁴⁾, as giving more accurate range of indication. This, however, is very much more tedious to use than TOPFER'S reagent, for it requires colour changes to be matched with those produced by standard acids.

RYFFEL⁽⁴⁵⁾ disagrees with COLE & ADIE, and considers TOPFER'S indicator as being sufficiently accurate for all practical purposes, and that organic acids in the stomach never attain an acidity great enough to affect it.

MATHEWS⁽⁴⁶⁾ supports this contention and finds that any organic acid occurring in the stomach would require to be present in a concentration of at least .5% before it would affect this indicator.

Lastly MACLEAN⁽⁴⁷⁾, while employing TOPFER'S reagent in the estimation of free HCl., entirely disagrees with RYFFEL, in supposing that dimethyl does not react to lactic acid in moderately strong concentration, just in the same way as it does with free HCl., entirely dis

All observers are in agreement in using the phenolphalein indicator in estimating the combined HCl.

In/

In quoting these divergent opinions, I have purposely refrained at this stage from expressing any opinion upon them, since a part of a later section in this thesis has been devoted to an investigation of the various tests employed for the discovery of free hydrochloric acid in the gastric contents, and conclusions are there arrived at as to their individual efficacy.

THE/

THE SIGNIFICANCE of ACHLORHYDRIA.

Anacidity, or absence of free HCl. in the stomach contents is due according to BOLTON⁽⁴⁷⁾ to :

- (i) Excessive neutralisation of the gastric juice, which may be in normal or diminished quantity consequent upon abnormal potency of the pylorus or the presence of gastric jejunostomy.
- (ii) To neutralisation by the alkaline or albuminous exudates from the surface of a malignant growth.
- (iii) To neutralisation and inhibition of acid secretion by an excessive output of mucus, as in chronic gastritis.
- (iv) To complete absence of the gastric juice as in achylia gastrica.

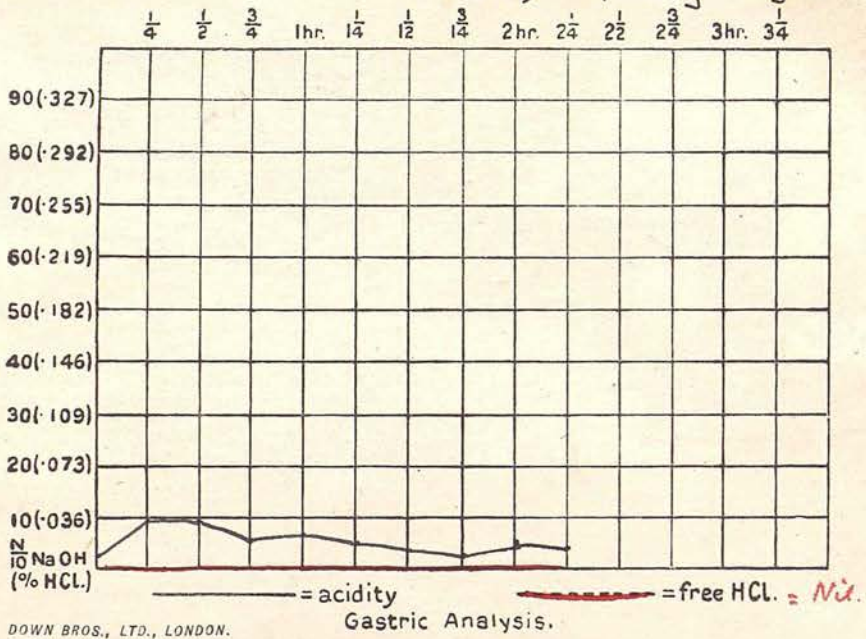
This latter which was first described by EINHORN⁽⁴⁸⁾ has by some, been presumed to depend upon atrophy of the gastric glands. FABER⁽⁴⁹⁾ regards it as a result of pathological changes consequent upon past gastritis. HURST⁽⁵⁰⁾, as also did MARTIUS⁽⁵¹⁾, regards it as an inborn error, and considers that gastritis is more often secondary to achylia than achylia to gastritis. The discovery of achylia in a small percentage of healthy men and in healthy members of some families with a history of Addison's anaemia, supports HURST'S view. ZWEIG⁽⁵²⁾ observed eight verified cases of development of cancer in middle-aged patients whom/

whom he had been treating for ten to fifteen years for gastric achylia. BRINTON⁽⁵³⁾, showed that scarlet fever is capable of producing a very severe desquamative gastritis, which may be the cause of subsequent achylia, and one of the four healthy men with achylia in BENNET & RYLE'S⁽¹⁷⁾ series, was found to have had scarlet fever in childhood.

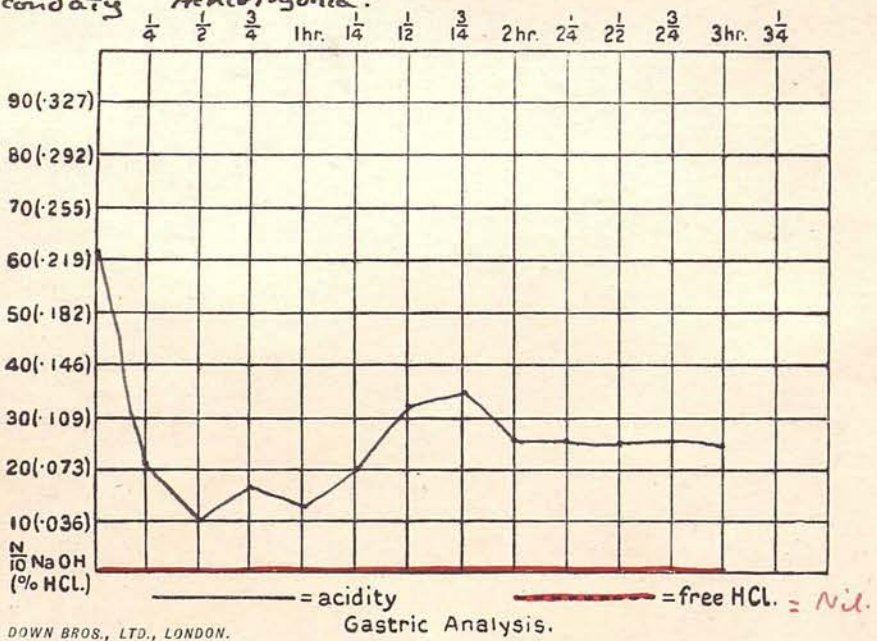
The term achylia should, strictly speaking, be limited to an entire absence of gastric juice and cases of this are rare in the extreme, being probably due to a congenital abnormality. An examination of the literature, shows that the vast majority of cases of achylia have been put into this category, without sufficient justification. Not only is the evidence that gastric secretion is entirely absent in these cases incomplete; but there is, especially in more recent accounts, strong evidence that a secretion of some sort is present. Thus CROHN⁽⁵⁴⁾, in a series of fractional test meals on subjects with so called achylia, shows that acid administered to such subjects is rapidly neutralised by dilution with watery gastric secretion and by mucus poured out by the gastric glands.

According to RYLE⁽⁵⁵⁾, there are no absolutely constant distinguishing features in the ordinary/

Principious Anaemia. (Ryle) Primary Achylia.



Carcinoma of the Stomach & Pyloric Stenosis (Ryle)
Secondary Achlorhydria.

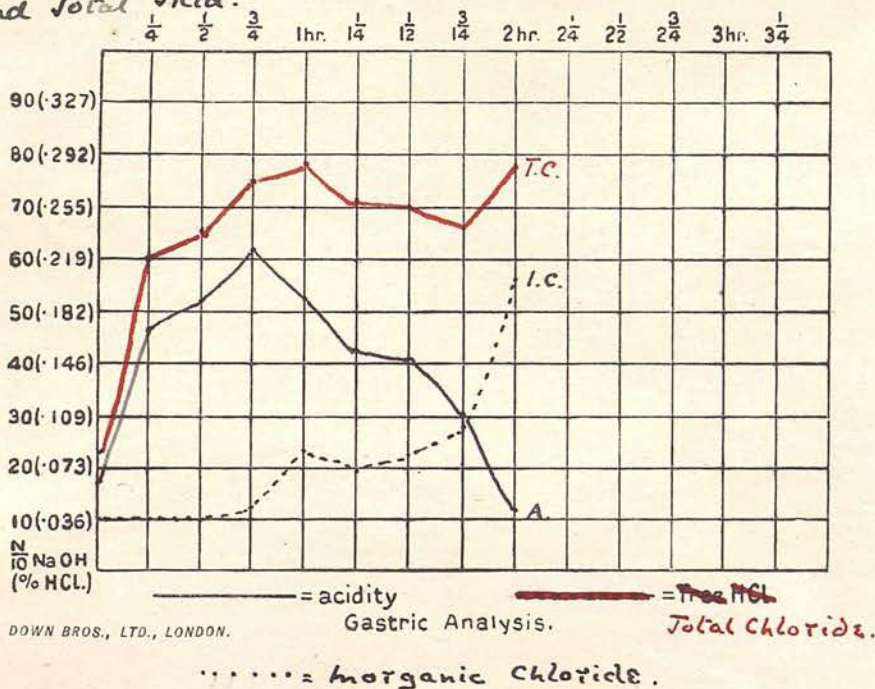


ordinary test meal curves between a secondary achlorhydria and a primary achylia. In primary achylia there is a very narrow interval and a close parallelism between the curve of total acidity and the base line. (Vide Charts.) A wide interval between the curve of total acidity and the base line and a lack of parallelism are more likely to occur in secondary achlorhydria.

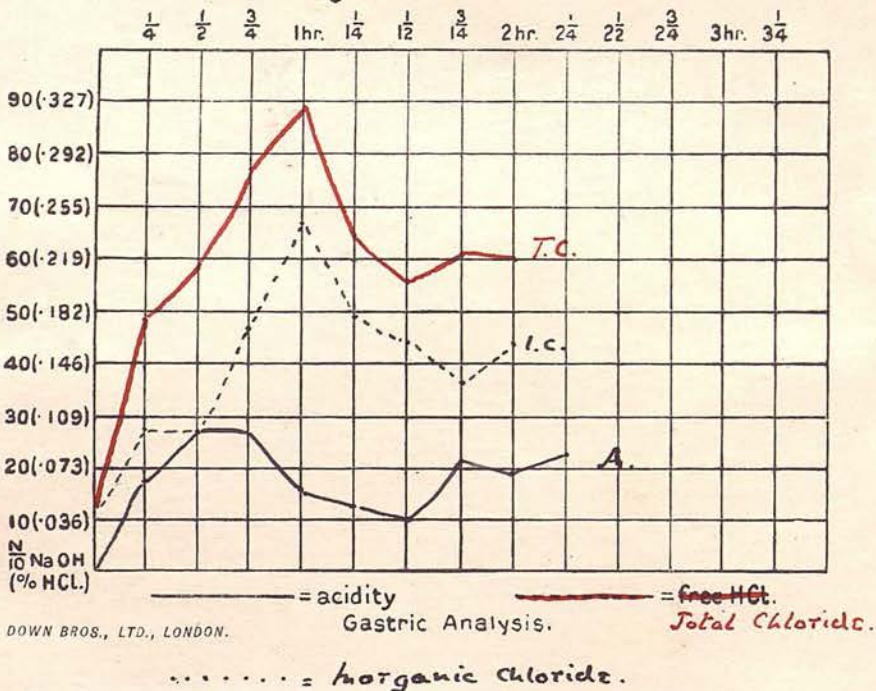
(47)
 BOLTON, stresses the importance of a complete chloride analysis in the condition of sub-acidity, for he points out that ordinary acid estimation is inaccurate as it takes no account of the neutralised HCl in the form of inorganic chloride. He points out that when the ordinary gruel meal is taken the percentage of total chlorides present (that is, free HCl and protein HCl + inorganic chlorides) represents as nearly as possible the percentage of total HCl. secreted, and the curve of the total chlorides is, therefore, the real secretory curve as nearly as can be obtained. By means of such total chloride estimations, he claims that achlorhydria due to excessive neutralisation of the gastric juice may be distinguished from simple diminution in the amount of gastric juice secreted and from achylia gastrica.

Excessive neutralisation of the gastric juice/

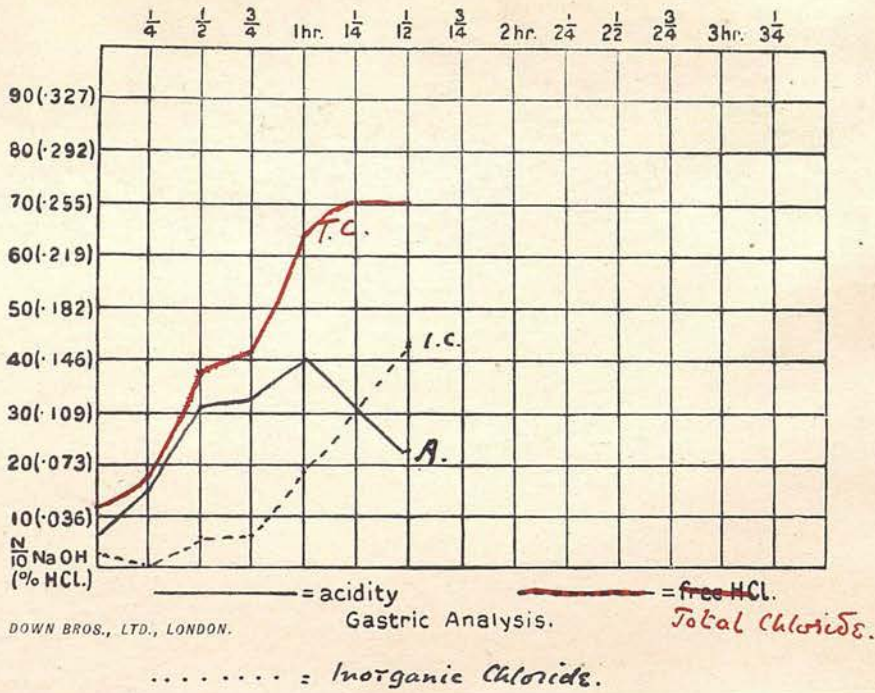
Normal Curve of Total Chloride, Inorganic Chloride
And Total Acid.



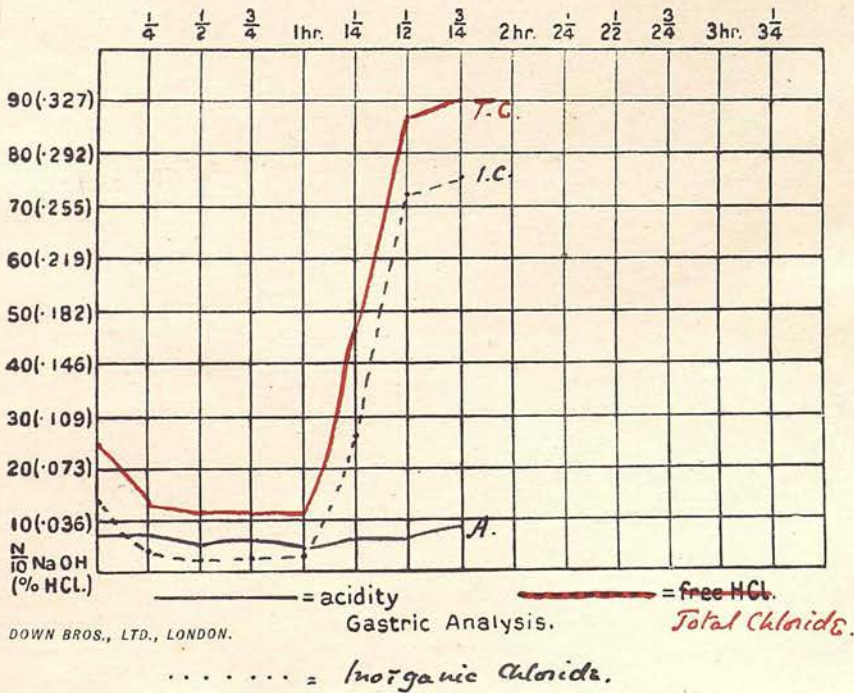
Excessive Neutralization. Functional Disorder.



Hyposecretion.



Pernicious Anaemia. Primary Achylia Gastrica.



juice, is demonstrated by the large increase in the amount of inorganic chloride present as compared with the diminution in the amount of protein HCl, free HCl being absent. A characteristic feature of the curves is that the inorganic chloride curve is higher than the acid curve during the whole of digestion, and it is uncommon for these two curves to cross as is usually the case. When the gastric juice is being secreted in normal quantity but is being excessively neutralised, the total chloride curve rises from 60 to 90. This rise occurs in the normal fashion and is accompanied by a corresponding rise in the inorganic chloride curve.

Simple diminution in the amount of gastric juice secreted is demonstrated by the total chloride curve standing at 60 or below, while the stomach contains food; otherwise the curves are like the normal but lower.

In achylia gastrica the total chlorides are low in percentage - under 30 - the curve practically drawing a straight line. (Vide Charts.)

(56)
ANDERSEN, found that cases of achlorhydria due to excessive neutralisation or to simple diminution of gastric secretion might be made to show free acid in the test meal analysis after hypodermic injection of histamine di-hydrochloride which stimulated/

stimulated the gastric secretion, and MATHESON and AMMON⁽⁵⁷⁾, using histamine acid phosphate came to much the same conclusion.

BENNET & RYLE⁽¹⁷⁾, in a series of 100 healthy students examined by the fractional method, found that 4 cases showed complete absence of free acid throughout the test, on each of the several occasions on which they were examined, and, therefore, concluded that achlorhydria cannot, in itself, be regarded as a pathological finding.

CAMPBELL⁽⁵⁸⁾, criticised these observations and suggests that the incidence of achlorhydria in healthy people is not nearly so high as 4%. In the large series of normal subjects examined by himself in collaboration with BAIRD & HERN, there were 3 cases of achlorhydria, but only one of these was shown to have a constant achlorhydria, and subsequent physical studies raised doubts as to the fairness of classifying him as healthy.

REHFUSS, BERGEIM & HAWKE⁽⁵⁹⁾, found achlorhydria in few, if any, of the normal subjects they examined.

In only one case out of the 58 normal students examined by BENNET⁽⁶⁰⁾, was free acid always absent.

KEEFER & BLOOMFIELD⁽⁶¹⁾, in 1500 analyses/

analyses found anacidity present in 390 (26%) cases forty-five minutes to one hour after the ingestion of an EWALD Test Meal, - the much higher figure being no doubt due to the employment of the less delicate one hour technique, instead of the fractional method. None the less they found that when the histamine test was applied the incidence of anacidity was reduced, so as practically to be limited to persons with definite disease such as cancer, gastritis and pernicious anaemia.

It would seem then, that though cases of achlorhydria and achylia may occasionally be encountered among apparently normal subjects, yet the phenomenon is very rare; but this is by no means so in persons suffering from disease.

(62)
BROWN , quotes the following conditions

in which achlorhydria has been observed:-

Pernicious anaemia; chronic gastritis; gout;
Arthritis deformans; tuberculosis; typhoid infections; intestinal parasitic infections; chronic nephritis; chronic myocarditis; pellagra; spine;
cancer of the stomach and other organs; diseases of the thyroid; linitis plastica; gastric atony; chronic cholecystitis; after severe psychic disturbances and during the menstrual period./

BARBER & RYLE⁽⁶³⁾, showed that acne rosacea was yet another disease with which achlorhydria is frequently associated; and HURST and BELL⁽⁶⁴⁾, found it constantly present in sub-acute combined degeneration of the cord.

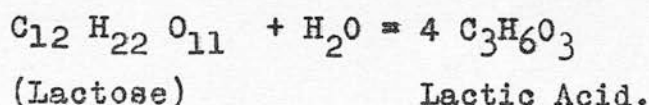
All authorities are in agreement, however, that the three diseases in which anacidity most commonly occurs are, -

Pernicious anaemia,
Gastritis, and
Carcinoma of the stomach.

LACTIC/

L A C T I C A C I D .

A-Hydroxypropionic acid is commonly known as lactic acid, so called because it is the chief acid formed when milk turns sour by fermentation. When milk is exposed to the air it is certain after a time to receive from the air a small quantity of an organism containing the enzyme lactose, which acts upon the milk sugar, or lactose and converts it into lactic acid. The chemical equation representing the action of the enzyme is:-



The enzyme is capable of turning other sugars besides lactose into lactic acid.

A variety of lactic acid is found in muscle and may be prepared from meat extract. It is named sarcolactic acid and possesses the same constitutional formula as the lactic acid derived from the carbohydrates. This acid and its mode of production must here be referred to in some detail owing to the theories advanced later on in this thesis.

Sarcolactic acid, like fermentation lactic acid, is a-hydroxypropionic acid. In all its chemical actions it behaves exactly like fermentation lactic acid, but differs from it in its effect upon polarised/

polarised light. We, therefore, have two different acids with only one formula; for although lactic acid and sarcolactic acid are absolutely similar in their chemical properties, yet they differ in their physical properties in such a way that they cannot be regarded as identical substances. (WALKER⁶⁵)

In 1795 VON HUMBOLDT⁽⁶⁶⁾ first showed that frog's muscle when excised keeps its irritability longer in oxygen than in air or in hydrogen, especially when the temperature is fairly high. In 1904 FLETCHER⁽⁶⁷⁾ came to the following conclusions as the results of his experiments on the effects of oxygen on muscular metabolism: that an abundant supply of oxygen markedly delays the loss of irritability in a surviving muscle; that it is able to abolish the visible phenomenon of natural rigor mortis; that the delay of rigor mortis and fatigue effected by the presence of available oxygen marks the completeness with which the dissociative processes of resting and active muscle in the presence of oxygen result in the formation of carbon dioxide; and that the hastening of fatigue and rigor when oxygen is withheld, is due to the accumulation of the products of metabolic activity of the muscle, which are the potential precursors of carbon dioxide and which have a toxic effect on the muscle.

It/

It has long been known that an acid reaction of muscle is a constant mark of the fatigued condition and a constant condition of the state of rigor mortis. Now if a muscle is extracted with alcohol sarcolactic acid may be obtained, but FLETCHER & HOPKINS⁽⁶⁸⁾, have pointed out that most of the methods previously used for the extraction of lactic acid from muscle caused the formation of lactic acid in this tissue. To obviate this difficulty they adopted the practice of freezing the muscles before cutting them out of the body and then dropping them into alcohol cooled to 0° centigrade. While immersed in this, they were finely divided with scissors and then pounded up in an ice cold mortar. In this way the tissue was destroyed at a temperature which did not allow the changes responsible for the production of lactic acid. Any lactic acid which there was in the muscle originally, was separated in the form of zinc sarcolate by boiling its partially purified solution with zinc carbonate.

