THE SIGNIFICANCE OF LACTIC ACID

IN THE

GASTRIC CONTENTS.

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By

A.B.Robertson, M.B.,Ch.B.

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For many years investigations have been carried out with the object of determining the cause of the acidity of gastric juice. Although it has now been definitely established that the chief acid concerned with this is hydrochloric acid, it is generally admitted that organic acids may also be detected. What the exact significance of the presence of the latter is, has caused considerable divergence of opinion. The chief of these organic acids is lactic acid, and not only does considerable doubt exist as to its significance, but there is also some dubiety as to its origin. The object of the present work, therefore, is to try to determine the origin of lactic acid, the conditions favouring its production, and its fate during the course of gastric digestion. From an investigation of these three points it is hoped that certain conclusions as to the actual significance of lactic acid in the stomach may be deduced.

One of the earliest investigations into the cause of the acidity of gastric contents was published in 1824 by Prout,(1) who found that, during the process of digestion, free, or at least "unsaturated", muriatic acid existed in the stomachs of certain animals. He was also able to detect this free acid in the fluid ejected from the stomach in severe cases of dyspepsia. His work was thus the basis of the early view that the chief acid of the stomach was hydrochloric acid, and the results he obtained were soon confirmed by Children[2] and Braconnot,[3] and also by Dunglison and Emmet.[4] The latter, working on Dr. Beaumont's well-known case, were able to obtain hydrochloric acid by distillation of gastric juice in a similar manner to Prout. Although now unchallenged, Prout's view was by no means generally accepted in his day.

A new theory of the cause of gastric acidity was put forward by Blondlot,[5] who considered that it was due in part to the presence of acid calcium phosphate. He thought that chemical action took place in the wall of the stomach between the sodium chloride and calcium phosphate of the blood. Resulting from this, acid calcium phosphate was produced, accompanied by traces of hydrochloric and phosphoric acids.

About the same time an entirely different view came into vogue, namely, that not hydrochloric acid, but lactic acid, was the important acid of the stomach. The chief supporters of this belief were Bernard and Barreswil,[6] who, in 1844, published their classical treatise on the subject. Their findings may be quoted briefly.

"From the results of our work we can assert that the acid reaction of the gastric juice is not due to biphosphate of lime, but that it results, on the other hand, from an acid existing in a free state in the stomach juices. We have never been able to prove the existence in the free state of hydrochloric and/

and acetic acids which have previously been demonstrated. We have consistently found the very distinct characters of lactic acid along with a small proportion of phosphoric acid. In our opinion lactic acid ought to be considered as a constant physiological phenomenon. In fact, no matter under what conditions of feeding animals are placed, we have never seen any variation in the nature of the chief acid of the gastric juice. Thus after a diet exclusively vegetable or animal, taken for several days, or even after a more prolonged period, we have always found free lactic acid present. In advancing the theory that lactic acid is the constant cause of the acidity of gastric juice, we do not wish it to be thought that this acid is, by its nature, endowed with certain special properties which render it indispensable for the phenomena of digestion. It follows, on the contrary, from the experiments of Blondlot (5) and others that, if an acid reaction is indispensable for the solvent property of the gastric juice to manifest itself, the nature of the acid which produces this reaction is immaterial. This equivalence of acids for the activity of the gastric juice appears even necessary; for, on every occasion, by the same act of feeding, the greatest variety of salts are introduced into the stomach, at the moment of formation of gastric juice. It is obvious that, if among these salts one is found whose activity can be displaced by lactic acid, the digestive functions will be infallibly disturbed, if the new acid, in its free state, cannot replace the normal acid."

This work soon received a large measure of support from other investigators, of whom one may mention Pelousse,[7] Thomson,[8] and Lehmann.[9] They all considered that the free acid of the gastric juice was lactic acid. The latter explained the presence of any hydrochloric acid in the gastric juice by the action of the lactic acid, which he considered the essential acid, on chlorides. This view was supported by Leuret and Lassaigne.[10]

Thus it came about that the views of Prout and his supporters were for a time discredited. As far as digestion was concerned, the presence of lactic acid was considered of prime importance, and if at times traces of hydrochloric acid were found, their presence was explained by Lehmann's theory.

The work commenced by Bernard and Barreswil, and extended by other investigators, did not, however, remain for long unchallenged, and there soon developed a reversion to the hydrochloric acid theory. This was largely due to the work of Bidder and Schmidt,[11] who showed, that in resting juice the free acid of the stomach was hydrochloric, but that juice removed during the course of digestion, contained, in addition, lactic acid.

That both hydrochloric and lactic acids were present in gastric juice now became more generally accepted, but it was not till 1872 that any explanation was advanced for the presence of two different acids. This was largely due to the work of Brücke,[12] who showed that starch could be converted into lactic acid by bacillary action in the stomach, and that this could occur without the intervention of ptyalin. He supposed that sugar was first formed by the action of the bacteria, but immediately became converted into lactic acid by their further activity.

About this time two further contributions of considerable interest appeared. The first was by Maly,[13,30] who discovered that lactic acid could be isolated from the stomach of the pig. He believed that it arose by the fermentation of carbohydrates, but that the acid so formed, reacting with sodium chloride, produced lactate and hydrochloric acid. This worker also found that lactic acid would decompose sodium chloride in this way in cold solutions.

The second publication at this period was that of Ufflemann,[14] who described the well known test for lactic acid, which commonly bears his name at the present time.

The view that lactic acid was derived from ingested carbohydrate by bacterial action was soon challenged. In fact it is remarkable how controversial were all these earlier theories connected with gastric function. Landwehr,[15] in 1886, postulated a new theory. He suggested that the lumen of the gastric glands was always more or less filled with mucous, and that, when the glands were stimulated, a ferment was produced which decomposed the mucin, forming lactic acid from its carbohydrate constituent. This author agreed with Maly that the lactic acid did not long remain as such, but soon became converted into hydrochloric acid and sodium lactate. He considered that the former was passed into the stomach, and the latter absorbed by the blood. In proof of the absorption of lactic acid by the blood, Drechsel,[(16)] by his investigations, was able to show that, during digestion, an increased amount of lactate would be detected in the blood. The possibilities of increased blood lactic acid being due to causes other than absorption from the stomach, would make one dubious of the results on which this theory is based.

An excellent conception of the differences in the views held at this time can be obtained by comparison of some of the contemporary text books. McKendrick,[(33)] in his "Outlines of Physiology", stated that a free acid always existed in gastric juice. This acid was usually hydrochloric acid, rarely lactic acid alone, and not infrequently a mixture of both acids.

Foster[(17)] considered that the acidity of gastric juice was due normally to hydrochloric acid. According to him this had been conclusively shown by the fact that the amount of chlorine present in gastric juice was more than would suffice to form chlorides with all the bases present, and that the excess, if regarded as existing in the form of hydrochloric acid, corresponded exactly to the quantity of free acid present. He was of the opinion that lactic and butyric acid, when they occurred, arose either by their respective fermentations from articles of food, or from the decomposition of their alkaline or other salts.

According to Halliburton[18] lactic acid was generally found in the stomach during a meal, especially if the meal contained carbohydrates. By fermentative changes in these, lactic acid was produced. This author supported the view of Maly,[30,13] namely that the lactic acid so formed soon became converted into hydrochloric acid and lactate. There is some difficulty, however, in accepting this theory, since carbohydrates are not always present in the food, and also because a flow of acid from the gastric glands can be excited by distilled water or mechanical irritation. This objection is met to some extent by the work of Landwehr,[15] previously quoted, who considered that lactic acid arose not from ingested carbohydrate, but from the carbohydrate constituent of the mucin commonly found filling the lumen of the gastric glands. Halliburton concluded by stating that, although there was very little doubt that hydrochloric acid was the acid, par excellence, of the gastric juice, lactic acid did occur during digestion. This consisted partly of sarcolactic acid derived from meat, and partly of fermentation lactic acid derived from carbohydrates. The amount of lactic acid was considerably increased in those conditions where excessive fermentation was taking place. Small quantities of acetic and butyric acids were apparently produced in a similar fashion.

The next important contribution to this study of gastric acidity was made a few years later by Ewald and Boas,[19] who obtained the material for their researches from patients attending a clinic in Berlin, established by the latter for the investigation of gastro-intestinal disorders. As the result of their work, they stated definitely that lactic acid was never present unless some digestive disturbance existed. Boas also discovered the bacillus which, in his opinion, caused the production of lactic acid by fermentation in the stomach. It must not be forgotten, however, that in 1857, nearly forty years earlier, Pasteur[20] had isolated an organism capable of producing lactic acid by fermentation, and since then, an immense variety of organisms, said to be capable of causing this reaction had been described.

At the end of the nineteenth century two works of outstanding importance were published; the first "The Work of the Digestive Glands" by Pavlov,[21] and the second, "A Text Book of Physiology" by Schafer.[22] Both writers pay particular attention to this problem of the occurrence and origin of lactic acid in the stomach.

Pavlov says:- "Nor is the possibility excluded that the continuation of starch digestion may depend on some entirely different condition; for example, the production of lactic acid from the carbohydrate constituents of the food. Possibly this is the explanation of the production of lactic acid, the meaning and importance of which have been but little cleared up." And again:- "As an aid to digestion nature itself constantly endeavours to prepare lactic acid in the stomach as well as hydrochloric acid. The former arises from the food introduced, and is constantly present." It is obvious that Pavlov, at that time, realised that comparatively little was known about the significance of lactic acid in the stomach, and that, in his estimation, the theories of previous investigators had been by no means definitely established.

Schafer,[(22)] likewise, made no very convincing statements on this question of lactic acid. In his opinion it had been conclusively demonstrated that hydrochloric acid was the chief acid of the gastric juice, and that in the purer samples, free from food, it was almost exclusively the only acid present. He also found that in gastric juice mixed with food, especially carbohydrate, lactic acid in addition might be found. He quoted the work of C. Schmidt, who, from a large number of analyses, concluded that the pure juice of carnivora, obtained after a fast of eighteen to twenty hours, contained only hydrochloric acid, and no trace of lactic and acetic acids. On the other hand, the gastric juice of herbivora contained, besides hydrochloric acid, small amounts of lactic acid probably derived from remnants of carbohydrate food. It is, of course, worthy of note that the stomach of the herbivora retains food for a much longer period than that of the carnivora. In the case of the sheep, for example, traces of food are usually found in the stomach even thirty-six hours after a meal.

In connection with the presence of lactic acid in the stomach, Schafer mentioned that where it occurred it did not persist for long; in fact, half an hour after gastric digestion commenced, lactic acid could usually no longer be detected. He apparently offered no explanation of this phenomenon.

In 1902, Herter (24) published his "Lectures on Clinical Pathology", and dealt at considerable length with the lactic acid question, chiefly from the pathological standpoint. He stated that, although fermentative and putrefactive processes might go on side by side in a large extent of the digestive tract, fermentation, in health, was unaccompanied by putrefaction during gastric digestion. In disease, on the other hand, a slight degree of putrefaction sometimes occurred in the stomach. Because of its frequency, lactic acid fermentation was considered a very important type of carbohydrate decomposition. In the normal conditions of the stomach, it was either not found at all, or only in small amounts. Whenever the stomach was unable to empty itself with physiological promptitude, lactic acid fermentation was liable to occur, especially if carbohydrates were freely eaten. According to Herter, two

two organisms, the Bacillus Acidi Lactici and the Bacillus Lactis Aërogenes, were chiefly concerned. Their action was favoured by the presence of protein, and by a neutral or slightly acid medium. They were, however, said to grow well even in the presence of hydrochloric acid of a concentration of .7%. A neutral medium was the most propitious, and this was often found where there was stomach disease with impaired secretory activity.

A further contribution was made in 1905 by Austin Flint,(25) and it is interesting to note that a degree of doubt even greater than that of Pavlov and Schafer appears to pervade his views. He stated that it was supposed that the gastric juice contained free hydrochloric acid, and probably also a small amount of lactic acid. It was generally admitted that the total acidity of gastric juice was variable, and that the normal acid could be replaced, without loss of the digestive properties of the secretion, by lactic, oxalic, acetic, formic, succinic, tartaric, citric, phosphoric, nitric or sulphuric acids.

From the time of the publication of Flint's book in 1905, till 1928, little work dealing with this question was apparently performed. Lactic acid was considered of common occurrence in those conditions conducive to tardy emptying of the stomach. Of these conditions gastric carcinoma was the commonest, and the occurrence of a very low concentration of free hydrochloric acid in this type of case was looked on as being exceptionally favourable for fermentation taking place.

To show, however, that, even at that late date, other ideas were held, it is worthy of note that Noël Paton,(32) in his "Essentials of Human Physiology", reverted to the view of Schafer that lactic acid could not be considered an abnormality during the first half-hour of digestion. It arose by fermentation of carbohydrate, and this process continued until the gastric contents became distinctly acid in reaction by the activity of the gastric glands. Paton likewise offered no explanation of the disappearance of lactic acid at the end of half an hour.

In 1928 came the somewhat astounding publication of Craven Moore and Roberts.(26) They considered that lactic acid was never found in gastric contents except in cases of gastric carcinoma. The same writers stated that it appeared earlier and more frequently in the rapidly growing types of neoplasm. According to them there was no evidence to show that lactic acid was formed by bacterial fermentation, but they considered that most probably it arose by the specific activity of the cancer cells on the glucose of the tissue fluids. In their opinion lactic acid was pathognomonic of gastric carcinoma.

Coming as they did after a lull of several years, these rather revolutionary assertions do not appear to have aroused the controversy one would have expected. Since the above investigation was published, nothing, throwing any further light on the question, has appeared, if one excepts Maclean's work on the thiophene test for the detection of lactic acid in the gastric contents, and a paper by Dodds and Robertson,[28] dealing with the application of the test.

The most recent view on the entire question is summed up by Lovat Evans[29] in the latest edition of Starling's "Text Book of Physiology", where one reads that "the acid of the gastric juice is entirely hydrochloric. When, however, one examines the gastric contents, composed of a mixture of gastric juice and semi-digested food, one will always find other acids besides hydrochloric, and of these the most important is lactic. It is produced by processes of bacterial fermentation occurring in carbohydrates, converting them first into sugar and then into lactic acid. As the gastric juice soaks into the food and renders it acid, it puts a stop to the bacterial activity."

Thus, after full consideration of all this work, it is obvious that complete unanimity has not yet been reached. It is universally accepted that hydrochloric acid is the predominant acid of the gastric juice, and that at times lactic acid may also occur. Some are of opinion that the latter is pathognomonic of cancer, although many others have found the acid under purely physiological conditions. There is still the further point that, even if one accepts the truth of the statement attributed to Schafer[22] and Noël Paton,[32] that lactic acid is commonly present during the first half hour of digestion and then disappears, no satisfactory explanation of this phenomenon has yet been offered. It appears a pity that a question at once so interesting and important clinically should not have been still further investigated.

It is believed that the results of the investigations, herein described, help to elucidate certain points in this rather controversial question.

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TESTS EMPLOYED FOR THE DETECTION

OF LACTIC ACID.

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A close investigation of the literature describing the tests employed for the detection of lactic acid, reveals the fact that only three methods, each with certain minor variations in technique, have been commonly utilised. The great difficulty is, of course, to find a test which is applicable to gastric contents, and it is generally admitted that each one of the above methods, presently to be described, comes into that category.

In 1884, Ufflemann,(14) published a description of the well-known test which now bears his name. He claimed that it was a thoroughly reliable method if applied to gastric contents, and carried out according to his technique. Unfortunately, as will be shown, the test has been considerably modified since Ufflemann's time, and although, in its new form, it is much more simple to carry out, the results obtained are by no means so satisfactory.

In his "Text Book of Physiology", published in 1898, Schafer (2 gives Ufflemann's test pride of place, but also states that - "a very dilute solution of ferric chloride, possessing only a trace of colour, is much deepened in colour on the addition of a mere trace of lactic acid." This appears to be the earliest mention of the now commonly employed Ferric and Mercuric Chloride Test.

For many years these two methods were the only ones employed qualitatively. With the introduction of the Thiophene

Test, however, a considerable advance was made. In its early form, as described by Hopkins, the technique was comparatively simple, but the results obtained were not considered satisfactory. In an attempt to improve the method, Maclean (27) carried out a series of investigations, and perfected a process, applicable to gastric contents, which is now known as Maclean's modification of the Thiophene Test. Unfortunately, in its new form, the test is more complicated, but the additional work entailed is well worth while, since the degree of accuracy has been considerably increased.

It is now proposed to deal with each test in greater detail with a view to determining which will give the most accurate results in the ensuing part of this investigation.

Ufflemann's Test.

The reagent (14) employed in this case consists, of course, of an amethyst-blue solution, made by adding a trace of ferric chloride to a one per cent solution of carbolic acid. If a few drops of lactic acid are added to this, a yellow colour is produced. It has to be remembered, however, that hydrochloric acid, while it fails to produce a yellow tint, is capable of discharging the blue colour of the reagent. For this reason it is unwise to apply the gastric contents, suspected of containing lactic acid, directly to the reagent. It is best to adhere rigidly to Ufflemann's original description of the mode of application of the test.

Realising the above difficulty, he suggested that the stomach contents should first be filtered and then extracted with ether. The ether should then be distilled off, and the residue extracted with water. A few drops of the solution so obtained should be added to a small quantity of the reagent. Provided the test was performed in the above manner, a positive result was said to be obtained with dilutions of lactic acid of one in ten thousand.

Owing to the delicacy of the colour produced by the presence of lactic acid the test is by no means foolproof, and those who have had any experience of the method, will no doubt agree that the possibility of fallacious interpretation cannot, by any means, be excluded. The difficulty which may arise from the presence of hydrochloric acid has already been pointed out. This can only be avoided by employing the ether extraction method.