A study of the lactic acid content of muscle by FLETCHER & HOPKINS⁽⁶⁸⁾ using the precautions described above, has shown that fresh muscle contains only minimal amounts of lactic acid; but if the muscle be left in the body after death, a steady accumulation of/

of acid takes place, being most rapid in the first few hours, but continuing until the muscle passes into rigor, when the amount does not increase, but rather exhibits an almost constant quantity of about 0.4%. They also found that the accumulation of lactic acid, when the circulation has been cut off, gradually brings about the coagulation of the proteins of the muscle, which bring about the condition known as rigor; and that varying quantities of lactic acid were produced during fatigue, the quantity varying according to the degree of fatigue induced.

Now we have already seen that in an atmosphere of oxygen the onset of rigor or fatigue may be almost indefinitely postponed, or at least very greatly belated, and that in these circumstances carbon dioxide is produced when the muscle is stimulated, whereas in an atmosphere of air or hydrogen very little carbon dioxide is produced, but lactic acid appears instead. It seems, therefore, that muscle produces on stimulation either carbon dioxide or lactic acid according to the amount of oxygen which is at its disposal for consumption, and it becomes of interest to find out whether we should regard the formation of lactic acid and carbon dioxide as alternative processes, or whether lactic acid is first formed and is then removed under the action of oxygen/

oxygen, undergoing partial or complete oxidation to carbon dioxide in the process. The evidence is distinctly in favour of the second hypothesis, and FLETCHER & HOPKINS regard lactic acid as a precursor of carbon dioxide, and that the muscle possesses in itself a chemical mechanism for the removal of lactic acid, since, if a fatigued muscle be exposed to pure oxygen all the lactic acid in it will be found to be gone after a few hours.

The normal occurrence of lactic acid in the stomach during digestion was formerly regarded as an established fact and generally ascribed to the action of lactic acid producing organisms which had been swallowed and which could exercise their activity so long as hydrochloric acid did not appear in the free state.

MARTIUS & LUTTKE⁽⁶⁹⁾ found "that the accurately determined curve of acidity referable to hydrochloric acid coincided in all respects, even at the beginning of the process of digestion; with the curve referable to the total acidity", so that lactic acid as a physiological constituent could not have been present. The researches of BOAS⁽⁷⁰⁾, moreover, prove beyond a doubt that in physiological conditions no appreciable amounts of lactic acid are formed during the process of digestion, provided no lactic acid is/

is introduced into the stomach in the form of food.

Under pathological conditions notable amounts (0.1 - 0.4%) are met with when stagnation of the gastric contents occurs. (VON NOORDEN⁷¹).

Most authorities believe that this only occurs in the absence of free hydrochloric acid, but SIMON⁽⁶⁹⁾ does not agree with this.

When this fermentation lactic acid is produced in large quantities, the well known long Boas-Oppler Bacilli are supposed to predominate among the organisms in the stomach. Careful investigation, however, by MILLER⁽⁷²⁾ and DAUBER⁽⁷³⁾ has shown that the formation of fermentation lactic acid in the stomach is by no means the prerogative of any particular organism, but can be caused by a whole host of different sorts.

The commonest method of testing for lactic acid in the gastric contents is by means of UFFEL-MANN'S reagent (a purple solution obtained by mixing carbolic acid and ferric chloride solutions), which is turned a canary yellow colour by lactic acid.

Hydrochloric acid will render the reagent colourless.

BEAUMONT & DODDS⁽⁷⁴⁾ and many other authorities consider the test practically worthless, since in a large majority of cases - particularly if EWALD'S test meal is employed - a characteristic reaction is not/

not seen, notwithstanding the presence of lactic acid, but a pale yellow, brownish or even grey colour is obtained instead, often leaving one in doubt whether lactic acid is present or not. The value of the test is also greatly diminished by the fact that glucose, acid phosphates, butyric acid and alcohol give the same reaction.

In order to avoid the fallacies of the
OFFELMANN test test MACLEAN ⁽⁴²⁾ has recently devised
a simple modification of the test, which he considers gives accurate results:

Two drops of 5% aqueous solution of ferric chloride are added to the filtered gastric contents, followed by five or six drops of a saturated aqueous solution of mercuric chloride, when, if lactic acid is present a distinctly yellow colour appears. As far as I can gather no one, besides MACLEAN, has published any results showing the efficacy or the reverse of this test.

VIEWS/

VIEWS on GASTRIC ANALYSIS in CARCINOMA of
THE STOMACH.

In 1879 the absence of free hydrochloric acid in gastric carcinoma was first noted, and since that time a very large amount of work has been done on the analysis of the gastric contents in patients suffering from this disease. Up till the last ten years or so, it was held that carcinoma of the stomach was almost invariably associated with complete achlorhydria, and many of the older physicians still believe that the presence of the slightest trace of free hydrochloric acid in the gastric contents is incompatible with the diagnosis of carcinoma.

It is interesting to review the theories which have been advanced to explain this absence of hydrochloric acid in this disease.

One theory which was very popular some years ago, depended upon the assumption that in carcinoma in general all the acidic processes in the body were suppressed and there was a tendency to alkalosis. This condition was manifested by absence of free hydrochloric acid in the stomach and a condition of alkalosis in the blood. It was even maintained that absence of free hydrochloric acid occurred in carcinoma situated outside the stomach, and thus cases of carcinoma of the breast, rectum etc., were described in/

in which no free hydrochloric acid occurred in the stomach. Very careful and extensive investigations have since gone far to prove this theory untenable, since achlorhydria is no more common in patients with malignant disease outside the stomach, than it is in patients suffering from non-malignant debilitating conditions.

A second theory which has appealed to many physicians of a physiological turn of mind, depended upon the view that the secretion of hydrochloric acid was normally brought forth by the gastric hormone secreted by the pylorus. It will be remembered that EDKIN'S theory was that when the bolus of food touched the pylorus it caused the cells of the musoca in this region to secrete into the blood serum a hormone called gastrin, and this circulated into the peripheral systemic blood and finally found its way back into the stomach, when it stimulated the organ to secrete a gastric juice. In other words this mechanism was the counterpart of the pancreatic stimulation by means of secretin. Now, since carcinoma usually occurs in the region of the pylorus, it was thought that the growth was outside the cells capable of producing gastrin, and therefore, the secretory mechanism would be interfered with. Again, extensive physiological researches have caused considerable/

considerable doubt to be cast upon the validity of this conception.

A third theory postulates an alkaline secretion from the cancer which neutralises the acidity of the gastric juice. This theory finds some support in the increase in mineral chlorides often associated with gastric carcinoma.

Lastly a more or less mechanical explanation of the achlorhydria has been put forward. Post-mortem examination in cases of carcinoma of the stomach reveals that the walls of the stomach are coated with a thick slime, and it has been suggested that this covering of the gastric mucosa prevents the test meal from getting into close contact with the wall of the stomach and thereby interferes with the secretion of the juice.

Since the cause of achlorhydria in gastric carcinoma has not been definitely established, it is perhaps not surprising that much of the current medical teaching on the subject in the most popular text books of medicine is vague in the extreme. There is a lack of agreement between the various writers, and a hesitancy on the part of most of them, that cannot but make the critical reader doubt whether gastric analysis is a real value in this disease.

HURST⁽⁷⁵⁾ . writing in Price's Text Book of
Medicine, says:-

"The/



"The absence of free HCl (in cancer of the stomach) is of less value, as achylia may also occur with chronic ulcers on the lesser curvature".

(76)
POULTON in Taylor's Practice of Medicine says:-

"In carcinoma of the stomach there is a great diminution in the active hydrochloric acid, and in the amount of free hydrochloric acid, and in the amount of free hydrochloric acid; but this also occurs in some normal people, as well as in a group known as achylia rosacea".

(77)
The last edition of Osler's Textbook states:-

"It may be said that free hydrochloric acid is absent from a large proportion of all cases of cancer of the stomach. Of 94 cases in which the contents were examined, in 84 free hydrochloric acid was absent. . . . Hydrochloric acid may be absent in chronic gastritis and in atrophy of the gastric mucosa. The presence of lactic acid is a valuable sign".

These three statements are fairly representative of the teaching accessible to the average medical/

medical student; they cannot be said to foster a belief that there is any great utility in gastric analysis, and the main impressions they convey are, first, that in most, but not all cases of gastric cancer there is no free hydrochloric acid in the gastric contents; and, secondly, that the test meal examination in carcinoma is similar to that seen in cases of chronic gastritis, pernicious anaemia, and achylia gastrica. No great emphasis is laid upon the presence or absence of lactic acid in the gastric contents - and there is certainly no suggestion that it may be possible to diagnose the majority of cases of gastric carcinoma by test meal findings alone.

Other authorities in gastric analysis, are no more unanimous in their conclusions.

In the records of the Mayo Clinic (78) . it is stated that the absence of free hydrochloric acid occurs in less than one half of the cases of carcinoma of the stomach; normal or even hyper-acid values may be expected in one quarter.

(79)
WHEELER , states that:-

"The presence of lactic acid and the absence of free hydrochloric acid may be regarded as a straw in the evidence to show which way the wind is blowing, but such a finding is of little or no aid towards early recognition". He believes that lactic acid is/

is only met with when actual pyloric stenosis occurs with stagnation and fermentation, and that free hydrochloric acid is generally found in the early stages of the disease.

HAYEM & LION⁽⁵⁰⁾ found achlorhydria present in 80% of cases of cancer of the stomach by this one hour test meal, but HARTMANN⁽⁵⁰⁾, by the fractional method found it present only in 50% of cases.

BENNET⁽⁸⁰⁾, however, believes that it is exceedingly rare for cases of gastric carcinoma to present themselves without the diagnosis being definitely established as soon as gastric analysis is performed. He states that even when a patient with gastric carcinoma has complete achlorhydria, the gastric analysis is rarely identical with that given by a patient with pernicious anaemia, chronic gastritis, or benign achylia. On the other hand, he finds that free hydrochloric acid is excreted in the stomach of the majority of patients with gastric carcinoma, and that it is not possible to effect a diagnosis on purely chemical grounds, or by discovery of some specific chemical substances secreted or produced by the tumour in the stomach. He bases his diagnosis on the evidence of stagnation, foul odour and the presence of blood.

HUNTER'S⁽⁸¹⁾ findings substantially agree with/

with those of BENNET.

(42)
MACLEAN, on the other hand, while agreeing with BENNET that carcinoma of the stomach can, in the vast majority of cases, be diagnosed with certainty by gastric analysis alone, entirely disagrees with him in regard to the question of achlorhydria in such cases; for in a large series of cases MACLEAN demonstrates achlorhydria to be present in fully 85% of cases, and in all such cases of achlorhydria lactic acid was found to be present. Further, he is convinced that this lactic acid is not necessarily the mere product of fermentation in the stomach, but is, in many cases, produced in some other unexplained way.

The views of these various authorities are thus sufficiently divergent to justify some further investigation of the subject.

OUTLINE/

OUTLINE and SCOPE of the THESIS.

The observations embodied in this thesis constitute an endeavour to elucidate several points in the technique of gastric analysis and in the results arrived at by this method, particular attention being paid to the question of the efficacy of gastric analysis as an aid to the early diagnosis of carcinoma of the stomach.

With this object in view, I have examined the gastric contents of 75 patients in Chalmers Hospital by means of the fractional method, of 15 patients in the Royal Infirmary, by means of the one hour method, and of 3 private patients by examination of the resting juice.

I am aware that it would have been desirable to have studied all my cases by means of an identical technique. This, however, proved impracticable; for had I relied entirely on the cases at my disposal in Chalmers Hospital, where I was not at liberty to employ the particular technique I desired and the one which I consider the most valuable, I should not have had sufficient cases for my purpose.

In the Royal Infirmary I was only permitted to examine cases by courtesy, and I was naturally not at liberty to dictate what technique should be there employed./

employed. The few cases in private practice which I have included in the series were all examined by me with a view to confirming or excluding a diagnosis of gastric carcinoma, and as a complete fractional examination was not possible, in the particular circumstances in which I found myself, I relied upon the examination of the resting juice, which, next to a complete fractional examination, I regard as being the most valuable method of gastric analysis in the diagnosis of this disease.

The series of cases examined by me in Chalmers Hospital by the fractional method, which constitutes the major portion of this work, were, in the main, cases of apparent gastric disorder admitted to the hospital irrespective of diagnosis. Many of these cases turned out on more exhaustive examination not to be primarily cases of organic or functional gastric disease, but cases of disease in other parts of the alimentary tract, such as the gall bladder or the appendix, showing secondary gastric symptoms. A few of the samples examined were obtained from patients suffering from such diseases as pernicious anaemia, rheumatoid arthritis, and the gastric crises of tabes, in which an examination of the gastric contents may be an aid in diagnosis or treatment.

Chalmers Hospital is divided into two sections/

sections - a private part and a public part. Patients admitted to the private wards pay about half a guinea a day, which fee includes all treatment, except X-ray examination. Those admitted to the public wards pay nothing, and are, therefore, on the same basis as patients in any other voluntary hospital. The male and female beds are present in almost equal proportions.

The cases, therefore, at my disposal varied somewhat from the usual run of hospital patients, so that there has been a rather wider field at my command, in which to carry out investigations than is usually the case.

All the analyses undertaken in the Hospital and the few which I have carried out in private practice, have been undertaken in the Hospital dispensary which is equipped with the usual simple apparatus employed in routine diagnosis. There was no elaborate apparatus, such as may be found in modern laboratories for clinical research.

All the tests have been performed in the same light, the same end point has always been taken in colour reactions, and an identical technique has been employed throughout, so that any error which I have made in reading colour changes should have been perpetuated in each case, and the results should thus be/

be strictly comparable one with another.

A series of cases examined by the one hour method in the Royal Infirmary were all patients either suspected of gastric carcinoma on purely clinical grounds, or patients who, for other reasons showed absence of free hydrochloric acid in the gastric juice. The analyses were conducted in the various siderooms of the wards which supplied me with cases, and the ward apparatus used, so that I cannot claim for these examinations the same identical conditions under which the tests were carried out in Chalmers Hospital. With the exception, however, of the decinormal soda solution used for titrating, I always carried with me my own reagents for carrying out the various tests employed.

In testing for free acid, I have used three tests on each occasion, namely: the Congo Red Test; the Dimethyl test; and the Gunzberg test. In the following pages, I have given tables to show the relative value of these tests, and have drawn conclusions therefrom.

TOPFER'S reagent has been used in estimating the free acid present, and the phenolphthalein indicator in estimating the combined acid.

No inferences can be drawn as to the prevalence of achlorhydria in general diseases of the stomach from the cases examined, for this would give an erroneously/

erroneously high impression as to the commonness of achlorhydria in general gastric diseases, since patients suffering from pernicious anaemia, chronic gastritis, carcinoma of the stomach and other diseases likely to cause achlorhydria, appear in my series of cases in a greater proportion than they would do had fractional test meals been invariably performed irrespective of diagnosis.

Lactic acid has been tested for in each case, and tables are given to show the type of disease in which it occurs in the gastric contents.

In testing for lactic acid both UFFELMANN'S TEST, and the test advocated by MACLEAN were employed on each occasion, and tables are given to show the relative value of these tests and conclusions drawn therefrom.

Some investigation has been made into the mode of production of lactic acid in the stomach, and from this a new theory is advanced as to the mode of production of lactic acid in some cases of gastric carcinoma.

In each case the contents of the stomach have/

have been examined for charcoal, starch, bile, blood and the Oppler Boas bacillus, and the presence or absence of foul odour noted. Tables are given showing the results arrived at.

I have examined carefully 17 cases of carcinoma of the stomach, and enquired into the possibility of diagnosing its presence or absence in a suspected case by gastric analysis, and of differentiating the test meal findings in this disease from findings in other diseases which give somewhat similar results on gastric analysis.

Finally, I have given the case histories with charts showing the test meal findings in all the cases which have come under my notice of patients suffering from gastric carcinoma, and of certain cases where examination of the gastric contents was found to be of use in excluding cancer of the stomach.

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TECHNIQUE EMPLOYED and RESULTS OBTAINED.

TECHNIQUE EMPLOYED.

- (i) The Series of cases examined by the fractional method.

The general procedure carried out in the series of cases examined by the fractional method will be considered in detail under the following headings:-

- (a) The preparations made for the test.
- (b) The passage of the tube, and the withdrawal of samples.
- (c) The method of examining the samples.

(a) PREPARATIONS MADE FOR THE TEST

(A) On the day before the test the patient received no drugs and his diet was a light one containing no meat, since his stools were tested for occult blood at the same time as the gastric contents were examined. On this day also, it was always my custom to explain to the patient the nature and purpose of the test, and to attempt to allay his anxiety. It was seldom that any patient was much perturbed at the prospect.

At 11.P.M. on the night before the test the patient was given a cup of milk containing two teaspoonfuls of charcoal and a charcoal biscuit.

(1)
BENNET'S custom was followed, of asking

all/

all patients not to brush their teeth on the morning of the test, lest blood be introduced into the stomach contents in this way.

(b) THE PASSAGE of the TUBE and the withdrawal of SAMPLES.

(B) The passage of the tube was commenced at 6.30 A.M. - no food or drink having been taken previously.

The tube used was a No.8 French rubber tube the bulbous end being that devised by RYLE⁽²⁾, which was described in the previous section. It is marked by transverse lines at 40 cm. and 57 cm. distance from the tip to indicate approximately the cardiac orifice and the pylorus respectively. The tube was boiled and kept lying in the water till required for use, when the end was lubricated with glycerine.

The patient sat upright in bed, and was told to take the weighted end of the tube into his mouth, together with two or three inches of tubing so that there was plenty of 'slack' in the mouth.

He was told to retain this in his mouth until it was thoroughly moistened with saliva, and then to work the bulbous tip towards the back of the tongue by ^{ac}passing his lips firmly round the tubing. The suggestion was then made that he should swallow the bulb as though it was a pill, and should he succeed in/

in 'getting it over', he was to swallow forcibly, two or three times in rapid succession, so as to force the bulb past the constriction corresponding to the cricoid cartilage, which is, according to RYLE⁽³⁾, the point at which the obstruction to the passage of the tube is most apt to occur. When he had got it passed this point, he was told to pause and take a few breaths to assure himself that he could breathe perfectly easily, and then to continue swallowing the tube quietly and taking his own time, till the mark indicating the pylorus was just reached, when the passage of the tube was stopped. If the patient felt any inclination to retch, while swallowing the tube, he was told to stop and take long breaths.

A few patients succeeded in swallowing the tube at the first attempt, but the majority had to make two or three efforts, before they could get the bulb past the constriction at the cricoid. In only two of the 75 cases examined by this method, was any great distress with severe coughing and retching caused, and in these the attempt to pass the tube was desisted from. These were the only two failures I have ever had in passing the tube, and an attempt to pass it has never been persisted in after four or five efforts have proved unavailing. In a few cases I found that by demonstrating
on/

on myself before the patient, how easy it was to swallow the tube, the patient, who had beforehand been convinced that the proceeding was impossible, gained such confidence as to swallow it readily.

When the tube had been swallowed as far as the pyloric mark, suction was commenced by means of a record syringe. Suction was applied with the patient sitting up, lying on his back, lying on the right side, then on the left side and finally lying on his face. No change in position was made till suction in the particular position only produced a little froth, and while in each position the tube was slightly lowered and raised so as to search the stomach thoroughly for contents. After this procedure, the patient was asked to maintain the tube so that the pyloric mark on it was just at the level of his lips, and thereafter, throughout the test, to spit out any saliva which accumulated in his mouth rather than swallow it, so as to prevent an artificial hypo-acidity due to excessive salivation, which occurred in a few of BENNET & RYLE'S ⁽⁴⁾ cases.

Of the aspirated contents, the first 15-20 cc. were placed in a test tube marked "o" and the remainder was placed in a bottle similarly marked.

The patient then sat up and with the tube still in situ, ate his 'test meal'. This consisted of/

of thin gruel, made by boiling two tablespoonfuls of oatmeal in two pints of water, until the total bulk was reduced to a pint, which was then strained through muslin. The result, though somewhat unpalatable, had the advantage of giving a colourless specimen on aspirating it from the stomach, so that when examined later, titration end points and other colour reactions could be determined with great accuracy.

After taking the meal, the patient was asked to lie down again and to remain lying for the rest of the test, reading or talking, so as to minimise as much as possible any psychological disturbance. The tube was clamped by a pair of small artery forceps, to prevent any leakage of gastric contents between the aspiration of the samples.

Samples were then withdrawn from the stomach, at intervals of a quarter of an hour, reckoned from the time the patient began to take the meal, care being taken to see that the pyloric mark was at the level of the lips before each sample was aspirated. The syringe was washed out thoroughly after each aspiration. Samples were withdrawn in this way for two hours, so that eight samples each consisting of from 15 to 20 c.c. were obtained.

The advisability of continuing the withdrawal of samples for a longer period, or until the stomach/

stomach was completely emptied, was carefully considered, and rejected. The inconvenience caused to the nursing staff made the procedure undesirable, and secondly, on examining the reports on 83 cases, on which fractional test meals had been performed by FABER, HOLST & NORGAARD ⁽⁵⁾, in which samples had been withdrawn for three hours, I was unable to find a single instance in which any more information had been obtained by the addition of an hour to the patient's discomfort.

The samples were placed in test tubes numbered '1', '2', '3', and so on, according to the order in which they were obtained, and after sample No.8 had been removed, the stomach was emptied completely by a similar procedure to that already described, when the resting juice was removed prior to the swallowing of the test meal. The contents obtained in this way, were placed in a bottle marked '8', and the tube was then withdrawn by a rapid movement.

(C) THE METHOD of EXAMINING the STOMACH CONTENTS.

(C). The samples for examination were contained in nine test tubes, marked from '0' to '8', and in two bottles marked '0' and '8'.

It was my custom to proceed as follows:-

The patient's name and the date of the test were/

were entered on a sheet of paper, which contained nine columns, one for each of the test tubes.

The odour of the specimens and their naked eye appearances were noted, each one being examined for the presence of bile, blood, pus and charcoal.

The specimen of resting juice was also examined microscopically for blood, pus and the Oppler Boas bacillus, and for evidences of stagnation.

Each tube sample was then tested qualitatively for the presence of free hydrochloric acid. Three tests for this were employed and the reaction to each test noted.

The three tests were:-

1. THE CONGO RED TEST. A piece of Congo Red Paper was dipped into the specimen; if the paper became blue, a positive result was noted.
2. THE DIMETHYL TEST. A drop of Töpfer's reagent was added to a small quantity of the specimen. If a red colour then appeared, the reaction was noted as positive.
3. THE GUNZBERG TEST. Two drops of Gunzberg's reagent - a small quantity of which I made up freshly each week - were added to five drops of the filtered gastric contents, in a porcelain basin. After mixing thoroughly the dish was very gently heated over a flame care/

care being taken that no charring occurred. A red colouration, or even a faint orange red appearing round the edges of the residue was taken to indicate the presence of free hydrochloric acid.

Each tube sample was then tested qualitatively for the presence of lactic acid. Two tests were employed, namely:-

1. **ÖFFELMANN'S TEST.** About 5 c.c. of Öffelmänn's reagent (Carbolic acid 1-20 10cc. Distilled water 20cc.) were placed in a test tube, and a few drops of the filtered specimen were added to it. A change in colour of the solution from blue to yellow was taken to be a positive reaction. (HUTCHISON & RAINY⁽⁶⁾).
2. **MACLEAN'S TEST.** Two test tubes were taken. To one $\frac{1}{2}$ - $\frac{3}{4}$ inch of the filtered gastric specimen was added, to the other an equal amount of tap water, and to each two drops of a 5% solution of ferric chloride. The tube with the gastric contents would then show a definite reddish colouration. To each tube five or six drops of a saturated solution of mercuric chloride were now added. If the reddish colour entirely disappeared a negative reaction was noted, but if the reddish appearance gave place to a distinctly/

distinctly yellow colour, the reaction was taken to be positive. Comparison with the control tube enabled one to determine the difference between them and to estimate the depth of the colour produced. (MACLEAN⁽⁷⁾)

Besides testing for blood by the naked eye appearances of the specimen and by the microscopical examination of the resting juice, the resting juice was also tested for it by chemical means.

Some of the solid was scraped off the paper used for filtering the contents in the tests for lactic acid. This was suspended in about one inch of water in a test tube, boiled and cooled under the tap. About $\frac{1}{2}$ inch of glacial acetic acid was added with shaking, then one inch of ether and the whole thoroughly shaken up. If the ethereal layer did not separate water was added without shaking. In each of two test tubes $\frac{1}{2}$ cc. of alcoholic solution of guiacum was placed, and 2 cc. of 3% peroxide of hydrogen. To one tube the clear ether extract was added with a pipette, while the other was used as a control. A blue colour appearing in the contents of the tube to which the ether extract had been added, was taken as a positive reaction. (BEAUMONT & DODDS⁽⁸⁾)

When, in a tube sample, the presence of free hydrochloric acid had been determined, this and the/

the total acidity were tested for quantitatively by titration against decinormal sodium hydroxide, using dimethylamine-adzeben^{enz}zol (TÖPFERS reagent) and phenophthalein solutions as indicators respectively. Amounts of 5 cc. of the unfiltered contents were used on each occasion. One of my predecessors in the hospital had found a 5 cc. glass phial of an ethyl chloride anaesthesia apparatus useful as a measure for this amount (McCRACKEN⁽⁹⁾). I made use of this phial also, since by using it there was a minimum of unnecessary contact between the sides of the measure and the gastric contents, such as occurs on using a larger or taller measure for this purpose.

After the measured contents had been poured into a small titration flask, the phial was filled with 5 cc. of water, the top closed with the finger, and the whole shaken thoroughly. This water was then added to the sample in the titration flask.

The acidity values were recorded in cubic centimetres of decinormal soda per 100 cc. of stomach contents, and the figures were translated into a graph by being plotted against a time basis.

The amounts of gastric content in bottle '0' and in tube '0' were added together, measured in cubic centimeters and recorded as the amount of 'Resting juice' present; while bottle '8' and tube '8' were similarly treated and recorded as 'Residue'.

Finally/

Finally a few drops of iodine solution were added to the remainder of the contents in each tube to show the presence or absence of starch.

(ii) In series examined by the one hour method.

The preparations made for the test in this series of cases, the passage of the stomach tube and the withdrawal of the gastric contents, which were performed at the Royal Infirmary, were not supervised personally by me.

The test meal consisting of a pint of weak tea with no sugar and only a few drops of milk, and a small piece ($\frac{1}{2}$ oz.) of toast was given early in the morning, the patient having fasted the night before, and one hour later an ordinary large size stomach tube was passed, and as much of the gastric contents as possible aspirated.

The volume of the contents obtained was measured and the analysis of the single specimen proceeded with in the same way as indicated above, with the exception that as no charcoal had been given previously it was not looked for.

(iii) In series examined by analysis of the Resting Juice only.

In this series of cases the sample was procured by an identical technique to that employed for procuring/

procuring the resting juice in the patients examined by the fractional method. The time of taking the sample varied in each case, but it was usually from nine to ten in the morning - the patient having had no food since the previous evening.

The technique employed in the analysis of the specimen was identical to that outlined above in the analysis of the resting juice of patients examined by the fractional method, except that no charcoal having been taken by this group of patients previously, it was not looked for.

RESULTS/

RESULTS OBTAINED.

In the following pages details will be found of the analysis of the gastric contents of ninety three different patients. Seventy five of these analyses have been performed by the fractional method, fifteen by the one hour method and three by examination of the resting juice.

These ninety three cases include:-

- (1) Forty eight cases showing the presence of free hydrochloric acid at some stage in the test, as demonstrated by the **GUNZBERG** reaction, in which gastric carcinoma, as far as could be ascertained, was not present. (43 by the fractional method, 4 by the one hour method and 1 by the examination of the resting juice).
- (2) Seventeen cases of gastric carcinoma. (9 by the fractional method, 7 by the one hour method and 1 by the examination of the resting juice).
- (3) Twenty eight cases showing absence of free hydrochloric acid throughout the test, in which gastric carcinoma, as far as could be ascertained, was not present. (23 by the fractional method/

method, 4 by the one hour method and one by examination of the resting juice).

It must be again pointed out that no significance can be attached to the percentage of cases showing achlorhydria in the ninety three cases examined. Such an inference would give an erroneously high impression of the occurrence of achlorhydria in general diseases, since the type of case likely to show achlorhydria has been particularly collected for the purposes of this research.

The first table shows some of the results arrived at in the first series of cases and represents an investigation into the delicacy of the various tests for the presence of free hydrochloric acid, and into the efficacy of UFFELMANN'S test for lactic acid.

The first column in the Table gives the number of the case, and the letter following the number shows the type of test employed:

F = Fractional Method.

E = EWALD'S one hour method.

R.J.= Examination of resting juice only.

The second column gives the diagnosis of
the/

the case.

The third column gives the reactions of the various tubes to GUNZBERG'S reagent. A positive or a negative sign indicates the presence or absence of free hydrochloric acid as demonstrated by the reaction and the numbers following the sign indicate the samples in which the positive or negative reaction occurred. Thus " - in 1,2," indicates that no free hydrochloric acid was found in the quarter and half hour specimens, but that it was present in all the other samples which are not mentioned.

The fourth and fifth columns show the reactions of the various tubes to the Dimethyl and Congo Red tests. Where the reactions differ from these given by the GUNZBERG test, the difference has been called attention to by printing the number of the tube in which the reaction occurred in red. When the reactions have been identical throughout to these given by the GUNZBERG test, the results have not been written over again, and instead the word "ditto" is inserted.

The last column shows the reaction of the various/

48 cases showing Free Hydrochloric Acid at some stage in the Analysis, as demonstrated by GUNZBERG'S reaction, in which Gastric Carcinoma was not present. To show the delicacy of the dimethyl and Congo Red tests and the efficacy of UFFELMANN'S reaction. MACLEAN'S test -ve. throughout.

CASE.	DIAGNOSIS.	GUNZBERG REACTION.	DIMETHYL REACTION.	CONGO RED REACT.	UFFELMANN'S TEST.
1 F.	Tabes	- in 1,2,	ditto.	ditto.	+ in 2
2 F.	Neurasthenia.	- " 0,1,2,3,6,7,8,	- in 0,1,2,3,4,6,7,8,	- in all.	+ " 0,1,7.
3 F.	"	- " 0,1,2.	ditto.	ditto.	-
4 F.	Chr. dyspepsia.	+ " all	ditto.	ditto.	-
5 F.	"	+ " 1,2.	ditto.	ditto.	-
6 F.	"	+ " all	ditto.	ditto.	-
7 F.	"	+ " "	ditto.	ditto.	-
8 F.	"	+ " "	ditto.	ditto.	-
9 E.	"	+ " "	ditto.	ditto.	-
10 E.	"	+ " "	ditto.	ditto.	-
11 F.	"	- in 0,1,8.	- in 0,1,7,8.	- in 0,1,2,7,8.	? in 0,8.
12 F.	"	- " 1.	ditto.	ditto.	-
13 F.	"	+ " all.	- in 1.	- in 1.	++ in 1.
14 F.	"	- " 1	ditto.	1,2.	-
15 F.	"	+ " all.	ditto.	ditto.	-
16 F.	"	+ " "	- in 1.	- in 1.	-
17 F.	"	- " 1,7,8.	ditto.	ditto.	? in 1,7,8.
18 F.	"	+ " all	ditto.	ditto.	-
19 F.	"	- " 0,1,2,3,4,7,8.	ditto.	ditto.	+ in 0,3,6.
20 F.	"	- " 1,2.	- in 1,2,8.	- in 1,2,8.	? " 2.
21 F.	"	+ " all.	ditto.	1.	-
22 R.J.	"	+ " "	ditto.	ditto.	-
23 E.	"	+ " "	ditto.	ditto.	-

T A B L E I. (contd.)

CASE.	DIAGNOSIS.	GUNZBERG REACTION.	DIMETHYL REACTION.	CONGO RED REACT.	UFFELMANN'S TEST.
24 E.	Chr. Dyspepsia.	+ in 1.	ditto.	ditto.	-
25 F.	T.B. Abdomen.	- " 0.	ditto.	ditto.	-
26 F.	Gall stones.	+ " all.	ditto.	ditto.	+ in 0.
27 F.	" "	- " 1,2,3.	ditto.	ditto.	? in 1,2,3.
28 F.	Gastric Ulcer.	+ " all	ditto.	ditto.	-
29 F.	" "	+ " "	ditto.	ditto.	-
30 F.	" "	+ " "	ditto.	ditto.	-
31 F.	" "	+ " "	ditto.	ditto.	-
32 F.	" "	+ " "	ditto.	ditto.	-
33 F.	Duodenal	+ " "	ditto.	ditto.	-
34 F.	" "	+ " "	ditto.	ditto.	-
35 F.	" "	+ " "	ditto.	ditto.	-
36 F.	" "	+ " "	ditto.	ditto.	-
37 F.	Colitis.	+ " 1,7,8.	- in 1,7,8.	in 1,7,8.	+ in 7.
38 F.	Rheumatoid Arthr.	- " 0,1,2,3,4.	- ditto.	- " 0,1,2,3,4,5.	+ " 0,1,2.
39 F.	Visceroptosis.	- " 1,2,8.	- in 1,2,7,8.	- " 1,2,7,8.	-
40 F.	" "	+ " all,	- ditto.	- " 1.	-
41 F.	" "	+ " "	ditto.	ditto.	" 3,6,8.
42 F.	" "	- " 1,3,6,7,8.	ditto.	ditto.	" 2.
43 F.	" "	- " 0,1,2,3.	ditto.	ditto.	-
44 F.	Chr. Pyelitis.	- " 1.	- in 1,2.	in 1,2.	-
45 F.	" Appendix.	- " 1.	ditto.	ditto.	-
46 F.	" "	+ " all	ditto.	ditto.	-
47 F.	Oxaluria.	- " 1.	ditto.	ditto.	-
48 F.	Carc. of Pancreas.	- " 0,1,2,8.	ditto.	ditto.	-

various samples to UFFELMANN'S test. When a negative sign appears all the tubes from "0" to "8" may be taken to have given a negative reaction for lactic acid. Where a positive sign occurs, the number of the tube in which the positive reaction has taken place is given. A mark of interrogation shows that the reaction has been doubtful. MACLEAN'S test for lactic acid was negative, in this series, at every stage of the test in every case.

It will be seen from the table given above that the dimethyl indicator failed to register the presence of free hydrochloric acid in eight samples, in which the GUNZBERG test had shown a clearly positive reaction. That is, after a drop of the dimethyl reagent had been shaken up with the sample the whole remained a bright yellow colour with no trace of red or pink in it. According to MACLEAN⁽⁷⁾, GUNZBERG'S test gives a distinctly positive reaction with such a low concentration as 0.003% of hydrochloric acid. It is apparent, therefore, that the dimethyl indicator is not quite so delicate a test, and that very small/

small quantities of free hydrochloric acid are not demonstrated by it.

In regard to the Congo red test it will be seen that in all the eight samples, in which the dimethyl indicator failed to give a positive reaction, the congo red test also failed. In addition, seven other specimens, which gave a positive reaction with both the GUNZBERG and with the dimethyl test, failed to change the colour of the red paper in any way. Since it was possible to estimate the quantity of free hydrochloric acid in these seven extra specimens by titration against the dimethyl indicator, it was found that congo red paper fails to give a positive reaction when the free hydrochloric acid is in a concentration of less than 0.015%

It seems, then, that if the GUNZBERG test is omitted a diagnosis of achlorhydria may be given, when, in reality, small quantities of free hydrochloric acid are actually present.

In all the specimens which were tested MACLEAN'S test indicated the absence of lactic acid.
It/

It will be seen, however, that UFFELMANN'S test gave a clearly positive reaction in fourteen specimens, and a doubtful (?) reaction in twelve more samples. It will be noted that free acid was absent, from all the samples in which a positive reaction occurred, since the reagent is decolourised by free hydrochloric acid. In none of the specimens in which a positive reaction was obtained was there any reason to suspect the presence of lactic acid, there being no evidence of stasis in the stomach with consequent fermentation, nor of gastritis or malignant disease - all conditions thought to favour the production of lactic acid. This consideration and the negative nature of the MACLEAN test throughout the series leads one to believe that lactic acid was not really present in any of these samples, but rather one of the many other substances which give a positive reaction with UFFELMANN'S reagent, such as phosphates or sugars. One cannot therefore regard a positive UFFELMANN reaction as being a reliable indication of the presence of lactic acid; and, indeed, any colour reaction which/

which so frequently leaves the observer in doubt as to its positive or negative nature, must be one of little or no practical utility.

TABLE II gives the results of the gastric analysis of the second series of cases, all the samples of which were obtained from patients suffering from carcinoma of the stomach.

A similar method of tabulation has been used, to that employed in TABLE I, but additional columns have been added showing the presence or absence of blood, charcoal, foul odour, and the OPPLER BOAS bacillus.

A positive sign is placed if blood was found in any sample throughout the test.

The test, in the case of the patients examined by the OPPLER BOAS bacillus was not looked for in every sample throughout the fractional method, but only in tube "O" containing the resting juice.

T A B L E II.

TABLE of RESULTS in 17 CASES of GASTRIC CARCINOMA.

CASE	GUNZBERG REACT.	DIMETHYL REACT.	CONGO RED REACT.	UFFELMANN	MACLEAN	CHARCOAL	FOUL ODOUR	BLOOD	OFFLER BOAS B.
1 F.	in all	in all	in all	++ in all	++ in all	-	-	-	-
2 F.	" "	" "	"6"	+++	+++	+++	+++	++	++
3 F.	" "	" "	"6"	-	-	+	+	+	-
4 F.	" "	" "	all	++	+	+	+	+	+
5 F.	" "	" "	" "	++	++	++	++	++	++
6 F.	" "	" "	"4"	+++	+++	+++	++	++	++
7 F.	" "	" "	all	+	+	-	-	++	-
8 F.	" "	" "	" "	+	+	-	-	++	++
9 F.	" "	" "	" "	+	+	-	-	++	++
10 E.	-	+	+	+++	+++	Not taken	+++	+	+
11 E.	-	-	-	+	+	" "	+	++	-
12 E.	-	-	-	++	++	" "	+	++	+
13 E.	-	-	-	+	+	" "	-	-	-
14 E.	-	-	-	++	++	" "	-	-	-
15 E.	-	-	-	++	++	" "	+	+	-
16 E.	-	-	-	++	++	" "	-	-	-
17 R.J.	-	-	-	+	+	" "	-	+	-

81a.

From the Table given it will firstly be seen that achlorhydria, as demonstrated by the GUNZBERG reaction was present in sixteen out of the seventeen cases examined. In Case 10, however, though the GUNZBERG test revealed no trace of the presence of free hydrochloric acid, yet both the dimethyl and congo red tests gave clearly positive reactions. We are thus faced with the apparent fallacy, that the test which the previous series of cases revealed to be the most delicate, is in this case seemingly less delicate than either of the other two.

CASE 10, as will be seen on referring to the case records given later, was a clear case of advanced gastric carcinoma - a diagnosis confirmed by laparotomy. The gastric contents had been examined at the Royal Infirmary and pronounced to contain a large quantity of free hydrochloric acid. This had been tested for by Congo Red paper and estimated quantitatively by titration, using the dimethyl indicator. GUNZBERG'S test had been omitted.

I obtained a sample from the same one hour specimen which had been previously tested, and repeated the analysis. Again the Congo Red and Dimethyl tests were strongly positive, but the GUNZBERG test/

test was definitely negative. The specimen obtained was abundant and intensely foul. The OPPLER BOAS bacillus was present in large numbers, there were numerous blood cells, and both MACLEAN'S and UFFELMANN'S test showed lactic acid to be present in great quantities. On estimating the total acid, it was found to be very high - (79 c.c. NaOH per 100 c.c. of gastric contents).

There seems no doubt, therefore, that the proper interpretation of the result is that "the large quantity of free hydrochloric acid", which was previously announced to be present, was not hydrochloric acid at all, but lactic acid; and that the high total acid reading was due, not to hydrochloric acid, but to organic acids.

If this supposition be correct, it follows that the dimethyl indicator must react with lactic acid, when this is present in strong concentration, just as it does with hydrochloric acid, and in this way, free hydrochloric acid may erroneously be supposed to be present, if GUNZBERG'S test is omitted. (10) Such a statement entirely disagrees with RYFFEL, who holds that organic acids in the stomach never attain an acidity great enough to affect TÖPFER'S reagent, and with MATHEWS (11), who states that any organic/

organic acid occurring in the stomach, would require to be present in a concentration of at least 0.5%, before it would affect this indicator; a concentration which, of course, they never attain. On the other hand, it substantiates the contention of COLE & ADIE⁽¹²⁾ and of MACLEAN⁽⁷⁾, who maintain that a positive reaction is sometimes given by TOPFER'S reagent when lactic acid is present in the stomach in fairly strong concentration.

The same thing is true, to an even greater extent, of the Congo Red test, since it was equally at fault in Case 10, and again showed a positive reaction in the sixth sample of Case 2, though GUNZBERG'S test - and in this case also - the Dimethyl test showed no free hydrochloric acid to be present in this specimen. In this case also, it will be seen that large quantities of lactic acid were present, and I have no doubt that it was this lactic acid not free hydrochloric acid which turned the red paper blue.

Seventeen cases, in sixteen of which achlorhydria was present, is not, of course, a sufficient number on which to come to any dogmatic conclusions as to the prevalence of achlorhydria in gastric carcinoma/

carcinoma. It is, however, suggestive; and it is permissible to speculate, once the fallacy of the dimethyl and congo red tests for free hydrochloric acid has been pointed out, whether this very fallacy has led many modern observers, such as BRUNET^{En} (13), and HUNTER⁽¹⁴⁾, to state that large quantities of free hydrochloric acid in the gastric contents are a very common finding in carcinoma of the stomach.

If GUNZBERG'S test is omitted, a quantitative estimation for free hydrochloric acid may be done in the usual way, and on addition of the dimethyl indicator a red colour is obtained. Under the impression that this red colour is due to free hydrochloric acid, an impression strengthened by the fact that a piece of congo red paper may have been turned blue by the sample, more and more alkali is added. The end point is indefinite and a large amount of alkali may be required to produce it. This is calculated as free hydrochloric acid, whereas, in reality, none may have been present and the reaction entirely due to a large quantity of lactic acid.

All this goes to prove that GUNZBERG'S test is the only reliable one for the detection of free hydrochloric acid in the gastric contents. It is, however, essential that the reagent should be fresh; since, if it is kept in a bottle for longer than a month/-

month - as must frequently be the case in ward side-rooms - it does not give satisfactory results. This, I have proved repeatedly, by testing a sample of gastric contents with the fresh reagent, and then with supplies which had been kept in bottles for varying periods.

In tube '6' in case 3, free hydrochloric acid was present in a concentration of just under 0.015%. As in previous cases quoted, the Congo Red test failed to indicate its presence, though the acid was present in a large enough proportion to be estimated by titration, with TOPFER'S reagent as indicator.

The most striking feature in this series of cases, is the absence of free hydrochloric acid and the presence of lactic acid. Lactic acid was present throughout the test in every case which showed achlorhydria - that is, in sixteen out of the seventeen cases. UFFELMANN'S test and MACLEAN'S test were in agreement throughout. It seems then, taking this and the previous series of cases into account, that though UFFELMANN'S test will always give a positive reaction when lactic is actually present, yet it will frequently give a positive reaction when lactic acid is, as far as can reasonably be ascertained, absent. It will be seen later, in the third series of cases, that this contention is/

is again borne out, since a positive reaction is once more given by UFFELMANN'S test in many cases where there is no likelihood of lactic acid being present in the gastric contents, and where MACLEAN'S test is invariably negative. MACLEAN'S reaction is, therefore, the more reliable of the two, and, as far as I can judge, an exceedingly simple, and trustworthy test.