In order to exclude any further fallacies which might be due to the presence of such substances as blood, pepsin, and bile, the writer investigated the test in the presence of these. It was found that blood and peptic extract did not apparently interfere with the accuracy of the test. Bile, on the other hand, as might be expected, caused considerable difficulty in interpretation.

From a study of the above results, the writer is satisfied that, unless carried out by the ether extraction method, the test is not suitable for application to gastric contents. Even so performed it is not sufficiently delicate for the ensuing work. The presence of bile renders the result of the test quite valueless.

Ferric and Mercuric Chloride Test.

The original description of this test is to be found, as has been previously stated, in Schafer's (22) "Text Book of Physiology". The form I have found most useful is as follows:

Two test tubes are filled to the same level, the one with filtered gastric contents, and the other with water. To each are added three drops of a five per cent aqueous solution of ferric chloride. The tube containing the gastric contents will often show a reddish-yellow coloration. To each tube are now added six drops of a saturated aqueous solution of mercuric chloride. In the presence of lactic acid the reddish appearance will give place to a yellow coloration; if no lactic acid is present the reddish colour will entirely disappear.

From the above description it will be seen that, in many respects, the test is similar to that described by Ufflemann. The colour change indicating the presence of lactic acid is, as in the previous case, a very delicate one, and for that reason the use of the control tube is absolutely necessary.

In the writer's opinion Ufflemann's test is superior to this one provided it is carried out by the ether extraction method. As might be expected, the presence of bile completely masks the end-point, and renders the test valueless. Blood, if present in minute traces, and peptic extract do not appear to introduce any fallacies, but larger quantities of the former as might be expected, cause considerable difficulty.

Thiophene Test.

In itx original form, as described by Hopkins, this test was not suitable for application to gastric contents, but various modifications, perfected by Maclean,(27) have now surmounted this difficulty. His method is as follows:

To 5 ccs. of filtered gastric contents previously boiled are added 5 ccs. of basic lead acetate solution. This is reboiled, allowed to stand for one minute, and cooled. 5 ccs. of ammonia and six drops of a saturated solution of ammonium sulphate are added. After mixing thoroughly, the whole is filtered, and 5 ccs. of the filtrate are evaporated almost to dryness. 5 ccs. of concentrated sulphuric acid, and one drop of saturated copper sulphate are added to the residue, and the whole is kept in a boiling water-bath for two minutes. After cooling, three drops of alcoholic thiophene are added, and the test-tube is reheated in the water-bath for two minutes. In the presence of lactic acid a cherry-red colour develops after a few seconds, and, if larger quantities are present, may even appear immediately on the addition of the thiophene without any further heating.

According to Maclean this method gives a positive reaction with a concentration of about .01%. The present writer has found that the minimum concentration of lactic acid in aqueous solutions which will give a positive result is .015%. When applied to gruel the concentration requires to be .02%. Two points have been found worthy of particular attention in carrying out the test. Charring is very liable to occur at a certain stage and can to a large extent be avoided by attending to these points. In the first place evaporation must be carried out very nearly, but not quite, to dryness. Secondly, the residue must be thoroughly cooled before the thiophene is added.

The delicacy of the test is in no way affected by the presence of blood, peptic extract, or hydrochloric acid. Unfortunately bile causes the same difficulty in interpreting the end-point as arose in connection with the two tests previously described. It has been found that where any quantity of bile is present in the gastric contents, a greenish-brown fluorescence develops when the residue, left after evaporation, is heated with the concentrated sulphuric acid. It is obvious that this will obscure any cherry-red colour which might appear, and that consequently, any results of an apparently positive nature can be accepted only with the utmost caution. The writer feels that, for the purposes of this investigation, and in order to reduce the possibility of error to a minimum, it will be advisable to neglect any results obtained in the presence of bile.

Apart from the two points mentioned, namely, the possibility of charring and the development of the fluorescence due to bile, the test appears to be in other respects an excellent one. In the writer's opinion the only drawback is the somewhat complicated nature of the technique employed. An attempt has therefore been made to simplify this, and the modified method is described by Paton,[31] Pembrey, and Cathcart in their "Text Book of Practical Physiology". It is carried out as follows.

5 ccs. of concentrated sulphuric acid, plus three drops of saturated copper sulphate, plus a drop of the suspected solution in alcohol, are placed in a boiling water-bath for five minutes. The tube is then cooled and the thiophene added as before.

This method appears to be of some value when applied to lactic acid in aqueous solutions. The writer has found, however, that it cannot be applied directly to gastric juice with accurate results on account of the excessive charring which generally occurs. This is apparently due to the fact that there has been no preliminary removal of protein from the gastric contents.

It is of interest to note that since the above observations were made by the author, similar views have been expressed by Dodds and Robertson.[28] They remarked on the difficulty which was caused by the presence of bile, and even went so far as to state that, in their opinion, the introduction of a quantitative method for the estimation of lactic acid was necessary, if reliable results were to be obtained. There seems little doubt, however, in my opinion, that, provided attention is paid to the points mentioned, very accurate results can be obtained except in the presence of excess of bile. Here certainly a difficulty arises, but it occurs in no less degree with the other tests.

It is not denied that the quantitative method, described by Dodds and Robertson, might possess certain minor advantages, but it is undoubtedly far too complex a process for general adoption.

In the subsequent work the writer has invariably used Maclean's modification of the thiophene test for the detection of lactic acid. In his opinion, it is, despite the difficulty due to bile, by far the most reliable of the three tests. The technique is not too complex for the average laboratory worker, and it is claimed that the results obtained are sufficiently accurate for all practical purposes.

It must be clearly understood that the test is in reality merely a qualitative one, but the writer claims, that a rough approximation of the relative amounts of lactic acid present can be obtained, by observing the rapidity with which the red colour appears after the addition of the thiophene, and also the intensity of the colour produced.

AN INVESTIGATION OF FIFTY FRACTIONAL

TEST MEALS.

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Modern workers, as a general rule, do not appear to pay very much attention to the presence or absence of lactic acid in the fractional test-meal. In the writer's opinion, the reasons for this are not far to seek. Owing to the unsatisfactory nature of the tests, it has apparently not been considered advisable to devote much time to them. Secondly, so much diversity of opinion exists regarding the significance of the presence of lactic acid in gastric contents, that, even if a reliable test was found, no interpretation of much value could be placed on the results.

Recently published books are singularly lacking in references to the presence of lactic acid in the stomach, and one sees many conflicting statements on the subject. Apart from reading that it is commonly found in cases of gastric carcinoma, associated either with an achlorhydria, or at most a very low concentration of free hydrochloric acid, one finds little mention made of it.

Since considerable uncertainty still exists, the following investigation has been carried out to discover whether or not lactic acid is of common occurrence in gastric contents, or whether its presence is pathognomonic of cancer. If lactic acid is frequently found, the opportunity will be taken of determining for how long it persists during the course of digestion.

The method employed in each case was as follows: At 8 pm.

on the evening prior to the examination, the patient had a light supper and a charcoal biscuit. Nothing more was taken until the test had been carried out. At 9 am. the following morning a Ryles' tube was swallowed, and any fasting juice present was withdrawn with a syringe and measured. With the tube in situ, the gruel was swallowed, and specimens withdrawn at fifteen-minute intervals up till the end of three hours. In some cases where there was rapid emptying of the stomach, nothing could be obtained after two hours. Any residue remaining was withdrawn as completely as possible at the last aspiration.

The test meal employed was the gruel meal commonly used in the Glasgow Western Infirmary. It is prepared by boiling two tablespoonfuls of fine oatmeal with a quart of water until the total bulk is one pint. The mixture is then strained through muslin.

Specimens, so procured, were examined as follows:

1. Estimation of free hydrochloric acid.
2. Estimation of total acidity.
3. Presence of bile, blood, and mucus.
4. Presence of lactic acid.
5. Time of disappearance of starch.

For the estimation of the free hydrochloric acid and the total acidity, Weiss' tube was not considered sufficiently accurate for the purposes of this investigation. These two estimates were therefore obtained, in the usual way, by titrating filtered gastric contents with $\frac{N}{10}$ caustic soda, using dimethylaminoazobenzol and phenolphthalein respectively as indicators.

Blood and bile were detected by the usual methods, while mucus was noted simply by its characteristic appearance. In every case the thiophene test was employed for the detection of lactic acid. The time of disappearance of starch from the stomach was determined by observing the point where a sample of the digest no longer gave a blue colour with iodine.

The results obtained by the above methods were plotted on gastric analysis charts, and grouped according to the type of curve produced. Usually the following classification is adopted:

(1) The normal or isosecretory type, in which there is a definite rise ending in a peak or short plateau, and followed by a more or less steep fall.

(2) The hyposecretory type, in which the acid concentration remains below normal during the whole course of the investigation.

(3) The hypersecretory type, in which the curve is distinctly higher than in the isosecretory variety.