Many modern observers have held that the absence of free hydrochloric acid and the presence of lactic acid are features only of advanced cases of gastric carcinoma, and that early cases do not give such results. Unfortunately I can only claim two cases out of the seventeen - (cases 1 and 7), which were admitted to hospital sufficiently early for the growth to be removed, and in case 7, pyloric stenosis had already occurred with consequent fermentation, and foulness of the gastric contents. It is not surprising, therefore, that achlorhydria combined with the presence of lactic acid, should have been found in case 7; but case 1 furnishes an example of a similar finding in a very early case indeed. The condition was diagnosed almost entirely by the test meal findings, since it will be seen, on referring to the case history, that the patient was admitted to hospital, not complaining/

complaining of stomach symptoms at all, but of sciatica. At the operation a nodule, confirmed by histological examination to be malignant, was found, which was not bigger than a sixpenny piece. There was no apparent involvement of glands and the growth was easily removed. There was no stagnation of the stomach contents, and the surgeon who operated, stated that it was the earliest case of gastric carcinoma that he had ever seen. (MERCER)⁽¹⁵⁾, Yet no free hydrochloric acid was found and lactic acid was clearly present.

Again, case 3, which was the only one to show free hydrochloric acid to be present, was one of the most advanced cases in the series, the patient dying a month after the analysis of the gastric contents had been performed.

It is, therefore, fallacious to imagine that the early stage of carcinoma of the stomach is associated with free acid in the gastric contents, and that it is only in the later stages that achlorhydria and the presence of lactic acid occur.

The general Text Book teaching concerning lactic acid in the stomach contents is to the effect that it is invariably caused by fermentation, due to stagnation of retained contents. There is no doubt that this is a frequent means of production of lactic acid/

acid, but that it is not invariably produced in this way can be seen from the fact that in cases 1, 8, 9, 11, 14, 15 and 17, there was no marked pyloric stenosis with consequent stagnation of the gastric contents and yet lactic acid was present in each case. Indeed, in cases 9 and 14, the stomachs, as demonstrated by X-ray screening, were 'leather bottle' in type, emptying very rapidly, and in cases 8 and 15, the cancer was situated at the cardiac end of the stomach.

Further, in case 2, where a marked degree of pyloric stenosis existed, causing stagnating and foul gastric contents containing a large quantity of lactic acid, I caused the stomach to be washed out until the return from it was perfectly clean - giving a negative reaction to MACLEAN'S test for lactic acid. Half an hour after this procedure, I caused a RYLE'S tube to be passed, and aspirated a small quantity of gastric juice, which was again tested for lactic acid by MACLEAN'S test. This time the test gave a clearly positive reaction.

It is apparent, therefore, that lactic acid must frequently be produced in the stomach in some other way than by mere fermentation of stagnating contents. A theory as to this alternative mode of production is advanced later, substantiated by certain observations in the third series of cases.

It will be seen that blood was found at some stage/

stage in the analysis in twelve cases out of the seventeen, charcoal in six cases out of the nine in which it had been previously taken by the patient, and the OPPLER BOAZ Bacillus in only five cases out of the seventeen. None of these findings were, therefore, so constant as the presence of lactic acid and the absence of free hydrochloric acid, which was observed in sixteen out of the seventeen cases.

(13)
 BENNET , who holds that it is exceedingly rare for cases of gastric carcinoma to present themselves without the diagnosis being definitely established once gastric analysis is performed, and who bases his diagnosis on the evidence of stagnation, foul odour, and the presence of blood, yet denies that it is possible to effect a diagnosis on purely chemical grounds, or by the discovery of some specific chemical substance in the stomach, would surely have been at fault in at least 4 of the cases in this series, namely Cases 1, 11, 14 and 15, since, apart from the absence of free hydrochloric acid and the presence of lactic acid, there was no evidence of stagnation, no evidence of blood or of any other sign of gastric carcinoma in any of the four stomach contents.

In case 3, the only one which showed free hydrochloric acid to be present, no lactic acid was found. The free hydrochloric acid was not present in great/

great quantity, never requiring more than 22 c.c. of decinormal soda per 100 c.c. of stomach contents to neutralise it at any stage of the test, and the total acid never more than 40 c.c. In this case blood and charcoal were present in the contents, which were very foul, so that there was little difficulty in effecting a diagnosis from the test meal findings.

With the exception of cases 3, 4, and 9, the diagnosis of gastric carcinoma was, in every case, confirmed by laparotomy or post mortem examination.. Cases 3, 4, and 9, are included in the series, as the physical examination, X-ray findings, and subsequent history of the patients, seemed to put the diagnosis beyond all reasonable doubt.

The case histories and charts showing the gastric analysis in detail of all the patients in this series are given later.

TABLE III, gives the results of the analysis of the gastric contents in the third series of cases, comprising twenty-eight cases showing absence of free hydrochloric acid throughout the test, as demonstrated by the GUNZBERG, and the dimethyl and congo red tests, in which, as far as could be ascertained, carcinoma of the stomach was not present. Since all the three tests for free hydrochloric/

hydrochloric acid were in agreement throughout this series, in giving a negative reaction. Those columns giving constantly negative signs, are not inserted in the table. In other respects the system of tabulation is the same as in TABLE II.

TABLE/

TABLE of RESULTS in 28 CASES of ACHLORHYDRIA, in which CARCINOMA of the STOMACH was not present.

GUNZBERG, CONGO RED and DIMETHYL reactions negative throughout.

CASE.	DIAGNOSIS	UFFELMANN.	MACLEAN	BLOOD.	CHARCOAL	FOUL ODOUR.
1 F.	Carcinoma of Oesophagus.	+ in all	+ in all	+	-	-
2 R.	" "	+ " "	+ " "	-	Not taken.	-
3 F.	Pernicious Anaemia.	- " "	- " "	-	-	-
4 F.	" "	- " "	- " "	-	-	-
5 F.	" "	- " "	- " "	-	-	-
6 E.	" "	- " "	- " "	-	-	-
7 E.	" "	- in all	- in all	-	Not taken.	-
8 F.	Carcinoma of Pancreas.	+ " 2, 3.	- " "	-	-	-
9 F.	" " Colon.	+ " all	- " "	-	-	-
10 F.	" " C.N.S.	- " "	- " "	-	-	-
11 F.	Banti's Disease.	- " "	- " "	++	-	-
12 F.	Rheumatoid Arthritis.	- " "	- " "	-	-	-
13 F.	Chr. Gastritis. (Alcoholic.)	- " "	- " "	-	+	+
14 E.	" "	- " "	- " "	+	Not taken.	-
15 F.	" "	- in all	- in all	-	-	-
16 F.	Cirrhosis of Liver. (Alcoholic).	- " " "	- " " "	++	-	-
17 F.	Chr. Appendix.	+ " " "	- " " "	-	-	-
18 F.	" "	- " " "	- " " "	-	+	-

T A B L E III. (contd.)

CASE.	DIAGNOSIS.	UFFELMANN.	MACLEAN	BLOOD.	CHARCOAL	FOUL ODOUR.
19 F.	Chr. Appendix & Cholecystitis.	? in all	- in all	-	-	-
20 E.	Chr. Cholecystitis.	++	-	-	Not taken.	-
21 F.	Melancholia.	- in all	- in all	-	-	-
22 F.	Glycosuria.	- " "	- " "	-	-	-
23 F.	Primary Achylia Gastrica.	- " "	- " "	-	-	-
24 F.	Chr. dyspepsia.	- " "	- " "	+	+	-
25 F.	" "	? " "	- " "	-	-	-
26 F.	" "	+ " 6, 7.	- " "	-	-	-
27 F.	" "	- " all	- " "	-	-	-
28 F.	" "	- " "	- " "	-	-	-

It will be seen from the above table that while UFFELMANN'S test and MACLEAN'S test are in agreement in giving positive reactions for lactic acid in cases 1 and 2, yet, in all the other cases, while MACLEAN'S test is consistently negative, UFFELMANN'S test is fairly frequently clearly, and sometimes strongly, positive; and in one or two more cases, it gives doubtful reactions. With the exception of cases 1 and 2, there was no reason to suppose lactic acid to be present in any of the cases in which a positive reaction was obtained with UFFELMANN'S test. This is consistent with the results obtained in the first two series of cases and substantiates the view previously expressed, that while the test is a good indicator of lactic acid when it is present, yet it gives a positive reaction so frequently with other substances besides lactic acid, as to entirely invalidate the test.

It is interesting to note that whereas lactic acid, as demonstrated by MACLEAN'S test, was present in all the cases of gastric carcinoma which showed achlorhydria, yet with the exception of the first two cases in this series, it was not present in a single other case in TABLE I., or TABLE III.

Cases 1 and 2, in which lactic acid appeared, were both early cases of carcinoma of the oesophagus/

oesophagus. I have tried to obtain the stomach contents for analysis from several other patients suffering from this disease, but in none of them has the growth been at an early enough stage to make the passage of the tube possible. In both cases 1 and 2 the swallowing of solids could still be accomplished fairly easily, when the analysis was made, so that it was exceedingly unlikely that any fermentation of stagnating foodstuffs was taking place in the oesophagus above the growth, nor was there any obstruction at the pyloric end of the stomach. None the less, a faint but clearly positive reaction to MACLEAN'S test was observed, on examining the stomach contents in each case, and this was confirmed by UFFELMANN'S reaction.

This observation, combined with those already mentioned, has confirmed me in the belief that lactic acid found in the stomach contents is not invariably fermentation lactic acid, but lactic acid which has been produced in some way by a malignant growth.

The work of FLETCHER and HOPKINS, on muscular metabolism, has already been referred to in some detail in an earlier section of this thesis. They showed that muscle produces on stimulation either/

either carbon dioxide or lactic acid, according to the amount of oxygen which is at its disposal for consumption, or that lactic acid is first formed and then removed under the action of oxygen undergoing partial or complete oxidation to carbon dioxide in the process. This full reaction, however, does not take place in an atmosphere deficient in oxygen. Now we know that the blood supply to the tissues of a malignant growth is always deficient, causing a necrosis in the centre of the growth; and since the blood supply is deficient, it must necessarily, follow that the supply of oxygen is also greatly diminished. It, therefore, seems possible and probable that in carcinoma of the stomach or oesophagus, imperfect oxidation occurs in the smooth muscle involved by the growth, so that lactic acid, a precursor of carbon dioxide or a product of incomplete combustion, is produced instead of carbon dioxide, and finds its way into the stomach contents; just as in diabetes, when fats are only being incompletely metabolised, ketone bodies make their appearance *in the blood.*

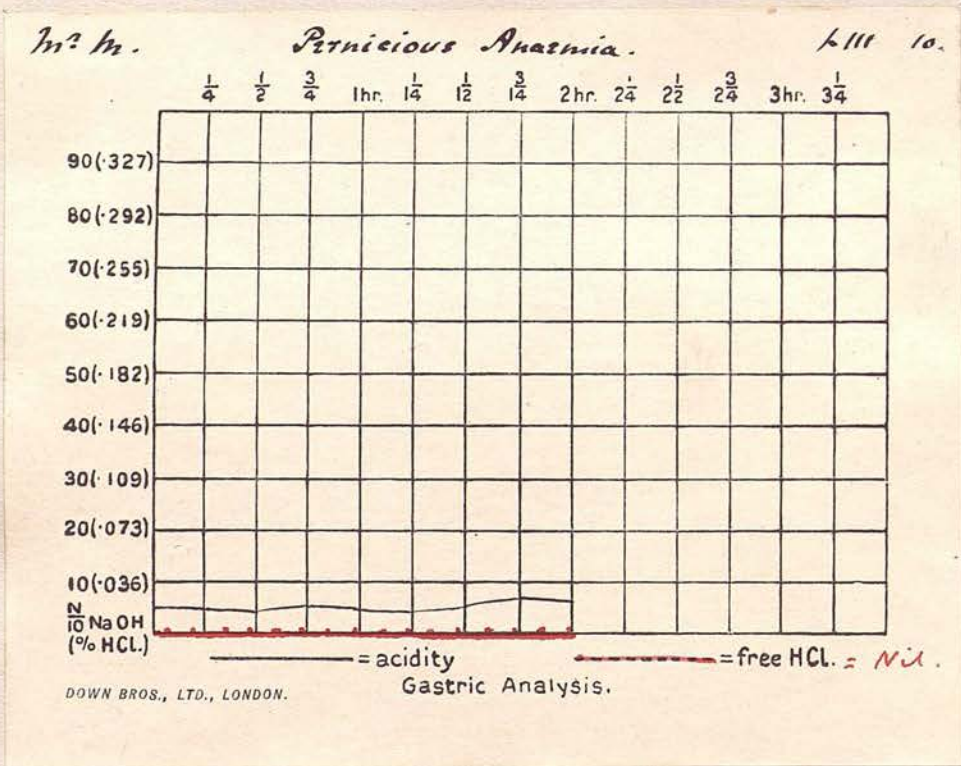
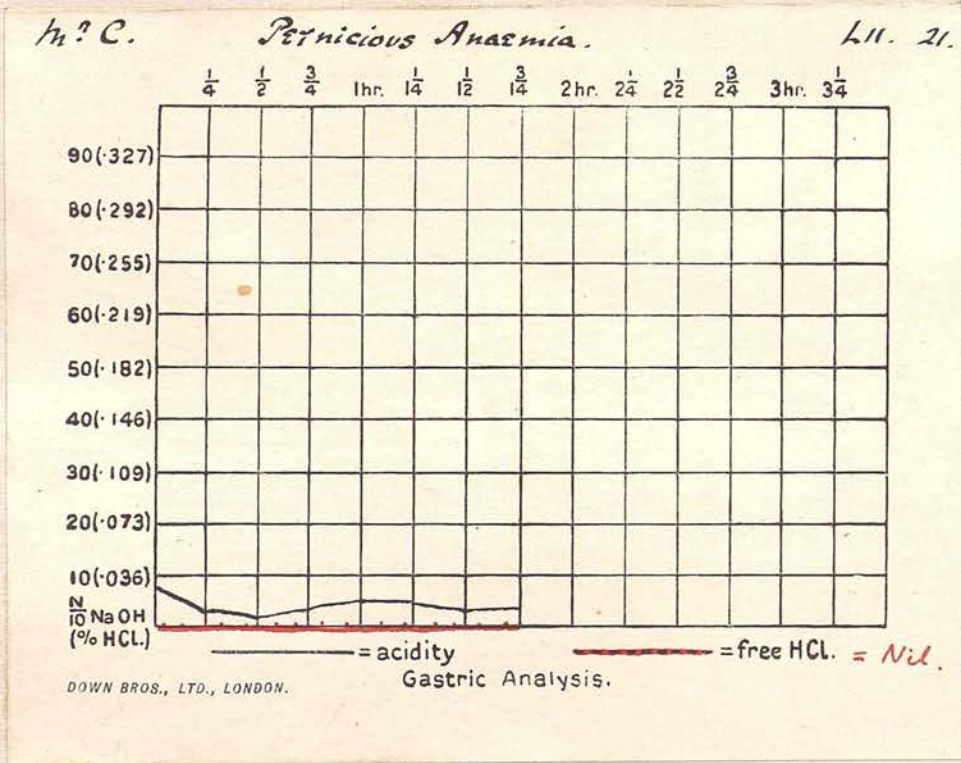
This theory, that lactic acid found in the stomach contents need not invariably be fermentation lactic acid, but may sometimes be sarco+lactic acid, would account for the presence of this acid in the/

the early stages of gastric carcinoma, when pyloric stenosis has not occurred and in carcinoma of the cardiac end of the stomach and in the oesophagus.

It is commonly held that small traces of lactic acid are frequently found in the stomach in cases of gastritis, and that achlorhydria is also present. The only three well authenticated cases of gastritis, which I have been able to observe, cases 13, 14 and 15, while showing achlorhydria in each case, showed not a trace of lactic acid on being tested by either MACLEAN'S or UFFELMANN'S test, though in two of the cases the samples were foul smelling.

The blood found in considerable quantity in case 11, where the specimen was obtained from a patient suffering from Banti's disease was due to a slight haematemesis at the end of the test; and the same explanation is true for case 16, where, owing to the cirrhosis of the liver, there were dilated veins at the lower end of the oesophagus.

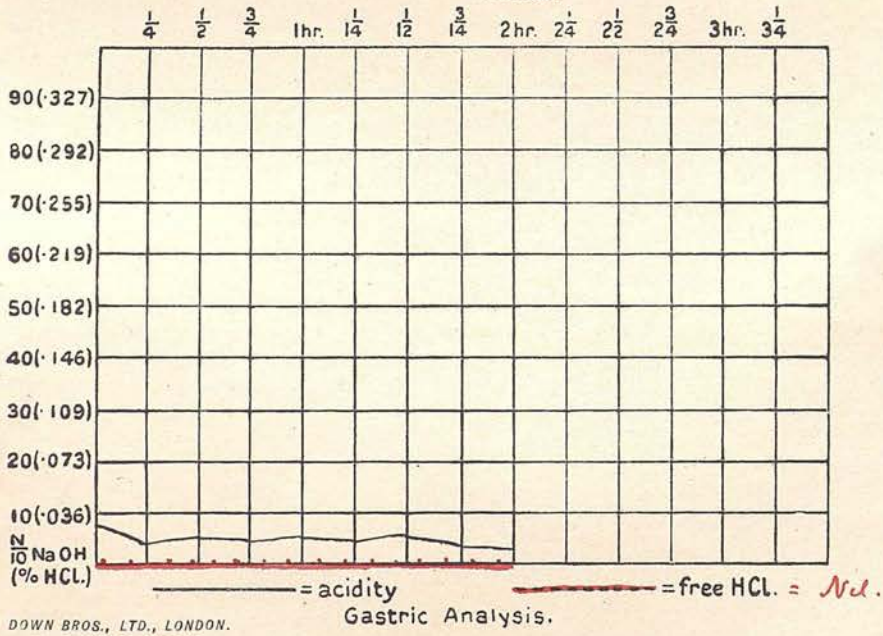
Lastly, the statement by RYLE ⁽¹⁶⁾, that in primary achylia and pernicious anaemia, there is a very narrow interval and close parallelism between the curve of total acidity and the base line, whereas a wide interval and lack of parallelism is more likely to occur in the secondary achlorhydria, such as may be caused/



M²⁵ W.

Perniciosa Anæmia.

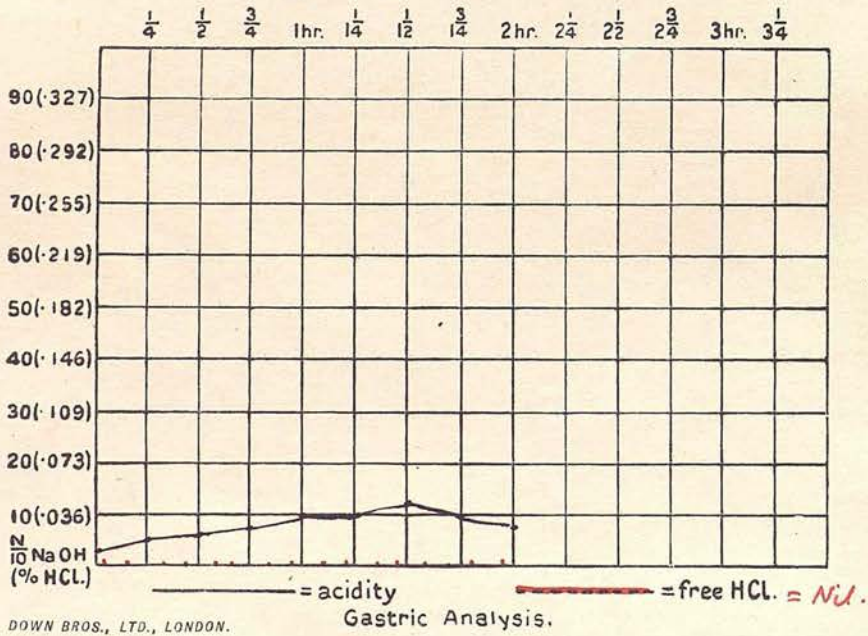
LVI. 1.



M²⁵ M.

Primary Achylia

LVI. 9.



caused by a malignant growth in the stomach, is well illustrated in the three cases of pernicious anaemia (cases 3, 4, 5), which I have examined by the fractional method, and in the one well authenticated case of primary achylia gastrica, which I have been able to observe. (Vide Charts). Comparison of the Graphs obtained from these four cases, with those obtained from the patients suffering from gastric carcinoma, shows very striking differences in the shape of the graphs obtained from the malignant and non-malignant cases.

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**CASE HISTORIES and CHARTS of the GASTRIC
ANALYSIS in 17 CASES of GASTRIC CARCINOMA.**

In the following pages the case histories and charts showing the details of the gastric analysis in the series of patients suffering from gastric carcinoma, are given. Where it has been possible to obtain the X-ray plate of the case, this is also inserted. The order in which the cases are given, corresponds to the order of their appearance in **TABLE II.**

The most striking feature, which has been brought out by the case histories, is the suddenness of the onset of symptoms in the majority of the cases. No case gave a history of symptoms for longer than one year, and in the vast majority the symptoms had started within five months prior to their admission to hospital. Without exception, all seventeen patients were quite definite that previous to the onset of their present illness, they had had no stomach trouble whatsoever, and had practically never had to bother about their digestions in any way.

When one remembers that many text books and authorities, on the assumption that cancer frequently follows upon a chronic gastric ulcer, state that the majority of cases of gastric carcinoma arise in patients/

patients who have had a long history of chronic dyspepsia, this observation in the history of these seventeen cases is somewhat striking.

With regard to the charts showing the details of the gastric analysis, certain abbreviations have been used.

M = Mucus.