(4) The hypersecretory type of marked degree, in which there is no tendency for the curve to descend, so that its highest point occurs when the stomach is empty. The well-known "climbing curve" is typical of this group.

Although this classification is undoubtedly the best for general clinical purposes, it was thought desirable, in the present series, to divide the hyposecretory group into two, thus separating those containing no free hydrochloric acid from those exhibiting merely a low concentration.

Thus, the following five groups were obtained:

(A) Those cases in which no free hydrochloric acid can be detected.

(B) Those cases with a very low concentration of free hydrochloric acid, and total acidity curves of lower concentration than normal.

(C) Isosecretory curves.

(D) Hypersecretory curves.

(E) Hypersecretory curves of marked degree.

This classification was adopted chiefly with a view to referring the presence of lactic acid to varying degrees of acidity. In the tables, presently to be described, these initial letters will be used to identify the different groups.

Findings in the Various Groups.

All the gastric contents, with two exceptions, were obtained from patients in the medical wards of the Glasgow Western Infirmary. From the clinical standpoint the cases investigated could be divided into two groups. To the first group belonged those who were suspected of suffering from some gastro-intestinal abnormality. These embraced such conditions as gastric ulcer, carcinoma of the stomach, hyperchlorhydria, pyloric stenosis, and duodenal ulcer. The second group consisted of those cases, used as controls, which did not show clinically any signs or symptoms of gastric disease. They were receiving hospital treatment for such conditions as cardiac disease, nephritis, rheumatism, arteriosclerosis, and organic disease of the nervous system.

The chief difficulty which the writer encountered during this investigation was the obtaining of sufficient quantities of digest to estimate the acidity and also to test for the presence of lactic acid. As a general rule this trouble did not arise till about two hours after the meal had been taken. Prior to that it was usually possible to carry out both examinations on each specimen. After two hours it was found most advantageous to use alternate specimens in order to estimate the acidity and examine for the presence of lactic acid. This was, of course, not necessary in every case. In every specimen where bile was detected the thiophene test was not carried out, as the results obtained under such conditions were not considered to be of sufficient value.

Reference to Tables I and II will show the results obtained. The most striking point is that lactic acid is of common occurrence in each group. Even in group C, the normal group, 50% show the presence of lactic acid. Not only is lactic acid present during the early stages of digestion, but it can also be detected even three hours after the taking of the gruel.

TABLE I.

Group	Number in Group	Number with Gastric Symptoms.	Number with no Gastric Symptoms.	Number Showing The Presence of Lactic Acid Throughout.
A	10	6	4	10
B	9	3	6	9
C	16	7	9	8
D	4	2	2	4
E	12	10	2	3
	51	28	[illegible]	

TABLE II.

	Group	Cases With No Symptoms. %	Lactic Acid Present %
	A	40	100
	B	66·6	100
	C	56·2	50
*	D	50))25	100))43·7
*	E	16·6)	25)

D. and E have been taken together since they are, in reality, merely subdivisions of the same Group.

It is most abundant in groups A and B, where hydrochloric acid is either absent, or of a very low concentration. As the acidity rises the percentage of cases showing lactic acid falls.

Apart altogether from the question of lactic acid, these tables are of interest. It appears remarkable that so many curves, considered abnormal in type, can be obtained from patients showing clinically no signs of gastric disease. It is equally important to note that, of the patients from whom isosecretory curves were obtained, no fewer than 43.8% were suspected, either from their history or as the result of clinical examination, of suffering from some gastro-intestinal condition.

It is thus obvious that lactic acid is commonly present even in the absence of any abnormal gastric condition. Its occurrence is not limited merely to those cases where there is an exceptionally low concentration of hydrochloric acid. Its presence is not incompatible with a hyperchlorhydria, nor is there any evidence that it commonly disappears half an hour after a meal is taken.

Having given this general survey of the entire series, the writer will now proceed to a more detailed account of each group.

- - - - - - - - - - - - - -

Group A. (Table III and Chart I).

Chart I is typical of the members of this group. Free hydrochloric acid is not found in any specimen, and the total acidity seldom reaches a higher concentration than .109. This is usually attained three-quarters to one hour after the taking of the meal.

Table III shows the following points. With two exceptions there is a considerable quantity of fasting juice in each case. In six cases there is an abundance of tough mucus throughout; in other two a smaller amount; and in the remaining two no trace of mucus visible to the naked eye. Blood is only found in traces on two occasions, and cannot therefore be taken as being of any clinical significance. In four cases bile is present in one or more specimens. No thiophene test was carried out on these specimens. Taking the absence of starch as an indication of the time of emptying of the stomach, it appears that in this group there is a tendency to rapid emptying.

Lactic acid is present in considerable amount in every case. There is absolutely no tendency for it to disappear half an hour after the commencement of digestion.

TABLE III.

	Fasting Juice.			Mucus	Blood	Bile	Starch Absent after.	Lactic Acid.
	ccs.	Free H.Cl.	T.A.					
1.	60	-	.03	+ +	-	+2¼,2½	2	Each Specimen + +
2.	5	-	.036	-	+ 2 hrs.	-	2	" " + +
3.	22	-	.036	+ +	+ 1½hrs.	-	1¾	" " + +
4.	20	-	.03	-	-	-	?	" " + +
5.	29	-	.09	+	-	+1¼,1½	1¾	Nothing obtained after 1 hr. Each Specimen + +
6.	23	-	.036	+ +	-	-	2	" " + +
7.	11	-	.073	+ +	-	-	2¼	" " + +
8.	3	-	.03	+ +	-	+1	?	Fasting Juice + + Insufficient for Test in others
9.	62	-	.073	+	-	+1,1½	2	Each Specimen + +
10.	12	-	.09	+ +	-	-	2¼	" " + +

Chart 1.

GASTRO-INTESTINAL ANALYSIS.

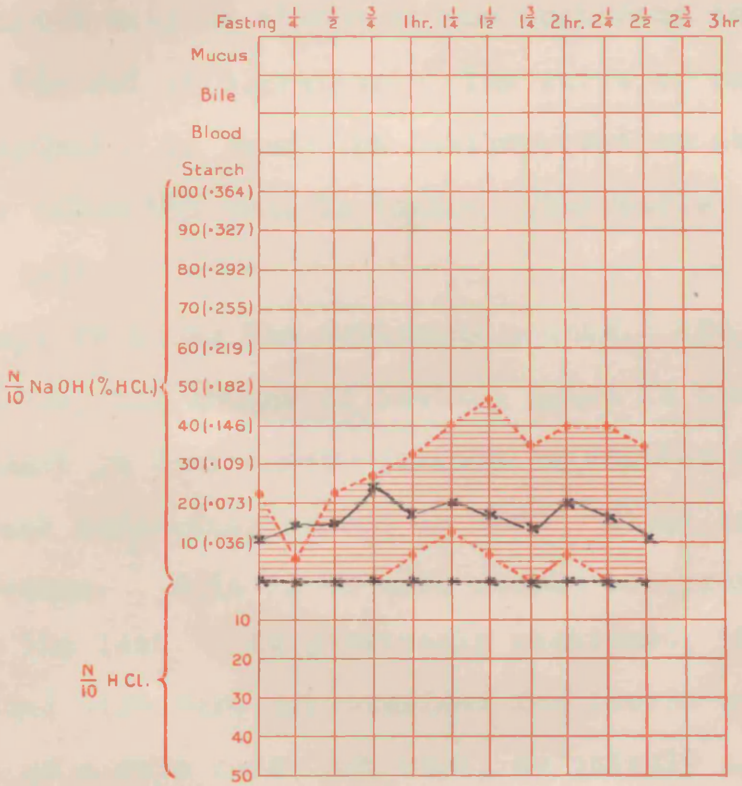
Name of Patient *Ward* *Bed*

1. FRACTIONAL TEST-MEAL. Date.

Fasting Juice.

Volume.

Cells.



One Hour Fraction

Free HCl.

Active HCl.

Total Chloride.

The shaded area represents the limits for free HCl. in 80% of normal people, and average rate of emptying (2-2½ hours).

———— represents free HCl.

– – – – represents total acidity.

Summary.

2. FÆCES.

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Group B. (Table IV and Chart II).

Chart II is typical of the members of this group. Free hydrochloric acid is absent at the beginning and generally towards the end of digestion. The curve of the total acidity rises gradually to reach its maximum, seldom above .146, about one hour after the meal is taken. Thereafter there is a gradual fall.

Table IV shows the following points. In this group, as in the last, the amount of fasting juice is considerable. Mucus is abundant in four cases, present in smaller quantities in three, and completely absent in two. Blood is not present in any specimen. Bile is of more common occurrence in this group than in the last. As previously mentioned, those specimens containing bile were not examined for lactic acid. The stomach as a rule does not empty so quickly in this group as in group A.

Lactic acid is again found in each case, and in six cases persists throughout. In one (9) it is not detected after 1¼ hours. In other two (6 and 7) it is absent during the first half hour and hour of digestion respectively. With one exception (9) there is no evidence of lactic acid disappearing during the course of digestion.

Chart II.

GASTRO-INTESTINAL ANALYSIS.

Name of Patient *Ward* *Bed*

1. FRACTIONAL TEST-MEAL. Date.

Fasting Juice.

Volume.

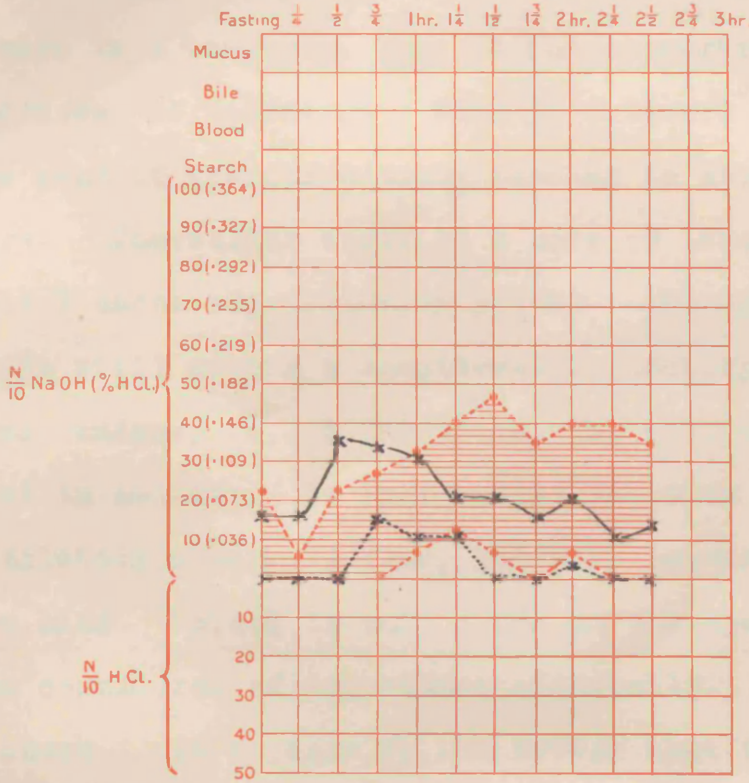
Cells.

One Hour Fraction

Free HCl.

Active HCl.

Total Chloride.



The shaded area represents the limits for free HCl. in 80% of normal people, and average rate of emptying (2-2½ hours).

——————— represents free HCl.

- - - - - - - represents total acidity.

Summary.

2. FÆCES.

Group C. (Table V and Chart III).

This group consists of normal curves. Chart III, typical of the members of this group, shows that after the meal is taken, there is a temporary fall in the concentration of acid, due, of course, to dilution. This is followed by a gradual rise, the peak of the curve being reached in about one and a half hours. Thereafter there is a more or less gradual fall.

Table V shows the following points. Though in many cases there still exists a considerable quantity of fasting juice, the tendency is, on the whole, for this to be somewhat diminished in amount. In three cases mucus is abundant, but it is completely absent in four, and only present to a lesser degree in nine. Blood is only found in one specimen, and cannot be considered of importance clinically. Bile occurs in five cases. It appears to the writer that this cannot always be due to the Rhyle's tube slipping into the duodenum. There would appear to be some regurgitation of duodenal contents. The stomach empties at a normal rate.

In five cases no lactic acid is present. It is copious in only two. In four cases it is present during the early stages of digestion, but cannot be detected later. In only two of these, however, does it disappear before one hour. In one case it does not appear till after half an hour, but it then persists throughout the further course of digestion.

TABLE V.

	Fasting Juice.			Mucus	Blood	Bile	Starch Absent after.	Lactic Acid.
	Ccs.	Free H.Cl	T.A.					
1.	41	.073	.146	+	-	-	$2\frac{1}{2}$	Each Specimen + +
2.	29	.17	.219	-	-	+$1\frac{1}{4}$, $1\frac{1}{2}$	3	" " +
3,	5	.02	.07	+ +	+$1\frac{1}{4}$	-	$1\frac{3}{4}$	" " + till 1hr.
4.	22	.03	.073	+ +	-	+2, $2\frac{1}{2}$	2	Each Specimen -
5.	5	-	.05	+	-	-	$2\frac{1}{4}$	" " -
6.	21	-	.06	+	-	-	$1\frac{3}{4}$	Each Specimen + till $\frac{1}{2}$hr.
7.	50	.03	.09	+	-	+2	$2\frac{1}{2}$	" " -
8.	19	-	.036	-	-	-	2	" " -
9.	-	-	.075	+	-	-	$1\frac{3}{4}$	Each Specimen + +
10.	4	.03	.109	+	-	-	2	" " + after $\frac{1}{2}$hr.
11.	20	.109	.18	+	-	-	$2\frac{1}{4}$	" " + till $1\frac{3}{4}$hr.
12.	9	.03	.06	-	-	+$2\frac{1}{4}$, $2\frac{1}{2}$	2	" " + " 2 "
13.	10	.07	.14	-	-	-	$2\frac{1}{2}$	Each Specimen + +
14.	2	.09	.182	+ +	-	+$1\frac{3}{4}$	$2\frac{1}{4}$	+ at $\frac{3}{4}$hr.
15.	51	.073	.12	+	-	-	$2\frac{1}{2}$	Each Specimen -
16.	25	.073	.109	+	-	-	2	" " +

Chart III.

GASTRO-INTESTINAL ANALYSIS.

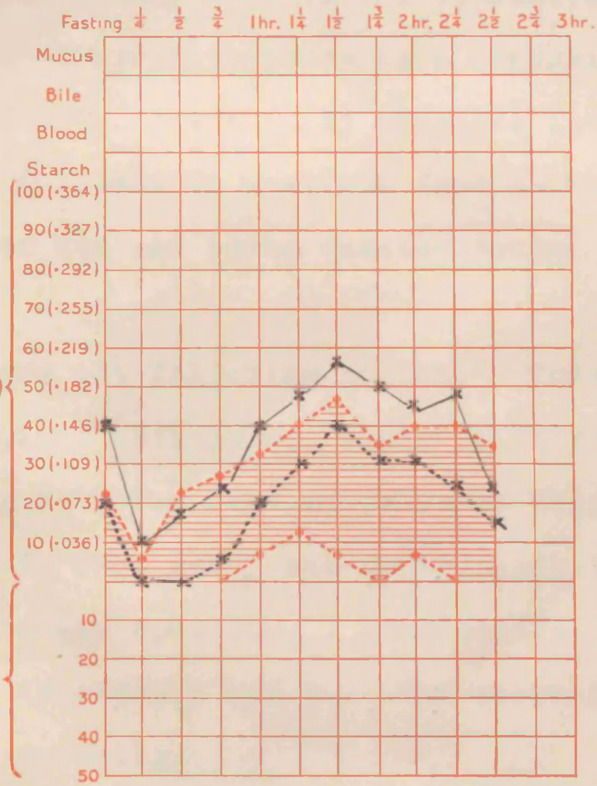
Name of Patient *Ward* *Bed*

I. FRACTIONAL TEST-MEAL. Date.

Fasting Juice.

Volume.

Cells.



One Hour Fraction

Free HCl.

Active HCl.

Total Chloride.

The shaded area represents the limits for free HCl. in 80% of normal people, and average rate of emptying (2-2½ hours).

——————— represents free HCl.

- - - - - - represents total acidity.

Summary.

2. FÆCES.

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Group D. (Table VI and Chart IV).

Chart IV, which is characteristic of this group, again shows a slight preliminary fall in the concentration of acid, due to dilution. Thereafter there is a gradual rise to a high degree of acidity, not usually attained for about two hours. This is followed by a slight fall in the curve, but even at the end of two and three quarter hours, the acidity is abnormally high.

Table VI shows the following points. There are only four cases which fall into this group, since it is really a sub-division of group E. The fasting juice is fairly copious. Mucus is present in each case, and is abundant in two. Blood is not detected in any specimen. Bile occurs in cases 3 and 4, but is absent in cases 1 and 2. The stomach empties rather more slowly than normally.

Lactic acid is present throughout digestion in three cases, and in one of these occurs in considerable amount. In case 2 lactic acid can only be detected in the fasting juice.

TABLE VI.

	Fasting Juice.			Mucus	Blood	Bile	Starch Absent after.	Lactic Acid.
	Ccs.	Free H.Cl.	T.A.					
1	21	-	.05	+ +	-	-	$2\frac{1}{4}$	Each Specimen +
2.	79	.036	.073	+	-	-	$2\frac{1}{2}$	Fasting Juice +
3.	12	.073	.146	+	-	+2, $2\frac{1}{4}$	$2\frac{1}{4}$	Each Specimen + +
4.	20	. -	.073	+ +	-	+2, $2\frac{1}{4}$	2	" " +

Chart IV.

GASTRO-INTESTINAL ANALYSIS.