B = Bile

S = Starch

Bl. Blood

C = Charcoal

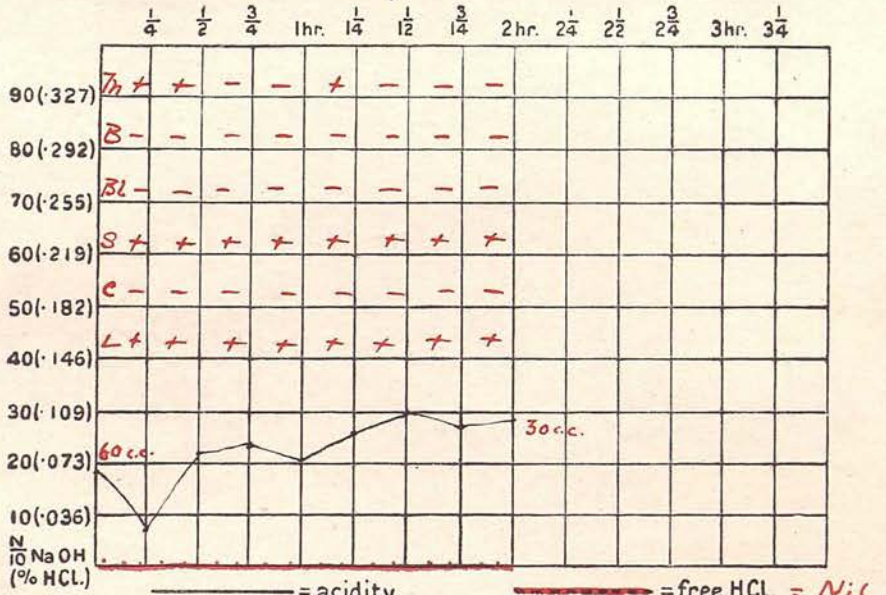
L = Lactic Acid.

The figures given at the beginning and the end of the curve of total acidity represent in cubic centimetres the volume of the resting juice and residue respectively.

M² G.

Carcinoma of Stomach.

LIII 18.



— = acidity ————— = free HCL. = Nil.

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Gastric Analysis.



CASE I. Mr. G. AGE 57. ENGINEMAN.

COMPLAINT. Sciatica.

HISTORY. The patient had suffered from occasional severe attacks of sciatica for years, and this was the reason of his admission to hospital.

Enquiry, during the taking of his case, revealed, however, that for a year before admission he had suffered from flatulence and eructation. For a month before admission, also, he had been losing weight, though his appetite had remained quite good.

ON EXAMINATION. The patient looked anaemic and thin. Nothing else abnormal could be made out on physical examination, except some slight tenderness on deep palpation in the region of the pylorus, and some slight splashing in the stomach two hours after a meal.

A test meal showed the absence of free hydrochloric acid and the presence of lactic acid.

The benzidene reaction was negative.

X-Ray examination showed a somewhat atonic stomach with an indefinite pylorus.

TREATMENT. The Test Meal findings were so suspicious/

suspicious that operation was advised. The patient was very loathe to agree, since his sciatica was the only thing which troubled him to any extent. Eventually, however, he agreed, and the abdomen was opened. A small nodule was found on the lesser curvature of the stomach, which histological examination later proved to be unquestionably malignant. The growth was not larger than a threepenny bit and there was no involvement of glands.

Pylorotomy and posterior gastro-enterotomy were performed.

PROGRESS. The patient made an uninterrupted recovery from the operation.

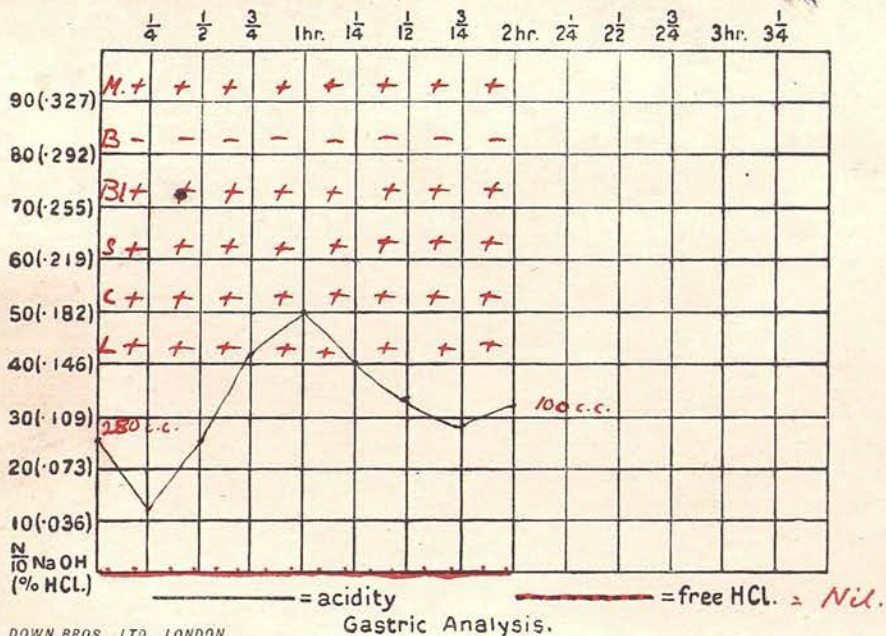
He reported for examination four months later in excellent health. A sample of his fasting juice was then taken and showed free acid to be present and no lactic acid.

Enquiry five and a half months after the operation showed him still to be in good health.

M³B.

Carcinoma of Stomach.

Aug. 21.



DOWN BROS., LTD., LONDON.

Gastric Analysis.



CASE II. Mr. B. AGE 51. STATIONMASTER.

COMPLAINT. Discomfort and pain in the stomach with vomiting.

HISTORY. Patient was in excellent health till 2 months before admission. He then - for the first time in his life - began to be troubled with indigestion. He had a sense of heaviness and distension after meals and began to loose weight rapidly.

Six weeks before admission he began to have a dull constant pain in the region of the stomach, and a fortnight later he started to vomit at night.

During the month before admission his symptoms got rapidly worse. Vomiting of dark foul material became very frequent so that he could take little or no solid food, pain was constantly present, and emaciation advanced with astonishing rapidity.

ON EXAMINATION. The patient showed the typical appearance of cancerous cachexia.

The distended stomach could be seen standing out against the emaciated abdominal wall with waves of peristalsis passing over it. A great deal of splashing could be elicited. A large mass could be felt in the/

the pyloric region, which was tender to palpate, and the liver was enlarged, nodular and tender. There was no enlargement of the supraclavicular glands.

Benzidene reaction was + ve.

The urine contained a trace of acetone.

The test meal gave the results shown opposite.

An X-Ray taken immediately after a bismuth meal showed all the bismuth in the cardia and body of the stomach, but none in the pyloric antrum.

TREATMENT. The stomach was washed out twice a day. On one occasion, after it had been washed out till a perfectly clear return was obtained which showed no lactic acid, a Ryle's tube was passed half an hour later and a small quantity of juice aspirated. This showed a definite quantity of lactic acid to be present.

Eight days after admission the abdomen was opened. A large malignant growth was found involving the pyloric antrum and completely blocking it. The pylorus itself was free. The posterior surface of the stomach was infiltrated and adherent to the transverse meso-colon. Some of the lymphatics on the anterior wall/

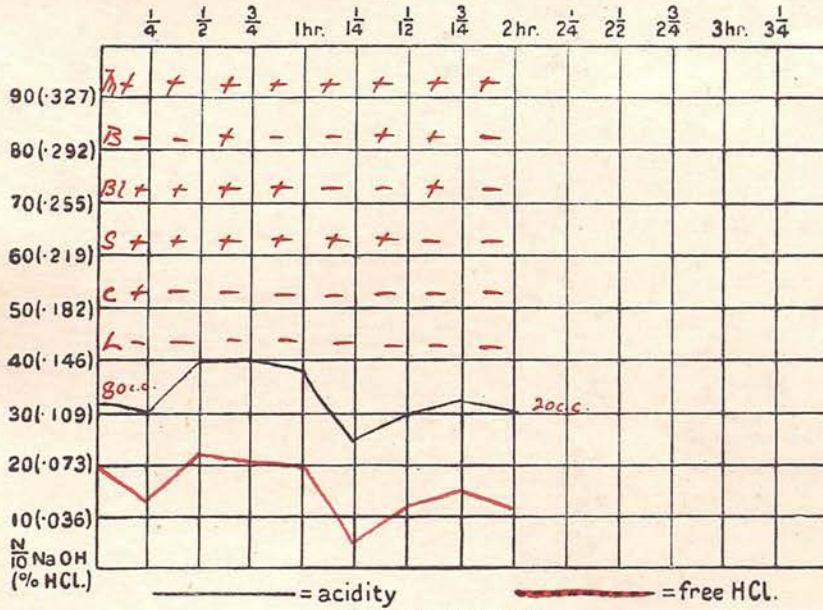
wall were also infiltrated with the growth. The liver was studded with secondary growths. A healthy area was chosen on the anterior surface of the stomach and an anterior gastro enterostomy was performed.

PROGRESS. The patient was relieved to a great extent by the operation, as vomiting entirely ceased and he was able to take fluids. His strength, however, did not rally and he died six days later.

Miss L.

Carcinoma of Stomach.

LVI. 5.



DOWN BROS., LTD., LONDON.

Gastric Analysis.



CASE III. Miss L.

AGE 68.

COMPLAINT. Vomiting and discomfort in the stomach.

Loss of appetite.

Loss of weight.

HISTORY. Three months before admission the patient, who "had never before known that she had a stomach" -being always healthy and strong, began to lose her appetite and to lose weight. The loss of appetite increased to a positive loathing of food, and she began to have a feeling of discomfort in the stomach, though no actual pain.

A fortnight before admission she started to vomit occasionally after food, and the loss of weight progressed more rapidly than ever.

ON EXAMINATION. The patient was very emaciated, but quite cheerful. The abdomen was very thin and a mass could be easily felt along the greater curvature of the stomach. There was no marked tenderness and the stomach was not enlarged.

There was no enlargement of the supra-clavicular/

clavicular glands or of the liver.

The benzydene reaction was positive.

X Ray examination showed the stomach to be quite empty five hours after a bismuth meal, Immediately after the meal a very definite massive carcinoma of the body of the stomach and of the pyloric antrum could be seen.

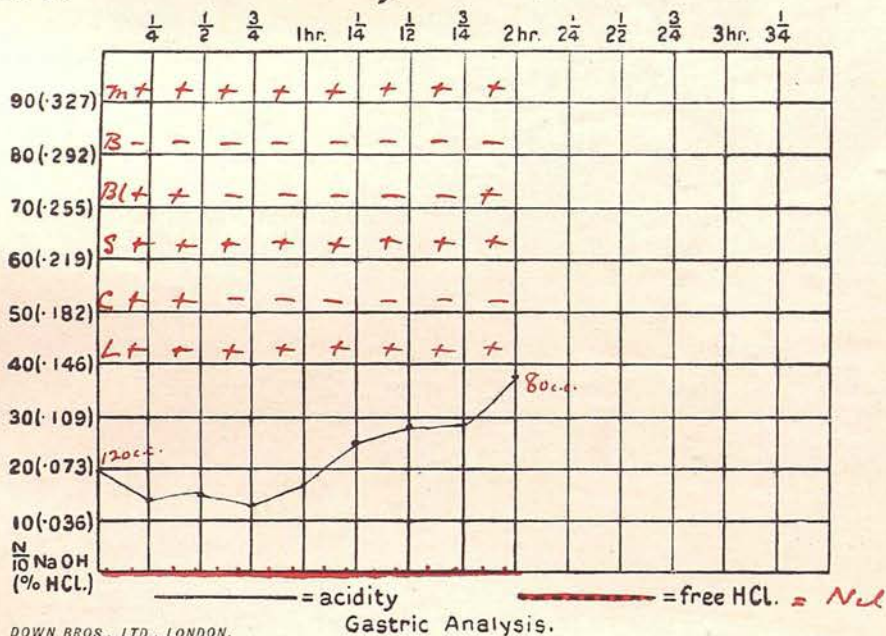
TREATMENT. Removal of the growth was considered out of the question, and, as there was no indication for a gastro-enterostomy, operation was not advised. The patient was given a very light fluid diet and small doses of opium.

PROGRESS. The patient died at home a month later.

Mt. C.

Carcinoma of Stomach.

hVI. 24.



DOWN BROS., LTD., LONDON.

CASE IV. Mrs. C. AGE 64.

COMPLAINT. Loss of appetite. Vomiting.
Weakness.

HISTORY. Patient was in good health till six months before admission, when she began to suffer from loss of appetite and indigestion. The loss of appetite increased in the next few months to a positive loathing of food, and for a few weeks previous to admission the taking of any solid food caused severe vomiting. Loss of weight and weakness advanced rapidly. There was no pain.

ON EXAMINATION. The patient was greatly emaciated, and quite prostrated. Anaemia was marked.

A large tumour could be felt in the left hypochondrium stretching to the right as far as the pylorus.

The liver could not be palpated and there was no ascites, but there were some enlarged hard supra-clavicular glands.

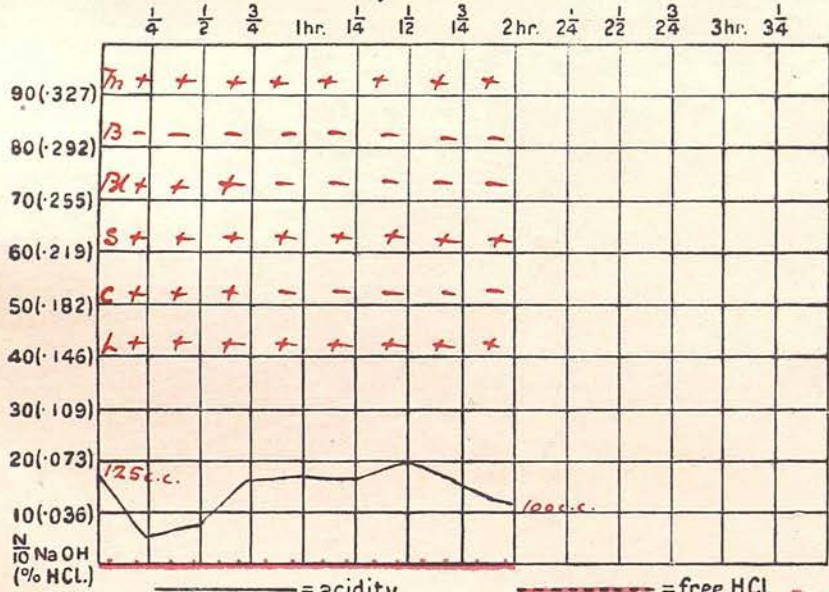
Benzidene reaction +ve.

X-Ray examination revealed a massive carcinoma/

carcinoma of the body of the stomach, stretching as far as the pyloric antrum. Unfortunately this plate could not be procured.

PROGRESS. The patient was so obviously on the point of death that no operative interference was thought of. She was taken home by her relatives where she died in a few days.

Int. F. Carcinoma of Stomach. Surgical.



DOWN BROS., LTD., LONDON.

Gastric Analysis.

11



CASE V. Mr. F. AGE 66. BUSINESS MAN.

COMPLAINT. Loss of appetite, flatulence and discomfort in the stomach. Weakness.

HISTORY. Six weeks before admission, the patient, who had previously had no stomach symptoms began to feel weak and easily tired. His appetite became bad and he was troubled with flatulence and discomfort in the stomach after meals. He also became constipated and started to lose weight. He had no pain and no vomiting, and had been going about his work till the day of admission.

ON EXAMINATION. Patient looked thin and anaemic.

A hard lump could be felt in the region of the pylorus, and there was splashing all over the stomach three hours after a meal. There were signs of slight ascites, but the liver was not palpable, and there was no enlargement of the supra clavicular glands.

The Benzidene reaction was +ve.

X-Ray examination five hours after a bismuth/

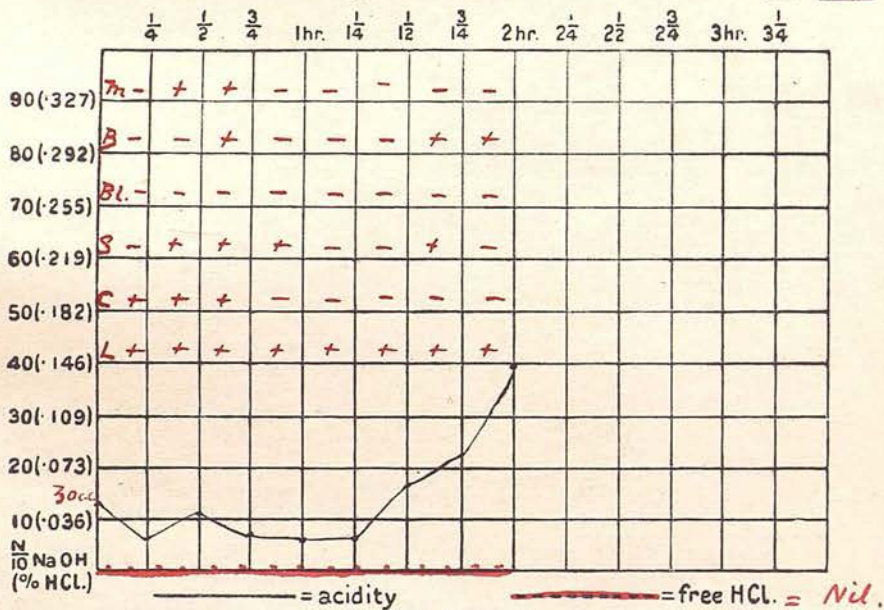
bismuth meal showed a third of the meal still in the stomach. Immediately after the meal a hypotonic stomach with a poor cap was seen.

TREATMENT. Five days after admission the abdomen was opened. An ulcerating carcinomatous growth at the pyloric end of the stomach was found, with extensive involvement of the glands along the lesser curvature. There was no obvious liver involvement, but there was a small amount of free fluid in the abdomen.

A posterior gastro-enterostomy was performed.

PROGRESS. The patient made an excellent recovery from the operation and was discharged home temporarily relieved of all his symptoms.

Miss A. Carcinoma of Stomach. Surgical.



DOWN BROS., LTD., LONDON.

Gastric Analysis.

CASE VI. Miss A. AGE 40.

COMPLAINT. Vomiting, weakness and constipation.

HISTORY. The patient had had no stomach trouble till a year before admission when she began to complain of indigestion, with occasional nausea and vomiting after meals.

For the few months previous to admission the vomiting had become more frequent, and she had experienced occasional pain in the stomach after meals. There had been a recent rapid loss in weight, and she had become obstinately constipated.

ON EXAMINATION. The patient was emaciated and markedly anaemic. A lump could be felt in the region of the pylorus, which was slightly tender, but there were no other physical signs.

X-Ray examination revealed considerable pyloric obstruction, about half the meal being still in the stomach five hours after the bismuth had been taken.

The Benzidene reaction was -ve.

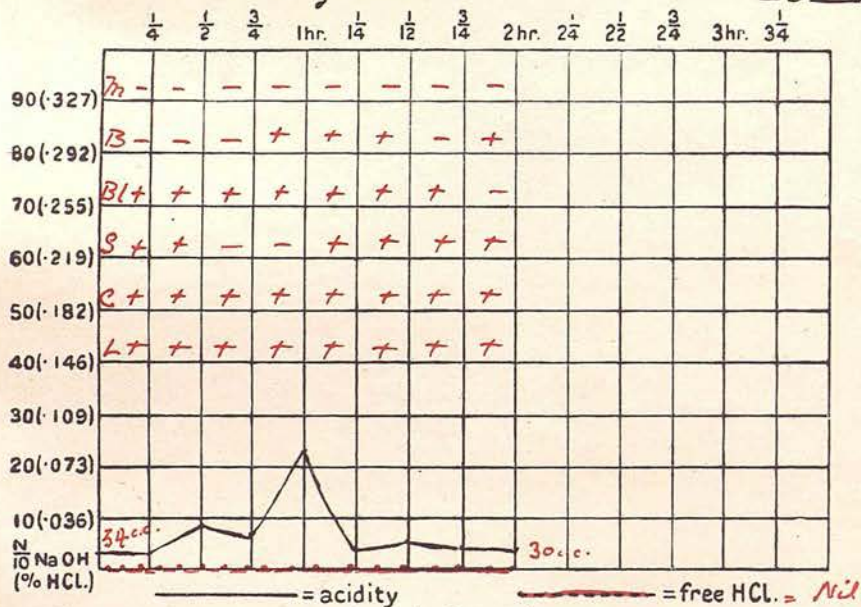
TREATMENT/

TREATMENT. Ten days after admission the abdomen was opened and an inoperable carcinomatous growth was found in the region of the pylorus.

Posterior gastro-enterostomy was performed.

PROGRESS. The patient made an uneventful recovery from the operation, and was discharged with considerable, though temporary relief from her symptoms.

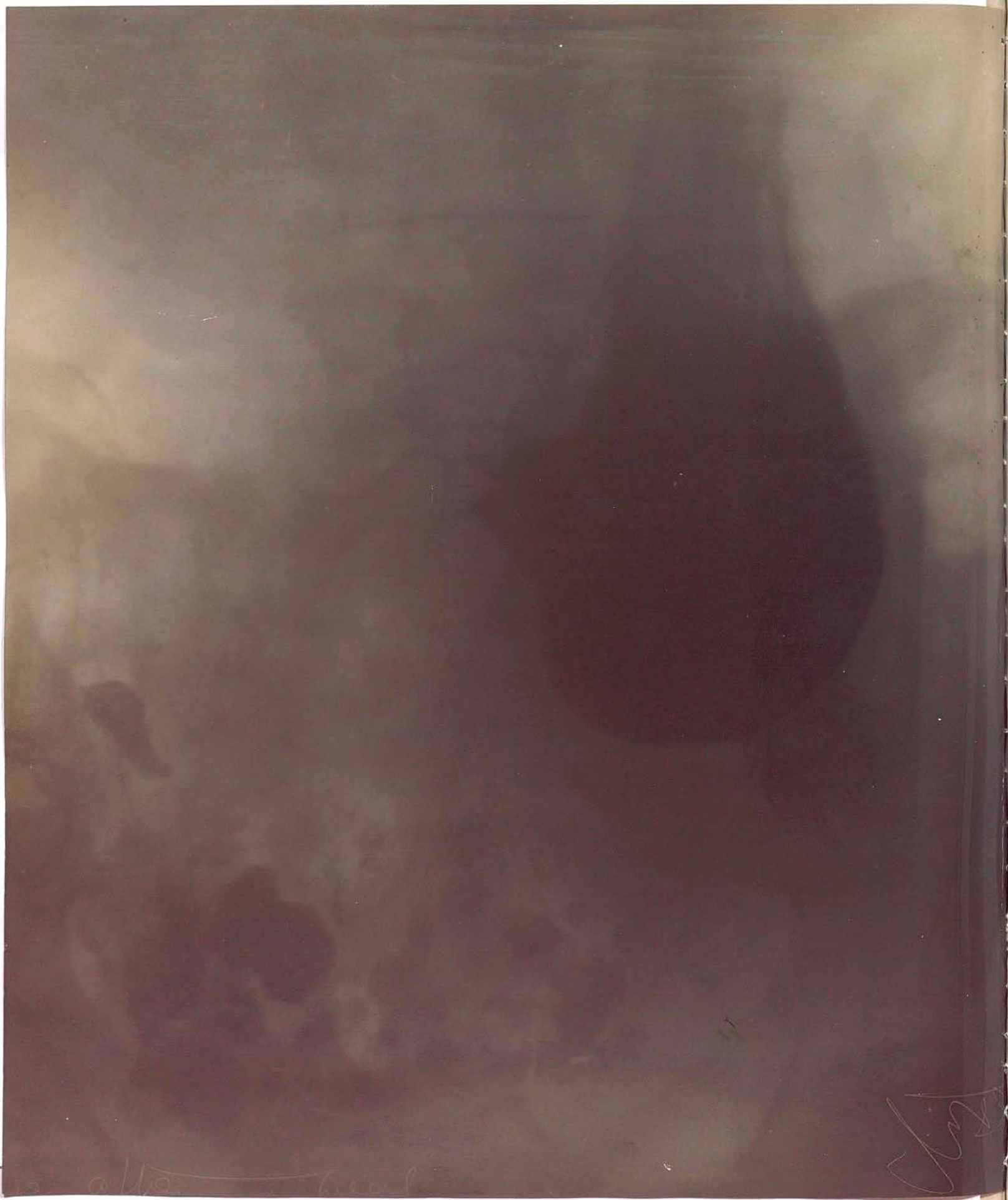
M^r W. Carcinoma of Stomach. Surgical.