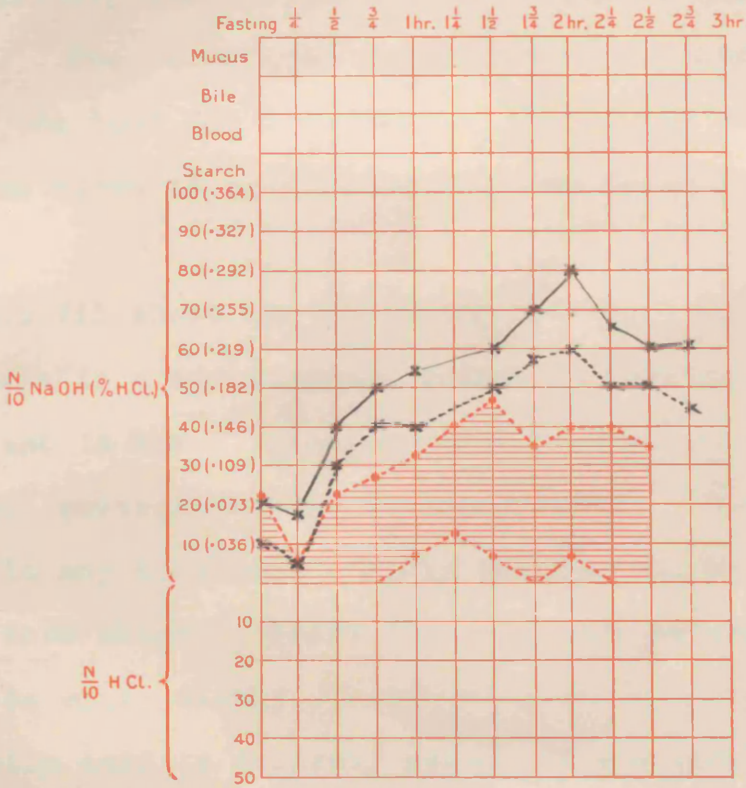
Name of Patient *Ward* *Bed*

1. FRACTIONAL TEST-MEAL. Date.

Fasting Juice.

Volume.

Cells.



The shaded area represents the limits for free HCl. in 80% of normal people, and average rate of emptying (2-2½ hours).

——————— represents free HCl.

- - - - - - - represents total acidity.

One Hour Fraction

Free HCl.

Active HCl.

Total Chloride.

Summary.

2. FÆCES.

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Group E. (Table VII and Chart V).

Chart V, which is typical of this group, again shows the preliminary fall in the concentration of acid due to dilution. The curve then rises rapidly to reach its maximum in about one hour and a quarter. Even after two and a quarter hours, the curve is showing no tendency to fall below this maximum.

Table VII shows the following points. With three exceptions there is a considerable amount of fasting juice. Mucus is abundant in three cases, present in smaller amounts in six cases, and entirely absent in three cases. Blood is not present in any specimen. Fifty per cent of this group contain bile at some stage. There is a distinct tendency for the stomach to empty slowly.

Lactic acid is entirely absent in six ~~hours~~ cases. It is present in small quantities throughout the course of digestion in three cases. In one it disappears at the end of two hours, and in another at the end of one and three quarter hours. In one case (12) it could only be detected in the fasting juice, and in the specimen withdrawn after a quarter of an hour. Thus even in these marked hypersecretory cases, lactic acid may persist throughout the course of digestion.

TABLE VII.

	Fasting Juice			Mucus	Blood	Bile	Starch Absent after.	Lactic Acid.
	Ccs	Free H.Cl.	T.A.					
1.	5	.146	.219	+ +	-	+2,2¼	2¼	Each Specimen -
2.	95	.182	.292	-	-	-	2½	" " -
3.	4	.109	.146	-	-	-	2	" " -
4.	21	.28	.3	+	-	+1,1½	2¼	" " + till 2hrs.
5.	32	.036	.109	+	-	-	1¾	" " + " 1¾ "
6.	11	.04	.109	+ +	-	-	2¾	" " -
7.	20	.219	.327	+	-	+ ¾	2½	" " +
8.	19	.255	.292	+	-	+1	1¾	" " -
9.	48	.182	.219	-	-	-	2¼	" " -
10.	24	.146	.219	+	-	-	2½	" " +
11.	26	.146	.182	+ +	-	+2,2¼	2	" " +
12.	2	.036	.109	+	-	+1¾	2¾	+ at 0 and ¼ hr.

Chart V.

GASTRO-INTESTINAL ANALYSIS.

Name of Patient *Ward* *Bed*

1. FRACTIONAL TEST-MEAL. Date.

Fasting Juice.

Volume.

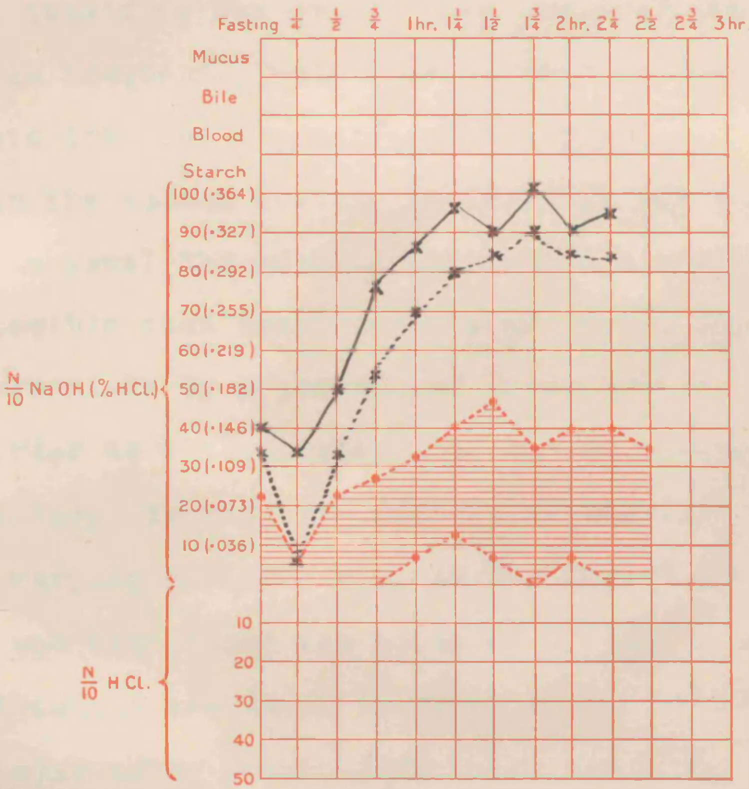
Cells.

One Hour Fraction

Free HCl.

Active HCl.

Total Chloride.



The shaded area represents the limits for free HCl. in 80% of normal people, and average rate of emptying (2-2½ hours).

———— represents free HCl.

——·—— represents total acidity.

Summary.

2. FÆCES.

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From the foregoing results it is obvious that lactic acid is of common occurrence in gastric contents. The possibility suggested itself to the writer that the positive results, obtained so frequently, might arise from the introduction of lactic acid into the stomach with the gruel.

It is the common custom, in hospital and elsewhere, to prepare the gruel the evening prior to the examination, and it seemed possible that small amounts of lactic acid might form in this overnight by a process of fermentation.

In order to investigate this, and so prevent the occurrence of any fallacy, freshly prepared gruel was kept at room temperature for varying periods, and, at the end of the stated times, filtered and tested for the presence of lactic acid. The results obtained are shown in Table VIII.

Not even after twenty-four hours could any lactic acid be detected. This investigation was repeated on several occasions with similar results each time.

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TABLE VIII.

Period of Incubation at Room Temp.	Lactic Acid.
6 Hours	-
9 "	-
12 "	-
15 "	-
18 "	-
20 "	-
24 "	-

THE FATE OF LACTIC ACID DURING THE COURSE OF DIGESTION.

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From a study of the results obtained by the detailed examination of the writer's series of fractional test meals, there is nothing to support the view that lactic acid, while it may occur during the first half hour of digestion, cannot be detected in the later stages also. If this theory, attributed to Schafer[22] and Noël Paton,[32] were true, then the lactic acid must either be absorbed or else destroyed as digestion advances. This point seemed to the writer worthy of further investigation.

Seven test-tubes were put up with the contents indicated, and incubated at body temperature for the times stated. The same amount of lactic acid was added in each case. At the end of the stated times the contents of the tubes were filtered. The thiophene test was applied to the filtrate.

The results are shown in Table IX. In no case where lactic acid was present at the commencement of the incubation did the writer fail to detect it at the end of two and a half hours.

It thus appears that, in the few cases in this series, where lactic acid disappeared towards the end of digestion, this was not due to destruction of the acid, but either to absorption or dilution.

TABLE IX.

Contents of Tube.	Hours of Incubation.					
	0	½	1	1½	2	2½
Water	-	-	-	-	-	-
Water + Lactic Acid	+	+	+	+	+	+
.2% H.Cl.	-	-	-	-	-	-
.2% H. Cl. + Lactic Acid	+	+	+	+	+	+
Water + Peptic Extract	-	-	-	-	-	-
Peptic Extract + Lactic Acid	+	+	+	+	+	+
.2% H.Cl. + Peptic Extract + Lactic Acid.	+	+	+	+	+	+

From the foregoing results it appears justifiable to draw the following conclusions.

(I) Lactic acid is of very common occurrence in the fractional test meal. Its presence is not by any means confined to those cases where some pathological condition of the stomach exists.

(II) Lactic acid does not disappear from the stomach half an hour after the meal is taken, as has been supposed by Schafer[22] and Noël Paton.[32] In a great many of the cases in this series, the writer has been able to demonstrate the presence of lactic acid after digestion has proceeded for two and three-quarter hours. It was, however, found that the intensity of the thiophene reaction often diminished after two hours. This is, of course, very different from a disappearance of lactic acid.

(III) Certain conditions in the stomach were correlated with the production of lactic acid, the chief of these being the quantity of fasting juice, its degree of acidity, and the presence or absence of mucus. Reference to the tables will show that the greatest amounts of lactic acid were detected where there was a considerable quantity of fasting juice containing no hydrochloric acid, or only a very low concentration, and where mucus was abundant. The tables also reveal the fact that a high degree of acidity is not incompatible with the presence of lactic acid.

MODE OF PRODUCTION OF

LACTIC ACID.

-oOo-

opinion concerning the active agent in its formation, it was felt that these further investigations were necessary.

In this investigation a total of fifty-one test meals was examined. In thirty-five of these lactic acid was present in the fasting juice, generally in considerable amount. Twenty-two specimens of fasting juice contained no free hydrochloric acid, and of these, all but three contained lactic acid. Mucus was also found in every specimen where lactic acid existed.

It might, therefore, be thought that, where lactic acid was found in the test meal during the entire course of digestion in the stomach, one was detecting that lactic acid which was originally present in the fasting juice, and not newly formed lactic acid. If this were so, however, it would be seen by a diminution, due to dilution, in the intensity of the thiophene reaction in each successive specimen. In the writer's experience the reverse rather is true. Generally the intensity increases for the first two hours of digestion. After that point is reached, a slight diminution may occur.

Regarding the method of production of lactic acid in the stomach, the more generally accepted theory is that of fermentation. If this is true the first question which arises is, whether lactic acid can be produced by the action of hydrochloric acid, peptic extract, or a combination of the two, on carbohydrate, or whether some other agent, in addition to these, is necessary.

In order to investigate this, gruel alone, and gruel in the presence of peptic extract and hydrochloric acid, was kept at body temperature for twenty-four hours. At intervals, samples were removed from each tube, and filtered. The filtrates were examined for the presence of lactic acid. The control tubes were employed, so that, in the event of a doubtful reaction being obtained, reference could at once be made to them. Each control tube contained a trace of lactic acid.

The results are shown in table X. In none of the four tubes was any lactic acid detected after incubation at body temperature for twenty-four hours. This series of observations was repeated on several occasions always with the same results.

It is thus obvious that, assuming the fermentation theory to be true, organisms must occur in the stomach. The fasting juice, therefore, seemed to the writer to be the most likely source of these organisms. If this supposition was correct, then it seemed quite justifiable to assume that lactic acid would be produced by incubating gruel along with fasting juice at body temperature. In an attempt to prove this the following experiments were carried out.

Five tubes were prepared containing respectively gruel, gruel + peptic extract + .2% H.Cl., gruel + fasting juice, gruel + peptic extract + fasting juice, and gruel + peptic

TABLE X.

	Contents of Tube.	Hours of Incubation.					
		½	1	2	4	6	24
1.	Gruel	-	-	-	-	-	-
2.	Gruel + .2% H.Cl.	-	-	-	-	-	-
3.	Gruel + Peptic Extract.	-	-	-	-	-	-
4.	Gruel + Peptic Extract + .2% H.Cl.	-	-	-	-	-	-
	Control Tubes.						
1.	Gruel + Lactic Acid	+	+	+	+	+	+
2.	Gruel + Peptic Extract + .2% H.Cl. + Lactic Acid	+	+	+	+	+	+

extract + fasting juice + .2% H.Cl. The first two tubes were employed to act as controls on the negative side, and a sixth tube, consisting of gruel + a trace of lactic acid, as a control on the positive side. All six tubes were then incubated at body temperature for four hours. At intervals samples were removed and filtered. The filtrates were examined for the presence of lactic acid.

The results are shown in Table XI. In each of the three specimens containing fasting juice, a trace of lactic acid was found after one hour's incubation. The longer the incubation, the greater is the amount of lactic acid formed, as evidenced by the intensity of the thiophene reaction obtained. The results just described were obtained by using a sample of fasting juice which contained no lactic acid. Such a specimen is difficult to obtain. In fact, when the above experiments were repeated a specimen had to be used which, to begin with contained a trace of lactic acid. As, however, the thiophene reaction became more intense as digestion advanced, it is obvious that production of lactic acid must have taken place.

That carbohydrate is necessary for the production of lactic acid is at once shown by the fact that lactic acid-free fasting juice, incubated at body temperature for six hours, does not produce any lactic acid. It therefore seems justifiable to assume that the active agent in the production of lactic acid exists in the fasting juice, and that the presence

TABLE XI.

	Contents of Tube.	Hours of Incubation.			
		1	2	3	4.
1.	Gruel	-	-	-	-
2.	Gruel + Peptic Extract + .2% H.Cl.	-	-	-	-
3.	Gruel + Fasting Juice	+	+	+ +	+ + +
4.	Gruel + Peptic Extract + Fasting Juice	+	+	+ +	+ + +
5.	Gruel + Peptic Extract + Fasting Juice + .2% H.Cl.	+	+	+ +	+ + +
6.	Gruel + Lactic Acid	+	+	+	+

+ = A trace of Lactic Acid
+ += Small amount of Lactic Acid
+ + += Large amount of Lactic Acid.

of carbohydrate is necessary for it to manifest itself. It is also evident that cancer cells cannot in themselves cause the production of lactic acid, as was supposed by Craven Moore and Roberts. Possibly the presence of the cells may produce specially favourable conditions for the activity of the agent contained in fasting juice.

It appeared to the writer that, if bacterial organisms were the agents concerned with the process, then boiling would sterilise the fasting juice and so prevent the production of lactic acid. In order to investigate this the following experiments were carried out.

A sufficient quantity of lactic acid-free fasting juice was obtained with some difficulty, boiled for two minutes, and then cooled. Six tubes were then prepared, containing respectively gruel, gruel + peptic extract + .2% H.Cl., gruel + fasting juice, gruel + peptic extract + fasting juice, gruel + peptic extract + .2% H.Cl. + fasting juice, and gruel + a trace of lactic acid. The first two tubes were used as controls on the negative side, and the last as a control on the positive side. All the tubes were incubated for four hours at body temperature. At intervals of an hour samples were removed and filtered. The filtrates were examined for the presence of lactic acid.

The results obtained are shown in Table XII. In no case, except the one where lactic acid was added as a control, was a

TABLE XII.

	Contents of Tube.	Hours of Incubation.			
		1	2	3	4.
1.	Gruel	-	-	-	-
2.	Gruel + Peptic Extract + .2% H.Cl.	-	-	-	-
3.	Gruel + Fasting Juice	-	-	-	-
4.	Gruel + Peptic Extract + Fasting Juice.	-	-	-	-
5.	Gruel + Peptic Extract + .2% H.Cl. + Fasting Juice.	-	-	-	-
6.	Gruel + Lactic Acid.	+	+	+	+

+ = A trace of Lactic Acid.

positive result obtained. This series of experiments was repeated, but the fasting juice used on the second occasion contained a trace of lactic acid. This persisted throughout the course of incubation, but there was absolutely no evidence of any production of lactic acid.

From the above results the conclusion is arrived at that the active agent concerned in the elaboration of lactic acid is contained in fasting juice, and is of such a nature that it is capable of being destroyed by boiling.

It was next considered advisable to determine whether the reaction of the fasting juice had any effect on its powers of producing lactic acid when added to carbohydrate. It has previously been stated that some observers hold that lactic acid is always associated with an achlorhydria, or at most a very low concentration of hydrochloric acid. The present writer's results do not agree with this. While the greatest amounts of lactic acid are found in those cases where the concentration of acid is low, a high concentration is by no means incompatible with the presence of lactic acid.

In order further to investigate this, the following experiments were carried out. Fasting juice was obtained in the usual way. Unfortunately it was found impossible to obtain a sufficient quantity which did not contain any lactic acid. The specimens used, however, showed only a trace. The fasting juice was then mixed with gruel, and a few drops of peptic extract were added. The mixture was divided into several portions. To each was added a known quantity of hydrochloric acid. In order to be absolutely certain of the degree of acidity so obtained, a titration with $\frac{N}{10}$ sodium hydrate was carried out. The tubes were then placed in the incubator, and kept at body temperature for four hours. At intervals of an hour samples were removed and filtered. The filtrates were examined for the presence of lactic acid.