DOWN BROS., LTD., LONDON.

Gastric Analysis.

(7)



CASE VII. Mr. W. AGE 56. BELL HANGER.

COMPLAINT. Pain in the stomach, vomiting, loss of weight.

HISTORY. The patient was in good health, and had had no previous stomach symptoms till four months before admission, when he began to feel discomfort in the stomach after food with nausea and eventually vomiting. The discomfort in the stomach rapidly developed into a dull constant gnawing pain. He lost weight rapidly, and had no desire for food.

ON EXAMINATION. The patient was thin and anaemic.

A definite lump could be felt in the region of the pylorus and splashing could be elicited three hours after a meal. Nothing else could be made out.

The Benzidene reaction was - ve.

X-Ray examination after a bismuth meal showed a third of the bismuth in the stomach five hours after the meal had been taken.

TREATMENT. Five days after admission the abdomen/

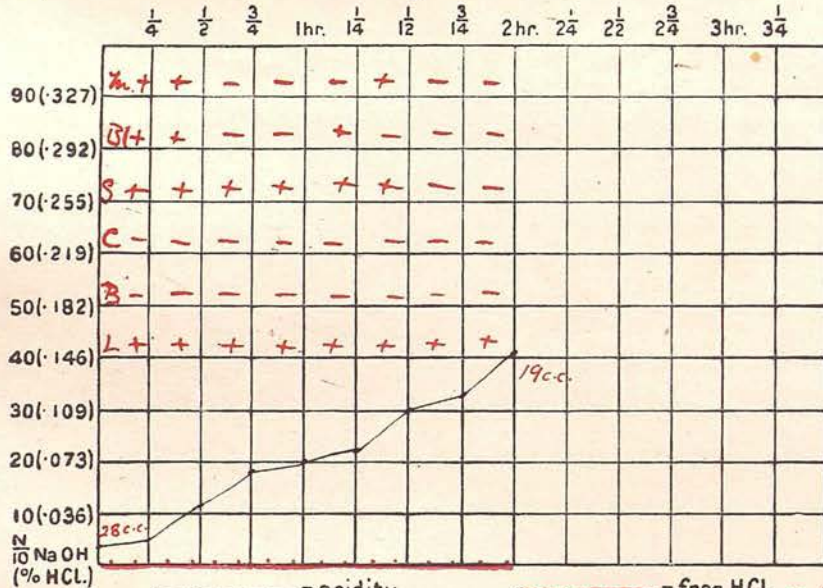
abdomen was opened and a large indurated mass was found involving the pylorus, and pyloric antrum. No glands were involved, and the liver seemed unaffected.

Pylorectomy and posterior gastroenterostomy was performed.

The pathological report showed that the tissue removed was definitely malignant.

PROGRESS. The patient made an excellent recovery. Enquiry nine months after the operation, showed him still to be in good health.

M²W. Carcinoma of the Stomach. R.I.E.



DOWN BROS., LTD., LONDON.

Gastric Analysis.

= free HCL. = Nil.

CASE VIII. Mr. W. AGE 48. FARMER.

COMPLAINT. Difficulty in swallowing.

HISTORY. For six months before admission to hospital the patient had experienced gradually increasing difficulty in swallowing solid foods. Latterly even fluids had caused him difficulty. This symptom was associated with a constant pain in the neighbourhood of the xiphisternum. There was no actual vomiting, but he put up a good deal of phlegm.

ON EXAMINATION. Nothing pathological could be made out, bar the fact that the patient had obviously lost weight.

X-Ray examination showed a "hold up" of the bismuth just before entering the stomach. The stomach itself was small, but otherwise apparently normal.

Benzidene reaction -ve.

The results of the test meal examination - which are given opposite - were quite consistent with carcinoma of the stomach, but as carcinoma of the oesophagus had been found in two other cases to/

to give similar findings, a provisional diagnosis of carcinoma of the oesophagus was given.

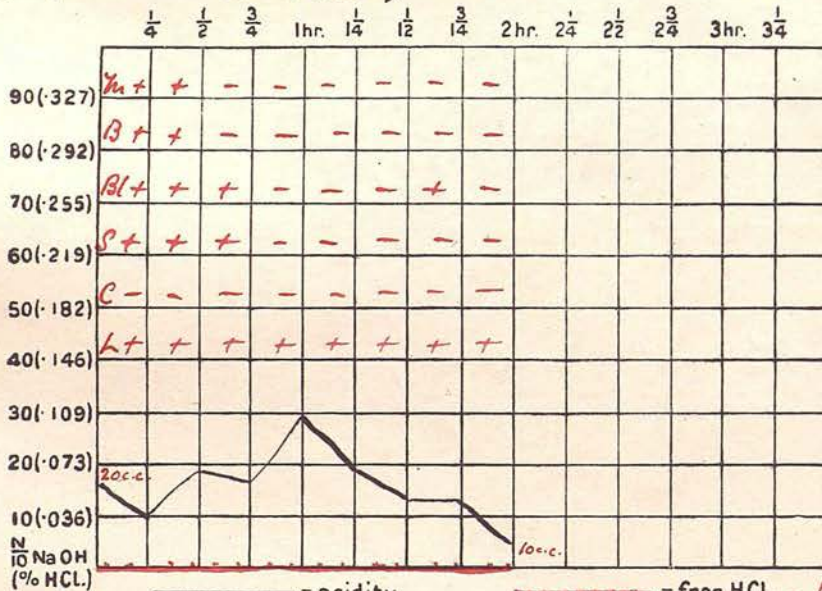
TREATMENT. The abdomen was opened, and the stomach as it presented in the wound looked perfectly healthy. On more detailed examination, however, a large ulcerating growth was found involving the cardiac portion and the cardiac orifice. Nothing could be done and the abdomen was closed.

PROGRESS. At the time of writing the patient is still in hospital.

7m² F

Carcinoma of Stomach.

LV 5.



DOWN BROS., LTD., LONDON.

Gastric Analysis.

— = acidity - - - = free HCL. = Nil.

CASE IX. Mr. F. AGE 68. GARDENER.

COMPLAINT. (i) Shortness of breath.
 (ii) Difficulty on micturition.
 (iii) Indigestion.

HISTORY. The shortness of breath and difficulty on micturition were the patient's main complaints, and his dyspeptic symptoms were only elicited on taking his history. This latter trouble had only lasted for two months, whereas his other two complaints had been getting gradually worse during the two years preceding admission to hospital.

The indigestion consisted of flatulence, anorexia, and discomfort in the stomach after food. On two occasions he had vomited a slight amount of "coffee ground" material. He had been losing weight rapidly since the dyspeptic symptoms appeared and he was obstinately constipated.

ON EXAMINATION. The patient was cyanotic. There was oedema of the feet. The body was emaciated.

He had marked auricular fibrillation. The prostate was enlarged and the bladder distended.

A mass could be felt along the greater curvature/

curvature of the stomach, and some of the supra-clavicular glands were enlarged and hard. The liver did not seem to be enlarged and there was no ascites.

The Benzidene reaction was ve.

X-Ray examination five hours after a bismuth meal showed the stomach to be quite empty with the bismuth far advanced into the transverse colon. Immediately after the meal a "steer horn" type of stomach was seen, with a patent pylorus so that it emptied very rapidly. The radiologist reported the stomach to be malignant, of the "leather bottle" variety.

PROGRESS. The patient refused operative treatment, and as he was not in a good enough general condition to stand it well, this was not pressed. Treatment was directed to the heart and bladder conditions, and when these had improved he was discharged. His stomach symptoms had, however, become more pronounced during his month in hospital and had not responded to treatment. He had also lost weight steadily.

I have not been able to trace this patient since discharge. I realise that the diagnosis of gastric carcinoma is in this case open to doubt.

Carcinoma of Stomach.

R.I.E.

	$\frac{1}{4}$	$\frac{1}{2}$	$\frac{3}{4}$	1hr.	$\frac{1}{4}$	$\frac{1}{2}$	$\frac{3}{4}$	2hr.	$\frac{1}{4}$	$\frac{1}{2}$	$\frac{3}{4}$	3hr.	$\frac{1}{4}$
90(.327)				U +									
80(.292)				B -									
70(.255)				B +									
60(.219)				S +			30 S.c.c.						
50(.182)				L +									
40(.146)													
30(.109)													
20(.073)													
10(.036)													
$\frac{N}{10}$ NaOH (% HCL.)													

————— = acidity - - - - - = free HCL. = Nil.
Gastric Analysis.

DOWN BROS., LTD., LONDON.

CASE X. Mr. C. AGE 69. SHEPHERD.

———— COMPLAINT. Loss of appetite. Vomiting.

HISTORY. Six months before admission to hospital the patient, who had never before had any gastric disturbance, began to lose his appetite and to feel nauseated after food. This was associated with wind and rumblings in the stomach. These symptoms speedily got worse, and he lost weight rapidly.

Three months before admission he started to vomit occasionally, then he would vomit foul material nearly every night, and latterly he vomited two or three times a day.

ON EXAMINATION. The patient was emaciated and cachectic looking. The stomach was enlarged and there was marked splashing over it. No tumour could be made out on palpation. Neither the liver nor the supra-clavicular glands were enlarged.

X-Ray showed evidence of marked pyloric stenosis.

The Benzidene reaction was +ve.

The test meal examination, the results
of/

of which are given opposite, reported that the stomach contents contained a large quantity of free hydrochloric acid, but on more detailed examination this was found not to be the case, and what had been previously taken to be free hydrochloric acid was, in reality, lactic acid.

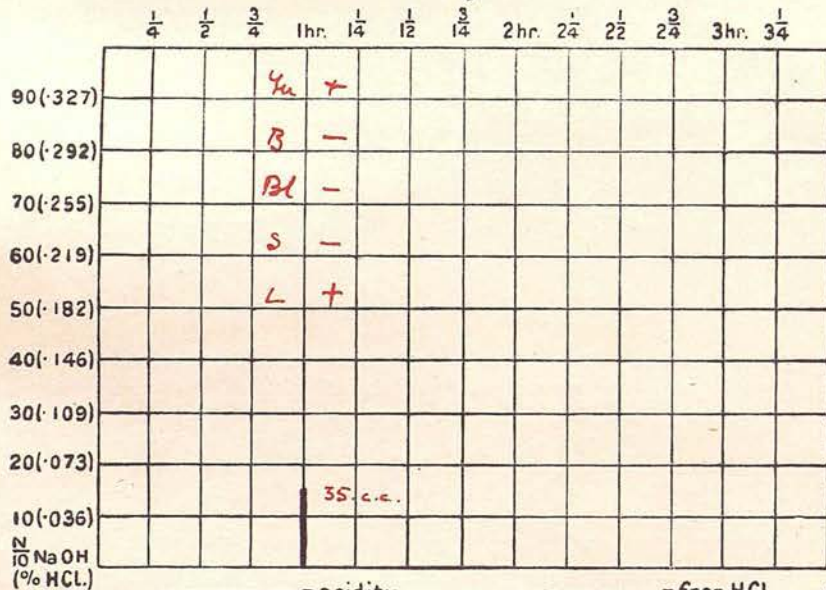
TREATMENT. The abdomen was opened and an inoperable carcinoma of the pylorus was found.

Posterior gastro-enterostomy was performed.

PROGRESS. The patient made a good recovery from the operation, and was discharged with his symptoms temporarily alleviated.

Carcinoma of Stomach.

R.I.E.



35 c.c.

————— = acidity - - - - - = free HCL. = N.U.

Gastric Analysis.

CASE XI. Mr. M. AGE 50. LABOURER.

COMPLAINT. Indigestion and pain in the stomach. Loss of weight.

HISTORY. For five months before admission the patient, who had had a previously healthy stomach history, had complained of discomfort and pain in the stomach after food. He had also lost weight rapidly.

Latterly the pain which was of a dull gnawing description had become continuous, he had vomited occasionally, and had lost all desire for food.

ON EXAMINATION. The patient was obviously in the last stages of cancerous cachexia.

A lump could be felt in the stomach, the liver was enlarged and tender, and there was some free fluid in the abdominal cavity.

The Benzidene reaction was +ve.

X-Ray examination showed a massive carcinoma of the body of the stomach. The pyloric region was unaffected.

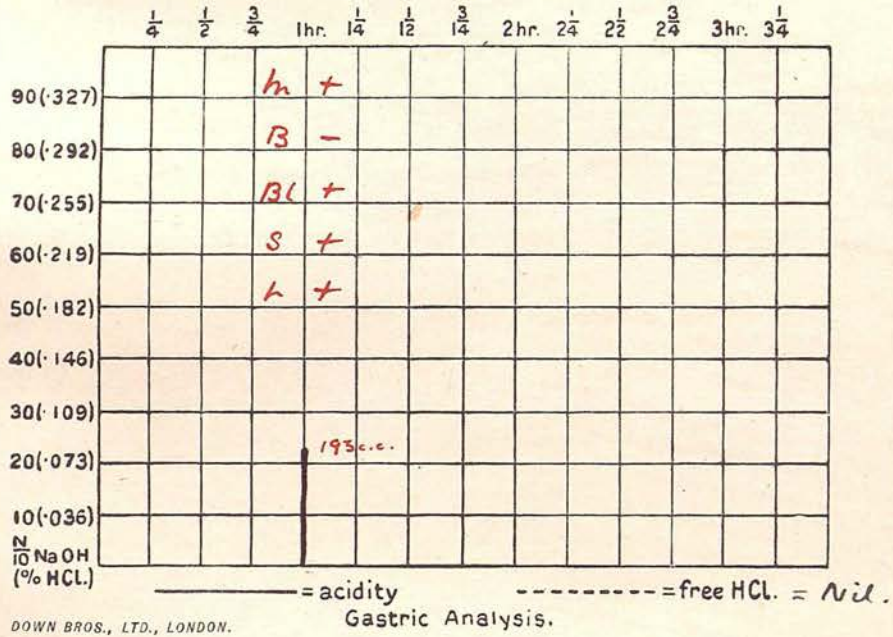
TREATMENT/

TREATMENT. Morphia in increasing doses.

PROGRESS. The patient died shortly after admission to hospital. Post mortem examination confirmed the diagnosis of gastric carcinoma.

Carcinoma of Stomach.

R.I.E.



CASE XII. Mrs. R. AGE 48.

COMPLAINT. Distaste for food, vomiting, loss of weight.

HISTORY. Three months before admission to hospital the patient began to complain for the first time of loss of appetite. Her digestion had up till then been always excellent. This loss of appetite quickly increased into an extreme dislike of food in any form, and latterly she had frequent attacks of vomiting - the vomited matter being very foul. All this time the patient lost weight rapidly.

ON EXAMINATION. The patient was considerably emaciated, and very anaemic.

The stomach was enlarged and peristaltic waves could be seen passing across it. No tumour could be made out, but the upper half of both recti, especially the right one, was held very rigid so that palpation in the region of the pylorus was difficult.

Nothing else could be made out on physical examination.

The/

The Benzidene reaction was +ve.

X-Ray examination revealed pyloric stenosis, and suggested pyloric carcinoma.

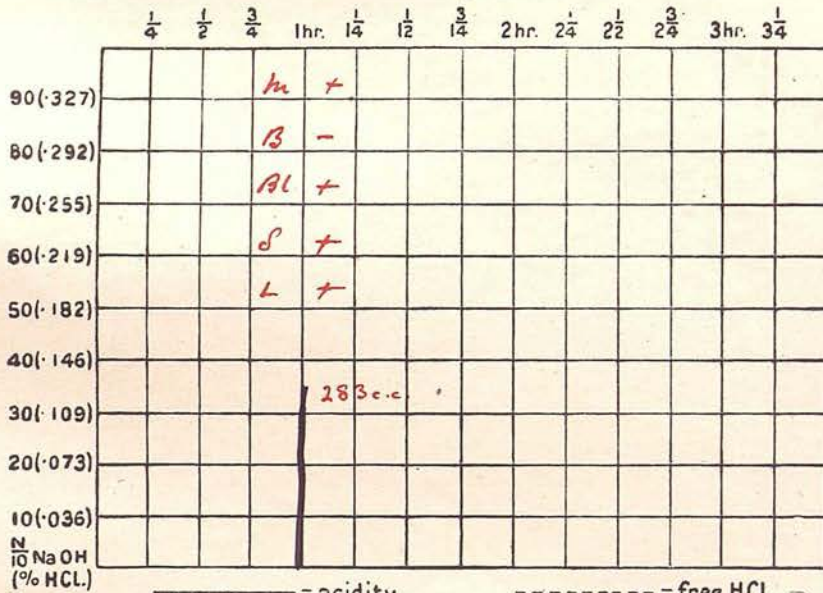
TREATMENT. The abdomen was opened and an inoperable carcinoma was found involving the pylorus and pyloric antrum.

Posterior gastro-enterostomy was performed.

PROGRESS. Patient made a good recovery from the operation and was discharged with her symptoms temporarily alleviated.

Carcinoma of Stomach.

R.I.E.



283 c.c.

————— = acidity - - - - - = free HCL. = N.U.

Gastric Analysis.

CASE XIII. Mr. L. AGE 51. LABOURER.

COMPLAINT. Pain in the stomach, vomiting, loss of weight.

HISTORY. Six months before admission to hospital the patient began, for the first time to suffer from dyspeptic symptoms after food. At first he merely experienced a feeling of great distension as though he had had a very large meal, after eating very little. This gradually gave place to nausea, and latterly he invariably vomited after taking solid food. He lost weight rapidly, and during the three weeks before admission he experienced pain in the stomach.

ON EXAMINATION. The patient was very emaciated and anaemic. A large tender lump could be felt in the region of the pylorus, and the liver was slightly enlarged.

The benzydene reaction was +ve.

X-Ray examination suggested carcinoma of the pylorus.

TREATMENT. The abdomen was opened, and a large/

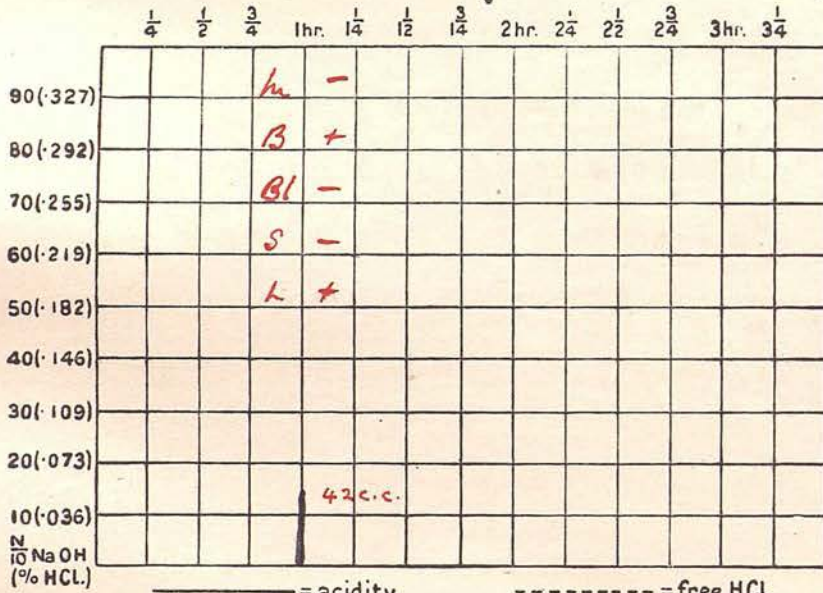
large carcinomatous mass was found involving the pyloric region of the stomach. The glands and liver were extensively involved.

Posterior gastro-enterostomy was performed.

PROGRESS. The patient did not rally after the operation and died shortly afterwards.

Carcinoma of Stomach.

R.I.E.



DOWN BROS., LTD., LONDON.

Gastric Analysis.

CASE XIV. Mr. B.

AGE 47.

MINER.

COMPLAINT. Indigestion, loss of weight, pain in the stomach.

HISTORY. Five months before admission to hospital the patient lost appetite, and began to be troubled with flatulence and eructation after meals, and of a disagreeable taste in his mouth. Previous to this his digestion had always been good.

The discomfort after meals became rapidly worse, and two months before admission he began to complain of pain in the stomach which soon became constant.

He became very constipated, and during the month before admission he lost weight with great rapidity, and became so weak that he could only walk a few steps. He vomited a small amount of coffee ground material on two or three occasions.

ON EXAMINATION. The patient was obviously in the last stages of malignant disease. He was exceedingly emaciated and quite prostrated.

The liver was greatly enlarged and tender and/

and there was some ascites. The supraclavicular glands were not enlarged, and no mass could be felt in the stomach, though he complained of great tenderness on palpation over it. The recti were held very rigid.

Benzidene reaction -ve.