The results are shown in Table XIII. In tube 6 there is no evidence of any production of lactic acid. In all the others there is. When, however, a concentration of .219 is reached, the amount produced begins to diminish. This diminution is greater as the concentration increases. It has to be remembered that, in the stomach, it is very rare indeed to find a fasting juice of such a high acidity as .219. In any case, even where this does occur, there will always be a period of half an hour or so immediately following the taking of the meal, when the acid will not have penetrated to the heart of the meal. During that space of time the acidity will be favourable for the organisms to act.

A final test was carried out in the same manner as the above, but the mixture was made neutral or very slightly alkaline. It was found that the results were in every way similar to those obtained where there was a low concentration of acid.

<u>TABLE XIII.</u>

	Contents of Tube.	Free H.Cl.	Hours of Incubation.			
			1	2	3	4.
1.	Gruel +	.036	+	+	+ +	+ + +
2.	Peptic Extract +	.073	+	+	+ +	+ + +
3.	Fasting Juice +	.146	+	+	+ +	+ + +
4.	H. Cl.	.219	+	+	+ +	+ +
5.		.255	+	+	+	+ +
6.		.327.	+	+	+	+

\+ = Trace of Lactic Acid
\+ += Small amount of Lactic Acid.
\+ ++= Large amount of Lactic Acid.

It has, therefore, been shown that, in vitro, lactic acid can be produced by the addition of fasting juice to gruel. It is formed by a process of fermentation of carbohydrate. The organisms are destroyed by boiling, and are inhibited in action by concentrations of hydrochloric acid exceeding .219. Their activity reaches a maximum in either a neutral, a faintly acid, or a faintly alkaline medium.

DISCUSSION OF RESULTS.

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It seems best to discuss the results obtained in this investigation by attempting to answer the following questions in the light of the findings previously described.

1. What is the most suitable test at our disposal for the detection of lactic acid in the stomach?

2. Is lactic acid of common occurrence in the stomach, or should its presence be regarded as a rarity?

3. Does lactic acid merely occur during the first half hour of digestion, or does it persist throughout?

4. What is the mode of formation of lactic acid in the stomach?

5. Are there any factors which influence the mode of production of lactic acid?

6. What is the clinical significance of lactic acid in the gastric contents?

It is now proposed to answer the above questions as briefly as possible.

1.

What is the most suitable test at our disposal for the detection of lactic acid in the stomach?

Three tests have been described and investigated by the writer. From the results obtained it is claimed that only Maclean's modification of the thiophene test can be employed, if reliable results are to be obtained. It is sufficiently accurate for all practical purposes, and, when applied to gruel, is capable of detecting lactic acid in a concentration of .02 per cent.

In the writer's experience there are two possibilities of error in applying the test. The first is due to charring and can be completely avoided by careful attention to the technique described. The second, unfortunately, one cannot at present combat. It is brought about by the presence of bile in the gastric contents, and, in order that, so far as the test was concerned, there should be no possibility of error in this investigation, those specimens containing bile were rejected.

The test is purely a qualitative one, but it is claimed that an idea of the relative amount of lactic acid present can be ascertained by noting the rapidity with which the end-point appears, and also the intensity of the colour produced. In the writer's opinion the use of a quantitative test for the detection of lactic acid, as suggested by Dodds and Robertson,(28) is unnecessary.

2.

Is lactic acid of common occurrence in the stomach, or should its presence be regarded as a rarity?

Four answers have already been given to this question by previous investigators. The first came from Bernard and Barreswil,[6] who considered lactic acid the chief acid of gastric juice. This was soon discredited. It was then generally believed that traces of lactic acid commonly existed in gastric contents. This theory was due to the work of Bidder and Schmidt.[11] In 1894 Boas,[19] as the result of his investigations, postulated that lactic acid would only be detected if some digestive disturbance existed. The last, and most recent answer to the question came from Craven Moore and Roberts,[26] who claimed that lactic acid was only found in cases of carcinoma of the stomach.

From the results, herein described, the present writer considers that lactic is by no means a rarity in the stomach. In his opinion it can be found in practically every test meal, certainly at some point in the course of digestion, and, in a great many, throughout.

3.

Does lactic acid merely occur during the first half hour of digestion, or does it persist throughout?

The necessity for answering this question is due to the statements of Schafer (22) and Noël Paton, (32) who both considered that lactic acid was commonly present during the first half hour of digestion, and then disappeared.

The present writer offers two conclusive proofs against this. In the first place, as the results of the in vitro experiments described, there is nothing to show that lactic acid is destroyed by the gastric digestive agents even after two and a half hours.

Secondly, from the results obtained in the routine examination of the fractional test meals, the reverse is seen to be the case. The amount of lactic acid present in the stomach generally increases for two hours and after that may show a slight diminution probably due to dilution.

If lactic acid did disappear at the end of half an hour, it might be due to one of two things; either destruction, or absorption. It has been shown that the former is not the case. It is claimed that the results obtained in the test meals discount the latter possibility. Since lactic acid arises from sources other than the stomach, the statement of Drechsel, (16) that there is an increase in the amount of lactic acid in the blood after a meal, cannot be accepted in support of the absorption theory.

4.

What is the mode of formation of lactic acid in the stomach?

There are two theories to explain this. The first is that it arises by a process of fermentation from ingested carbohydrate. The second, attributed to Craven Moore and Roberts,(26) is that it arises by the specific action of cancer cells on the glucose of the tissue fluids.

Since it has been conclusively shown that lactic acid is of common occurrence, and not present merely in cases of gastric carcinoma, it seems, justifiable to assume that the latter method is not the chief one, although it may play a part in those conditions where cancer exists. In the writer's opinion it is more likely that the presence of a neoplasm produces conditions specially suitable for bacterial action taking place.

There are, however, ample grounds for concluding that fermentation is the mode of production of lactic acid. The organisms must either be present in the stomach or be introduced with the food. Since gruel itself, in the presence of hydrochloric acid and peptic extract will not elaborate any lactic acid, it seems that the organisms do not exist in the food. On the other hand, if gruel is incubated at body temperature along with a small amount of fasting juice, then, in every case, it can be demonstrated that lactic acid is produced.

It therefore appears justifiable to assume that the active agent is present in the gastric juice. That carbohydrate is necessary before fermentation can occur, is shown by the fact that fasting juice, incubated at body temperature in the absence of any carbohydrate, produces no lactic acid.

It is thought that the process is due not to any particular organism, but to a wide variety of lactic acid-forming organisms acting under suitable conditions.

It seems likely, as mentioned by Halliburton,[18] that lactic acid may not be the final product of fermentation, but that, under suitable conditions, the process may continue the formation of butyric acid, as indicated by the equations:

(1) $C_{12}H_{22}O_{11} + H_2O = 4C_3H_6O_3$
(Lactose) = (Lactic Acid)

(2) $2C_3H_6O_3 = C_4H_8O_2 + 2CO_2 + 2H_2$
(Butyric Acid)

5.

Are there any factors which influence the mode of production of lactic acid?

It has been found, as the result of the examination of the series of test meals, that there are three conditions of the fasting juice conducive to the production of lactic acid. It was invariably found that the greatest amounts of lactic acid were detected in those cases where the fasting juice was large in amount, had a low concentration of acid, and contained mucus. On the other hand it must be noted that a high concentration of acid is by no means incompatible with the production of lactic acid.

As the result of experiments carried out in vitro, it was found that the most propitious medium for fermentation taking place was one where the reaction was neutral, slightly acid, or slightly alkaline. It was, however, necessary to raise the acidity above .255 before there was any appreciable inhibition in the activity of the organisms.

It was also found, as the result of these experiments, that boiling the fasting juice for two minutes destroyed the causal organisms, and so prevented the formation of lactic acid.

6.

What is the clinical significance of lactic acid in the gastric contents?

From the investigations, just concluded, it is, in the writer's opinion, unjustifiable to conclude that the presence of lactic acid is a sign of disease. In his experience it occurs very commonly where there is nothing to suggest the presence of any pathological condition of the stomach. Still less can it be said to be a sign of one specific disease, gastric carcinoma.

On the other hand, it may be stated with some confidence that the amount of lactic acid will be increased where conditions exist which favour fermentation. The chief of these would appear to be gastric stasis, hypochlorhydria, and pyloric stenosis.

It is, however, possible to detect large amounts of lactic acids in cases showing a normal type of curve, and even in those which give a very marked hypersecretory curve. For these reasons it seems that the finding of lactic acid in gastric contents will never prove very helpful as an aid to diagnosis.

Conclusions.

1. Lactic acid is of common occurrence in the stomach even in apparently healthy individuals.

2. Its presence is not limited to the first half hour of digestion.

3. It generally increases in amount for two hours after a meal is taken.

4. It is produced by a process of carbohydrate fermentation.

5. The best conditions for this process taking place are a low concentration of acid, a large amount of fasting juice, and the presence of mucus.

6. The presence of lactic acid in the stomach is not of any special clinical significance.

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