TREATMENT. Morphia in increasing doses.

PROGRESS. The patient died a fortnight after admission. The post mortem examination revealed quite a small malignant growth in the body of the stomach, on the lesser curvature. The liver, however, was crammed full of secondary deposits.

Carcinoma of Stomach.

R. I. E.

	$\frac{1}{4}$	$\frac{1}{2}$	$\frac{3}{4}$	1hr.	$\frac{1}{4}$	$\frac{1}{2}$	$\frac{3}{4}$	2hr.	$\frac{1}{4}$	$\frac{1}{2}$	$\frac{3}{4}$	3hr.	$\frac{1}{4}$
90(.327)				h -									
80(.292)				B -									
70(.255)				BI -									
60(.219)				S +									
50(.182)				L +									
40(.146)													
30(.109)													
20(.073)													
10(.036)													
$\frac{N}{10}$ NaOH (% HCL.)													

39 c.c.

————— = acidity - - - - - = free HCL. = Nil.
Gastric Analysis.

DOWN BROS., LTD., LONDON.

CASE XV. Mr. S. AGE 53. LABOURER.

COMPLAINT. Loss of weight, pain in the lower part of the chest.

HISTORY. For two months previous to admission to hospital the patient had been losing weight. During this time he suffered from slight indigestion after food and felt weak and run down.

A month before admission he began to experience pain of a dull gnawing nature in the region of the xiphisternum, and this pain was at its worst immediately after swallowing food.

ON EXAMINATION. The patient was rather white looking, but otherwise looked a fairly healthy man, and was still stout, though he stated that he had lost weight.

Nothing pathological could be made out on physical examination, except some tenderness on exerting pressure to the left of the xiphisternum.

Benzidene reaction -ve.

X-ray examination revealed nothing abnormal.

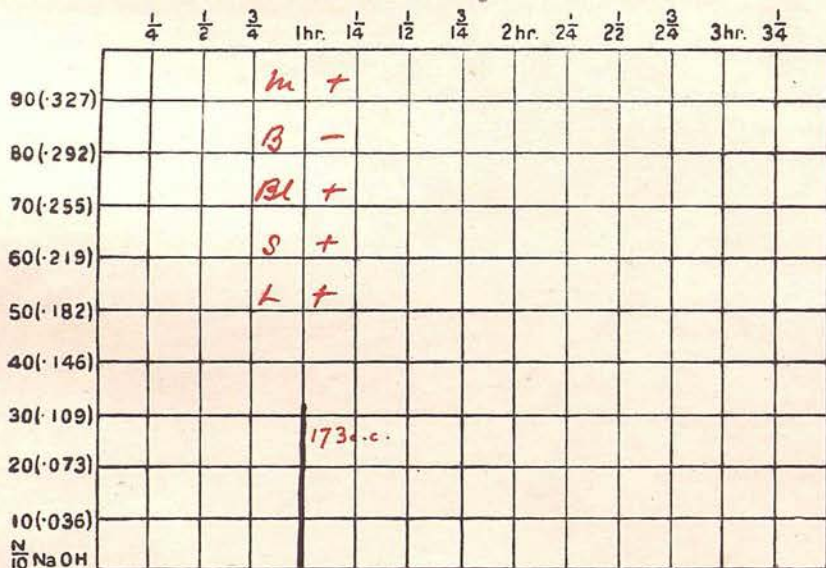
TREATMENT./

TREATMENT. The results of the test meal examination and the history made operation advisable. The abdomen was, therefore, opened and an inoperable carcinoma at the cardiac end of the stomach was found. The abdomen was closed.

PROGRESS. The patient recovered from the operation and was discharged home.

Carcinoma of Stomach.

R.I.E.



173 c.c.

$\frac{N}{10}$ NaOH
(% HCL.)

————— = acidity - - - - - = free HCL. \approx Nil.
Gastric Analysis.

DOWN BROS., LTD., LONDON.

CASE XVI. Mr. R. AGE 60. RAILWAYMAN.

COMPLAINT. Indigestion. Vomiting.

HISTORY. Two months before admission to hospital the patient lost his appetite and began to complain of nausea and eructation after food. The nausea rapidly got worse, the patient losing all taste for food, and vomiting of dark material took place frequently, but particularly at night. He complained of no pain, except a feeling of great weight in the upper part of the abdomen. He was very constipated and had lost weight. He had never had any previous stomach trouble.

ON EXAMINATION. The patient had obviously lost weight and was anaemic. A large mass could be felt in the stomach. Neither the liver nor the supraclavicular glands were enlarged.

Benzidene reaction positive.

X-ray examination revealed pyloric stenosis and was diagnostic of a massive carcinoma of the stomach.

TREATMENT. The abdomen was opened, and
the/

the whole stomach was found to be one mass of malignant growth, in spite of the very short history. Curiously enough there did not seem to be any involvement of the liver. There was not a sufficiently large healthy area on the stomach to do a gastroenterostomy and the abdomen was closed.

PROGRESS. The patient died in a few days.

Carcinoma of Stomach.

Nursing Home.

	$\frac{1}{4}$	$\frac{1}{2}$	$\frac{3}{4}$	1hr.	$\frac{1}{4}$	$\frac{1}{2}$	$\frac{3}{4}$	2hr.	$\frac{1}{4}$	$\frac{1}{2}$	$\frac{3}{4}$	3hr.	$\frac{1}{4}$
90(.327)	K+												
80(.292)	B-												
70(.255)	B+												
60(.219)	S-												
50(.182)	K+												
40(.146)													
30(.109)													
20(.073)													
10(.036)													
$\frac{N}{10}$ NaOH (% HCL.)	10 c.c.												

————— = acidity - - - - - = free HCL.

Gastric Analysis.

DOWN BROS., LTD., LONDON.

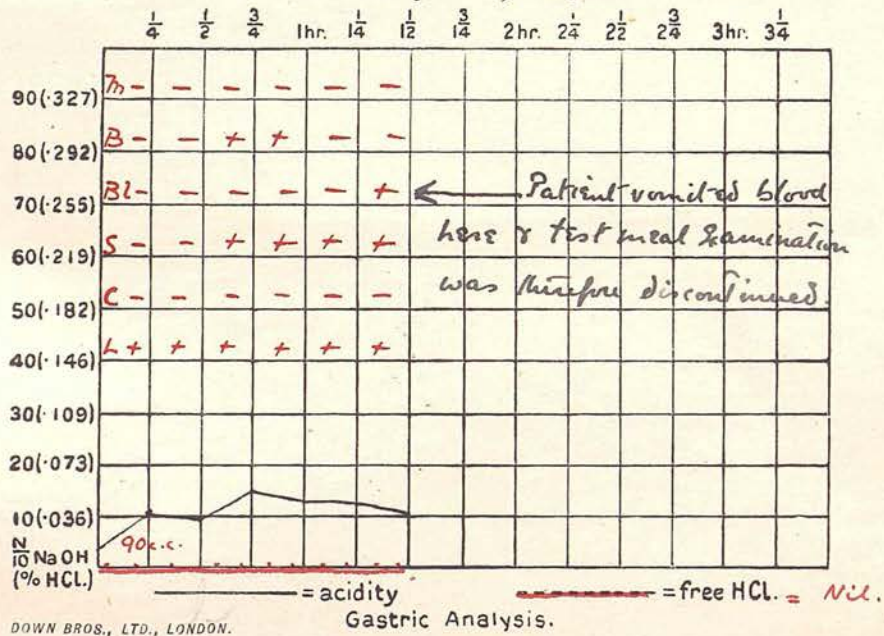
TREATMENT. The abdomen was opened and an inoperable carcinoma of the body of the stomach was found. The abdomen was closed.

PROGRESS. The patient recovered from the operation, but has since died.

h² m.

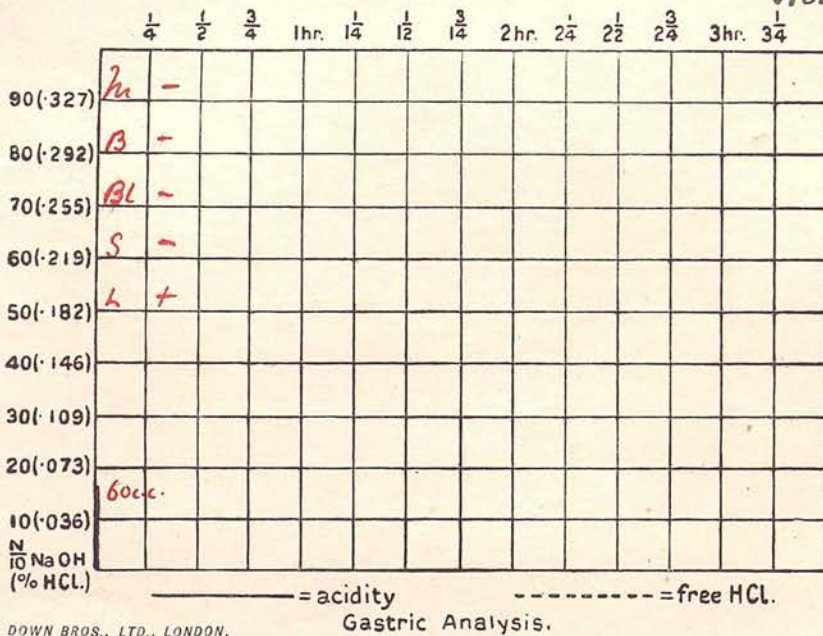
Carcinoma of Oesophagus.

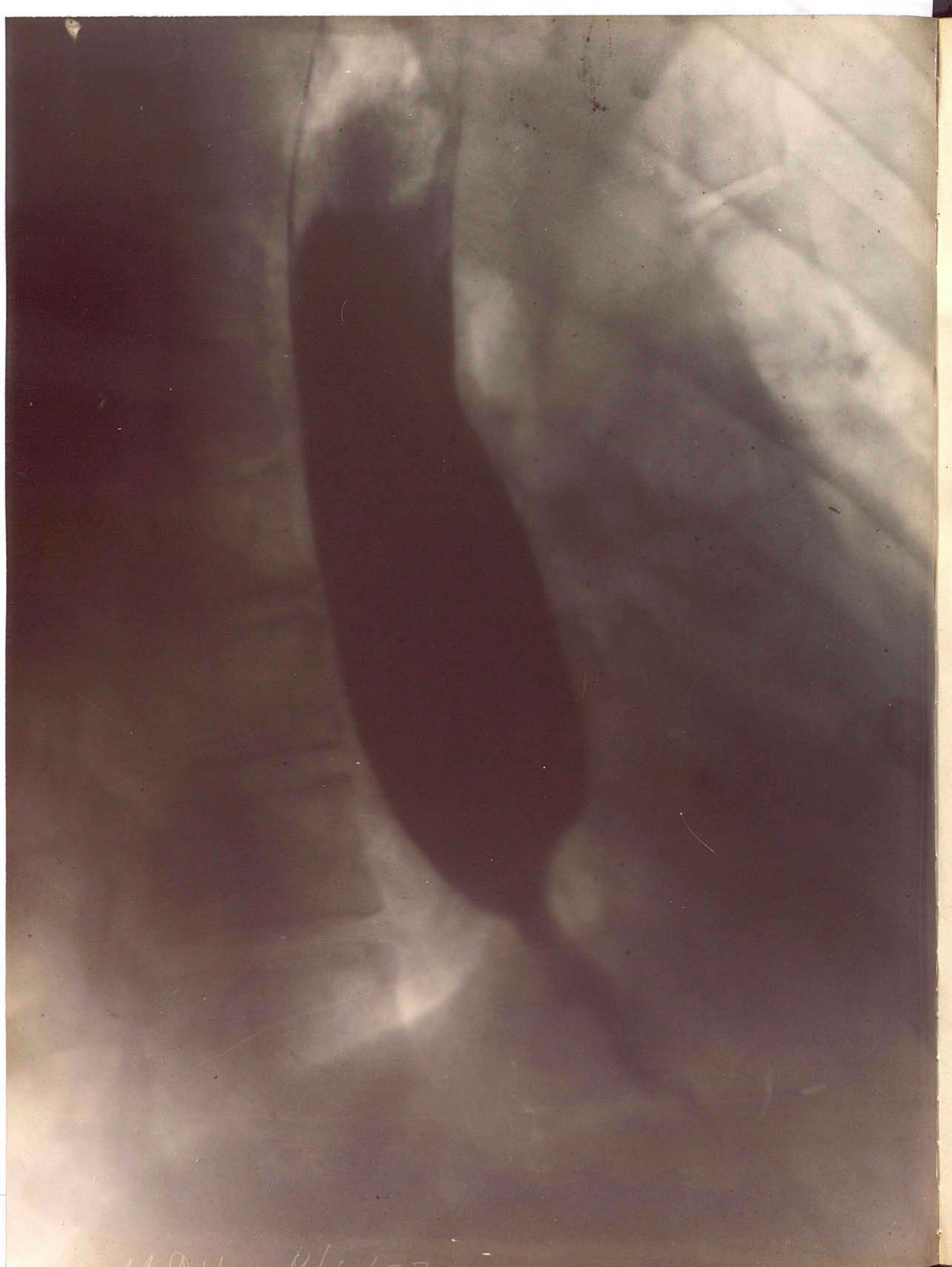
LIII 2.



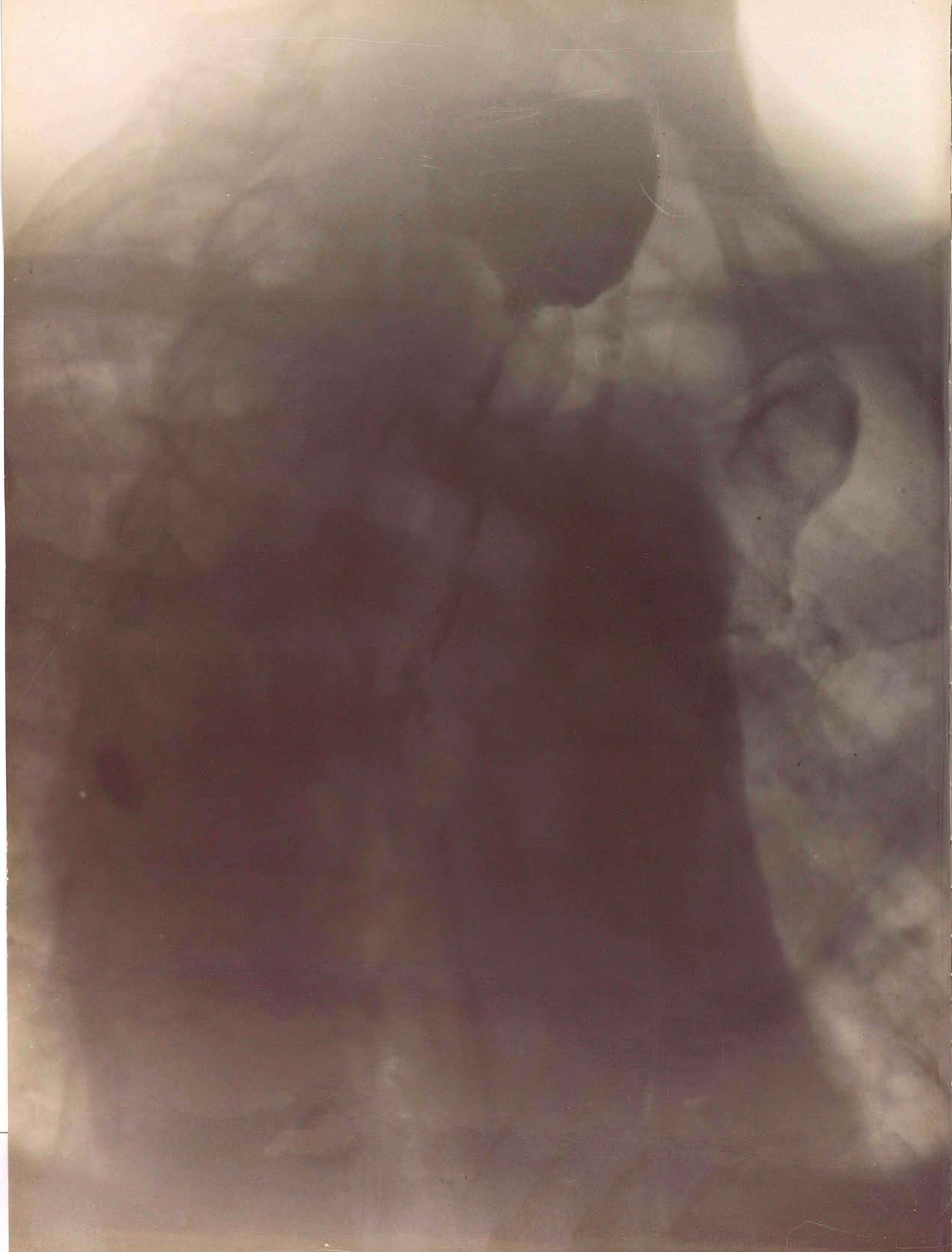
Carcinoma of Oesophagus.

Nursing Home.





1101 01/177



The charts of the gastric analysis and the X-rays of the two cases suffering from carcinoma of the oesophagus are now given. (Cases 1 and 2.

TABLE III.)

The X-ray photographs were taken at a late stage in the disease in both cases, when the X-ray appearances had become marked, whereas the gastric analyses had been conducted at an early stage, when the swallowing of solids was still possible.

Case 1 showed a carcinoma of the lower end of the oesophagus, some two inches above the cardiac orifice, whereas Case 2 - in which the resting juice only was tested - showed the constriction to be about the level of the sterno clavicular junction.

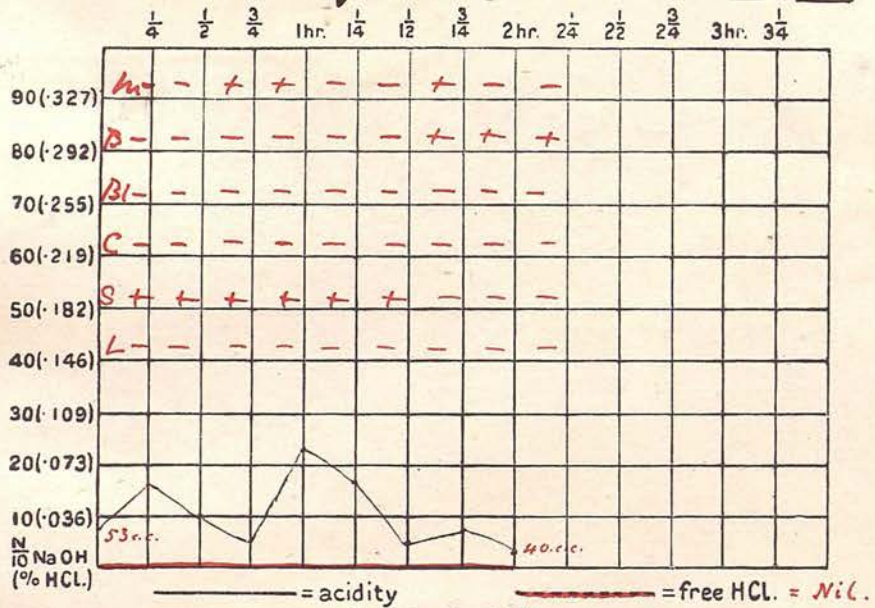
Both cases died following a gastrostomy.

In the following pages are given the case histories and the charts giving the results of the gastric analysis of seven cases showing achlorhydria. These seven cases correspond to cases 16, 20, 24, 25, 27, and 28 in TABLE III respectively, and include one case of carcinoma of the pancreas, one of cholecystitis and five, which, for want of a better name have been termed cases of functional achlorhydria.

They have been chosen to illustrate the value of MACLEAN'S test as a means of excluding the possibility of gastric carcinoma. In all seven cases the case history and physical examination were, to varying extents, suggestive of cancer of the stomach, all of them showed absence of free acid in the gastric contents, but in none of them was MACLEAN'S test for lactic acid found to be positive.

The subsequent histories of all the patients proved them not to be suffering from malignant disease of the stomach.

M^{rs} S. Carcinoma of Pancreas. Surgical.



DOWN BROS., LTD., LONDON.

Gastric Analysis.

CASE I. Mrs. S. AGE 66.

COMPLAINT. Pain and discomfort in the upper part of the abdomen. Lack of appetite. Weakness.

HISTORY. For six months before admission the patient had suffered from indigestion and lack of appetite. This had been associated latterly with pain in the upper part of the abdomen, not associated with taking food. She had lost much weight, was obstinately constipated and had become extremely weak.

ON EXAMINATION. The patient was emaciated and prostrated.

There was a feeling of resistance, suggestive of a tumour in the neighbourhood of the pylorus; and tenderness was complained of on palpation in this region. Nothing else could be made out, but the history and general appearances were very suggestive of carcinoma of the stomach.

Benzidene reaction negative.

X-ray examination showed nothing pathological in the stomach.

The results of the test meal were not suggestive of gastric carcinoma, for lactic acid was absent/

absent though achlorhydria was present.

TREATMENT. Owing to the fact that it was thought a lump could be made out operation was undertaken.

The stomach, gall bladder and liver were found to be healthy, but an advanced carcinoma of the pancreas was found.

PROGRESS. The patient died sometime later, developing jaundice a few days before death for the first time.

M²⁵ N.

Gall Stone.

R. I. E.

	$\frac{1}{4}$	$\frac{1}{2}$	$\frac{3}{4}$	1hr.	$\frac{1}{4}$	$\frac{1}{2}$	$\frac{3}{4}$	2hr.	$\frac{1}{4}$	$\frac{1}{2}$	$\frac{3}{4}$	3hr.	$\frac{1}{4}$
90(327)				M -									
80(292)				B -									
70(255)				Bx -									
60(219)				S +									
50(182)				G. +									
40(146)				L -									
30(109)													
20(073)													
10(036)													
$\frac{N}{10}$ NaOH (% HCL.)													

= acidity

----- = free HCL. = Nil.

Gastric Analysis.

DOWN BROS., LTD., LONDON.

CASE II. Mrs. N. AGE 53.

COMPLAINT. Indigestion, loss of appetite, nausea.

HISTORY. For seven months the patient, whose digestion had been excellent previously, had complained of loss of appetite, flatulence and nausea after meals. On one occasion she had vomited what she called dark brown material. She had never had any actual pain, but was conscious of a great feeling of weight and distension in the stomach. She stated that she used to be a fat woman but in the last few months had lost weight rapidly. She had no other symptoms.

ON EXAMINATION. The patient was still quite well nourished, but had evidently lost some weight, and was white and ill looking.

The upper part of both recti were held very rigid. Tenderness was complained of on palpation over the stomach, and some splashing could be elicited nearly three hours after taking a meal.

Benzidene reaction negative.

X-ray/

X-ray examination showed some stasis in the stomach, and the appearances round the pylorus were exceedingly suggestive of a pyloric carcinoma.

Test meal examination did not confirm this view, in that no lactic acid was demonstrated by MACLEAN'S test, even though the contents showed no free acid. UFFELMANN'S test, however, was positive, and there was some charcoal in the resting juice.

TREATMENT. The whole picture was so suggestive of gastric carcinoma, apart from the negative nature of MACLEAN'S test and the lack of blood in the stools, that operation was undertaken.

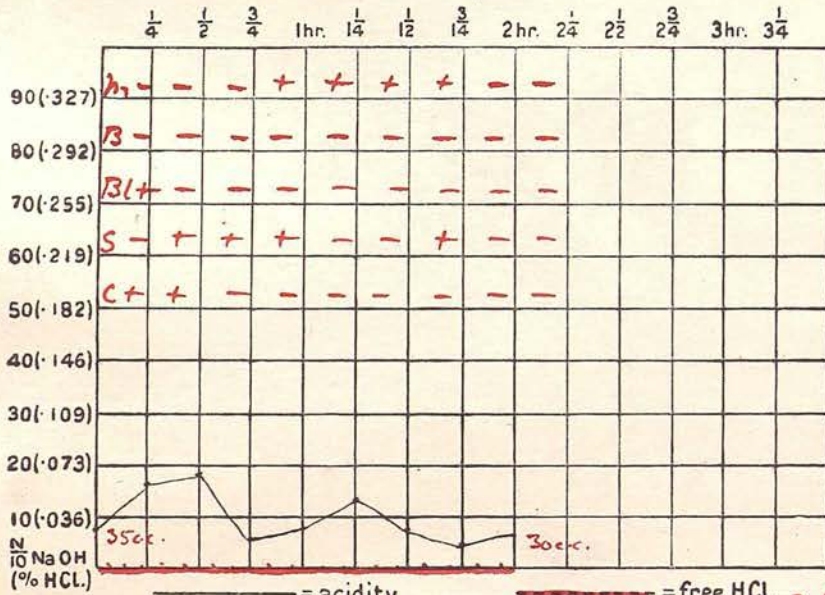
On opening the abdomen the stomach was found to be large and atonic, but otherwise healthy. A large single stone was found in the gall bladder. This was removed and the gall bladder drained.

PROGRESS. The patient made a good recovery from the operation and was discharged, having obtained complete relief from all her symptoms.

In: m.

Functional Achlorhydria.

XLIX 7.



DOWN BROS., LTD., LONDON.

= acidity = free HCl. = Nil.
Gastric Analysis.

CASE III. Mr. M. AGE. 37.

COMPLAINT. No appetite, flatulence, bad taste in the mouth.

HISTORY. For about a year before admission to hospital the patient who had previously been very healthy had not been taking his food well.

Five months before admission he started to complain of a bad taste in the mouth, and a good deal of flatulence and feeling of weight in the stomach after meals. He had latterly lost some weight. There was no vomiting or actual pain.

ON EXAMINATION. The patient was thin and pale looking.

Beyond some rigidity of the upper part of the recti nothing could be made out on physical examination.

Benzidene reaction negative.

X-ray examination shows slight delay in emptying.

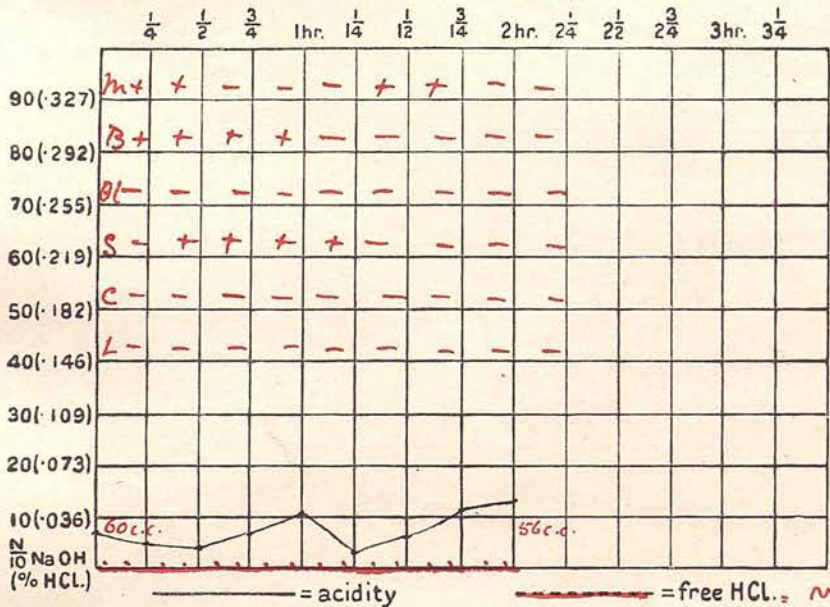
As will be seen, the test meal examination was quite consistent with a diagnosis of gastric carcinoma/

carcinoma, had lactic acid been present as well as achlorhydria. Lactic acid, however, was absent, and operation was therefore not advised.

TREATMENT. Large doses of Acid Hydrochlor. dil.

PROGRESS. Patient did very well, and increased rapidly in weight. His symptoms entirely disappeared. On leaving hospital, however, he discontinued his medicine, and his symptoms recurred. He consulted another medical man, who advised operation. On the abdomen being opened the stomach was found to be somewhat atonic, but otherwise perfectly healthy. The appendix was removed and reported to be slightly inflamed.

Miss M. Functional Achlorhydria. XLVIII. 22



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Gastric Analysis.

CASE IV. Miss M. AGE 50.

COMPLAINT. Indigestion, pain in the stomach.

HISTORY. For a year before admission to hospital the patient had had indefinite dyspeptic symptoms, flatulence after food, loss of appetite, and weakness.

For the month previous to admission she had also been troubled with a good deal of pain in the stomach about an hour after meals. She had lost some weight.

ON EXAMINATION. The patient was fairly well nourished and healthy looking.

Nothing pathological could be made out on physical examination.

Benzidene reaction negative.

X-ray examination showed nothing abnormal in the stomach.

The test meal results were not suggestive of gastric carcinoma.

TREATMENT. Dietetic. Acid tonic in large doses/

doses.

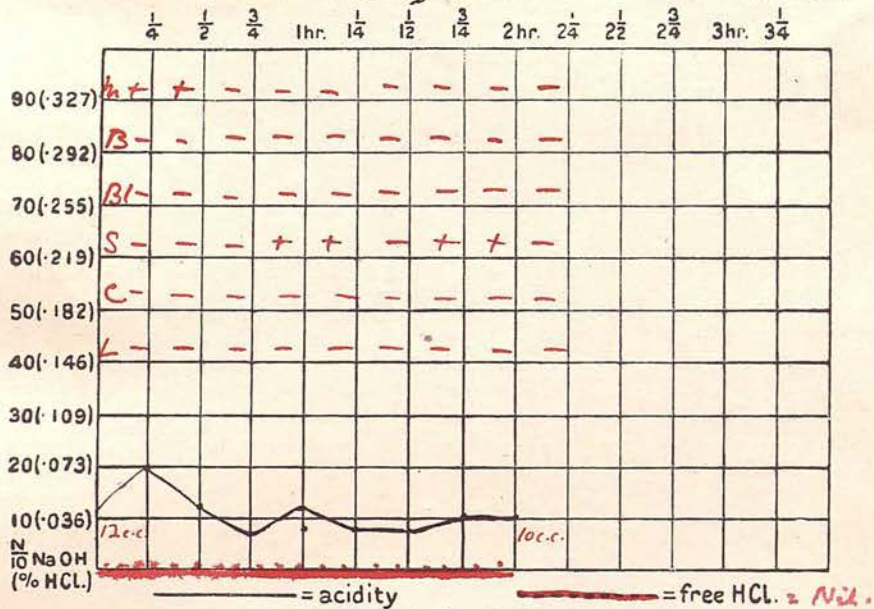
PROGRESS. Great improvement while in hospital. All her symptoms had disappeared by the time she was discharged.

Enquiry some months later revealed her to be in good health.

M^r W.

Functional Achlorhydria.

L-23.



DOWN BROS., LTD., LONDON.

Gastric Analysis.

CASE V. Mr. W. AGE 43.

COMPLAINT. Discomfort in the stomach after meals.

HISTORY. The patient had always been a strong and healthy man till six months before admission to hospital. He then began to complain of flatulence, feeling of weight in the stomach after meals, and lethargy. He had no other symptoms, except constipation and only consulted a doctor to please his wife.

ON EXAMINATION. The patient looked well nourished, and nothing pathological could be made out on physical examination.

X-ray showed a normal stomach.

Benzidene reaction negative.

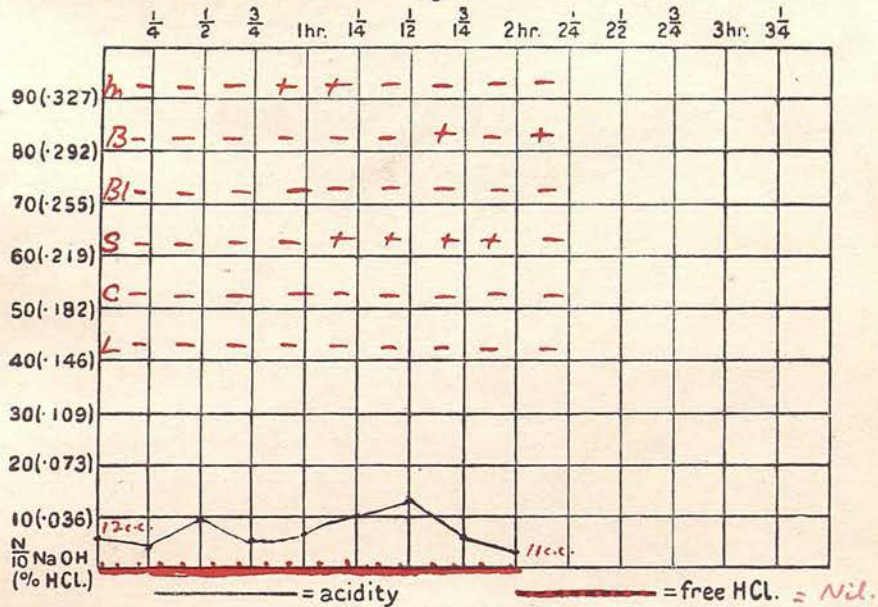
The test meal, apart from the achlorhydria, was not suggestive of gastric carcinoma.

TREATMENT. Stimulating tonic containing dilute hydrochloric acid, pepsin, nux vomica and gentian.

PROGRESS. Left hospital feeling very well.

Reported some months later in robust health.

M. R. *Functional Achylia.* *XLVI. 3.*



DOWN BROS., LTD., LONDON.

Gastric Analysis.

CASE VI. Mr.R. AGE 57.

COMPLAINT. Indigestion, pain in the stomach.

HISTORY. The patient had never had any stomach trouble till six months before admission. He then began to complain of constant pain in the stomach, which had no particular reference to the taking of food. This was accompanied by flatulence, nausea, loss of appetite, and very marked constipation. There had been no vomiting. He had lost some weight.

ON EXAMINATION. The patient looked thin but wiry.

There was rigidity over the upper part of both recti, but nothing else could be made out on physical examination.

Benzidene reaction negative.

X-ray showed a normal J shaped stomach, with no delay in emptying.

Apart from the achlorhydria the test meal results were not suggestive of carcinoma of the stomach, lactic acid being absent.

TREATMENT./

TREATMENT. Dietetic. Acid hydrochlor. dil.
in large doses.

PROGRESS. Appetite improved greatly while
in hospital, and the pain, flatulence and constipa-
tion disappeared.

On enquiry some months after discharge
the patient, who was persevering with his acid tonic,
was in good health.

M^oC. *Functional Achylia Stia.* R.I.E.

	$\frac{1}{4}$	$\frac{1}{2}$	$\frac{3}{4}$	1hr.	$\frac{1}{4}$	$\frac{1}{2}$	$\frac{3}{4}$	2hr.	$\frac{1}{4}$	$\frac{1}{2}$	$\frac{3}{4}$	3hr.	$\frac{1}{4}$
90(.327)			M +										
80(.292)			B +										
70(.255)			B -										
60(.219)			S +										
50(.182)			Ext										
40(.146)			L -										
30(.109)													
20(.073)													
10(.036)													
$\frac{N}{10}$ NaOH (% HCL.)													

23 c.c.

————— = acidity - - - - - = free HCL. = Nil

Gastric Analysis.

CASE VII. Mr. C. AGE 47. LABOURER.

COMPLAINT. Indigestion, lack of appetite.

HISTORY. For five months before admission to hospital the patient, following some domestic difficulties, had lost all appetite and was nauseated at the sight of food. This was his principal symptom, but he had also lost weight with great rapidity, and had become very weak and run down. He stated that he had vomited repeatedly, and was certain that something was wrong with his stomach.

ON EXAMINATION. The patient was greatly emaciated and very strained and nervous looking.

The upper part of both recti were held rigid, and he complained of pain on palpation over the stomach.

Benzidene reaction negative.

X-ray examination was negative.

Test meal examination, though showing achlorhydria in the one hour specimen was not otherwise suggestive of gastric carcinoma.

TREATMENT. The patient was treated as a nervous /

nervous dyspeptic, with suggestion and tonic treatment. He improved greatly while under hospital discipline and put on weight rapidly. He suddenly decided to go out, and it has since been impossible to trace him. The marked increase in weight, however, under treatment rules out the possibility of carcinoma.

S U M M A R Y.

INTRODUCTION.

Emphasis has been laid on the importance of gastric carcinoma to the nation and the world, its increase, its supposed earlier age incidence and the failure of the medical profession to solve the problem of its etiology or to deal with it by other than surgical means. It has been pointed out that, in the absence of prevention, the early diagnosis of the condition is the real problem on which attention should be concentrated, since it is the exception for a case to be brought for operation till the disease is so advanced as to make surgical interference of no avail. The obvious disadvantages of the exploratory laparotomy, in every suspicious case, have been dwelt upon, and the advantages of some simple laboratory test which would definitely establish a diagnosis stressed.

RESUME/

RESUME of LITERATURE etc.

A brief account of the histology of the gastric glands has been given.

The earlier views on gastric secretion have ~~there~~ been outlined, including an account of **PAWLOW'S** observations on the secretion induced by psychic excitation and the nerve supply of the stomach, of **EDKIN'S** work on the gastric hormone, and of **CANNON'S** theory of the acid control of the pylorus.

The evolution of the test meal has been followed in some detail, and the advantages of the fractional method of gastric analysis over the older one hour method pointed out. The possible fallacies of the fractional method have been dealt with, and in this connection the results of certain experiments on myself are given to show that the psychic disturbances induced by the test had little affect upon the acid secretion.

The more recent views on gastric secretion have been indicated, and it has been shown how the theories of **PAWLOW** and the older observers have had to/

to be modified in the light of recently acquired knowledge.

The methods used for the discovery and estimation of free hydrochloric acid have been described, and the rival views as to ^{the} efficacy of the various reagents used in these tests contrasted.

The views of various authorities on achlorhydria and its incidence and significance in health and disease have been given.

The chemistry of fermentation lactic acid and of sarcolactic acid has been outlined, and the method of the production of the former in the stomach contents and of the latter in muscle discussed. Two tests for the presence of lactic acid in the gastric contents are described and the views of various authorities as to their respective efficacy given.

Several theories as to the cause of the achlorhydria so often observed in gastric carcinoma have been stated and many authorities are quoted to show the conflict of opinion which exists as to the frequency of its presence in this condition. It has been shown that while some observers doubt the utility/

utility of gastric analysis as an aid to an early diagnosis of cancer of the stomach, others hold it to be invaluable; but of these latter, few are in agreement as to the particular results of the analysis upon which a diagnosis should be based.

OUTLINE and SCOPE of THESIS.

A brief outline of the scope of the original research has been given, and the type of patient upon whom the investigations have been conducted has been described.

It has been pointed out that with a view to elucidating several points in the technique of gastric analysis and of testing its value as a factor in the early diagnosis of gastric carcinoma, analysis of the stomach contents had been conducted in ninety three cases of general disease, including seventeen cases of gastric carcinoma. The great majority of these cases were examined by the fractional method, a few by examination of the one hour specimen only and two or/

or three by examination of the resting juice only.

TECHNIQUE EMPLOYED, and RESULTS OBTAINED.

The varying techniques employed in procuring the specimen of gastric contents for examination and the method of conducting the analysis has been described in some detail.

The relative delicacy of the congo red, dimethyl and **GUNZBERG** tests for the presence of free hydrochloric acid has been investigated. It has been found that the **GUNZBERG** reaction is the only reliable one, since it registers the presence of exceedingly small traces of free hydrochloric acid, which are not indicated by the dimethyl and congo red tests. It has also been found that whereas lactic acid has no affect upon the **GUNZBERG** reaction, it will, when present in a large quantity in the specimen, give with the congo red and dimethyl tests a similar reaction to that given by free hydrochloric acid.

It has been pointed out that this latter inaccuracy/

inaccuracy in the congo red and dimethyl tests for free acid may account for the fact, so frequently stated by modern observers, that free hydrochloric acid is present in the stomach contents of the majority of patients suffering from gastric carcinoma.

It has been demonstrated that UFFELMANN'S test for lactic acid is valueless, since it gives a positive reaction with many other substances which may be found in the stomach besides lactic acid; but that MACLEAN'S test for lactic acid is simple and trustworthy.

The results of the test meal examination in seventeen cases of gastric carcinoma have been tabulated. These results suggest that gastric analysis is a valuable aid in the diagnosis of gastric carcinoma, since, in all the seventeen cases a diagnosis could have been made from the results of the test meal examination alone. In sixteen out of the seventeen cases free acid was found to be absent and lactic acid present. This was the most constant finding in the series. Blood, charcoal and foul odour were commonly/

commonly present, though not constantly so, in the gastric contents. The OPPLER BOAS bacillus was seldom found.

It has been demonstrated that achlorhydria and the presence of lactic acid are not necessarily an indication of the stage of advancement of malignant disease of the stomach, as such results may be observed in both the early and late stages of the condition. Similarly the discovery of free hydrochloric acid in the stomach contents of a patient suffering from gastric carcinoma is no criterion of an early stage of the disease, as is sometimes stated, since free hydrochloric acid may be present when the cancer is far advanced.

It has been shown that lactic acid, when found in the stomach, is not invariably the result of the fermentation of stagnating contents, but may, on occasion, be present when no stasis in the stomach has occurred, probably due to the production of a sarcolactic acid by the tissues involved by the malignant growth.

Lactic acid was found in none of the other seventy/

seventy six cases, in which malignant disease of the stomach was absent, except in two cases of carcinoma of the oesophagus, where the tissues involved by the growth had probably produced a sarcolactic acid which had been passed into the stomach. The appearance of lactic acid in the stomach is thus a point of first rate diagnostic significance.

The case histories of all seventeen cases of gastric carcinoma have been given together with charts showing the results of the gastric analysis in each case. It has been observed that none of the cases gave a previous history of stomach trouble which suggests that the development of cancer from an old standing gastric ulcer is not as common as many suppose.

Graphs of the curves of the total acidity are given in three cases of pernicious anaemia and one case of primary achylia gastrica to demonstrate the difference in the shape of the curves obtained in these cases ^{from} ~~and~~ those obtained from cases of secondary achlorhydria due to gastric carcinoma.

The/

The charts showing the results of the gastric analysis and the X-ray photographs of the two cases of carcinoma of the oesophagus, in which lactic acid was found in the gastric contents, have been inserted.

Finally the case histories and the results of the test meal examination are given in seven cases showing achlorhydria, in which gastric carcinoma was proved to be absent, to show the diagnostic value of a negative test for lactic acid in such cases.

C O N C L U S I O N S .

As the result of my investigations the following conclusions have been arrived at. It must be realised, however, that, as it has only been possible to study a limited number of cases, certain of these conclusions must not be taken as dogmatic assertions, but rather as expressions of opinion based upon a limited number of results.

1. Gastric carcinoma may be diagnosed or excluded in the vast majority of cases, by examination of the stomach contents alone.

2. The results of the gastric analysis on which importance should be placed, in the diagnosis of this disease, are the presence of:
 - (a) Achlorhydria.
 - (b) Lactic acid.
 - (c) Blood.
 - (d) Evidences of stagnation.

3. Absence of free acid and the presence of lactic acid are found in the great majority of patients suffering from gastric carcinoma, and such a dual finding, with the exception of carcinoma of the oesophagus, probably occurs in no other condition.
4. The absence of lactic acid in stomach contents which show no free acid, or the discovery of large quantities of free hydrochloric acid make the presence of gastric carcinoma exceedingly improbable.
5. The absence of free acid and the presence of lactic acid is not necessarily evidence of an advanced condition of the carcinoma, nor is the presence of free acid necessarily evidence of an early stage in the growth.
6. Lactic acid found in the stomach is not invariably caused by the fermentation of stagnating gastric contents, but may be sarcolactic/

sarcoplactic acid produced by the tissues involved by the growth. It may therefore occur in the stomach contents when no pyloric stenosis is present.

7. Graphs of the total acidity curve in gastric carcinoma can usually be distinguished from those found in pernicious anaemia and primary achylia gastrica from the shape of the curve.

8. The congo red and dimethyl tests for free hydrochloric acid in the gastric contents are not trustworthy, since:
 - (a) They do not indicate free hydrochloric acid when it is present in very small quantities.
 - (b) They react to large quantities of lactic acid in the same way as they react to free hydrochloric acid.

9. GUNZBERG'S test, when the reagent is freshly prepared, is an entirely reliable one/

one for the presence of free hydrochloric acid.

10. UFFELMANN'S test for lactic acid is valueless, as it gives a positive reaction with many other substances, which may be found in the stomach contents, besides lactic acid.
11. MACLEAN'S test for lactic acid is simple and trustworthy.