"Peptic Activity of Gastric Contents and Urine in disorders of the Stomach with special reference to Carcinoma Ventriculi".

A Thesis for M.D. (Glasg.) degree

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In recent years ever since the epoch making discovery by Van der Velde that Hydrochloric Acid is diminished in Cancerous stomachs the estimation of HCl. - free and bound - has assumed a foremost place among the Chemical estimations on which a diagnosis of Gastric trouble could be built up.

The chief reason for this has been the fact that HCl. could itself be demonstrated and estimated as a separate and distinct chemical body.

Pepsin, on the other hand, although playing a rôle in gastric digestion equal to that of HCl. has never assumed a place of any importance in gastric diagnosis beyond practically that of academic interest. This is startling when we must be convinced that it undergoes changes in pathological conditions, but it is a ferment, a body in other words whose structure we do not know and which has never been isolated - it cannot be estimated as a separate entity on this account and its estimation can be achieved only from the results of its action. In other words we know it only from its work. On this account its estimations have had to take a second place very far behind those of HCl.

However one is convinced that Pepsin must be influenced, in quantity formed &c in all manner of Gastric derangements and the object of this investigation, carried out in a Cancer Research Laboratory, was primarily to determine the value of some of the more recent methods of Pepsin estimations in stomach juice and urine, and the value of such estimations in assisting a differential diagnosis of cases of Achylia Gastrica of benign and malignant origin.

The subject matter of the following paper may therefore be divide roughly into two parts - the first dealing with estimations of pepsin in the Gastric contents and the second dealing with pepsin - or more correctly put - Pepsinogen in the urine, and the questions which surround the second are from the nature of things different

from those around the first.

When one reviews the numbers of methods of estimating Pepsin in the Gastric juice one is struck by the large number of these, which have been evolved and found in more or less wide use - this has been especially the case in Germany where one recent writer on the subject apologised for having given only eleven methods.

It is not therefore my intention to attempt to criticise methods or results which are old but to confine myself here to a review of a few of the more recent methods and the results which have been achieved by means of them by recent investigators. As is always the case where many methods exist for some particular purpose - each claiming an outstanding excellence over its fellows it may be safely assumed that no perfect method for estimating pepsin yet exists, and is not to be expected until the body itself can be isolated and estimated.

The most widely known and generally accepted method for estimating pepsin in gastric juice is that of Mett, which has found its way into most books of Physiology and of clinical methods but hardly into the daily use of the clinician in this country.

This method consists simply stated in the use of egg albumen coagulated in glass tubes of capillary calibre - These tubes are placed in the ferment solution to be tested and after a time the amount of egg albumen digested out is read off. The length of albumen dissolved is proportional to the square root of the content of the fluid in pepsin - according to the Schutz - Borissow law.

The method was essentially simple and although having many modifications - it has remained the same. The most striking and successful modification was that of Mirenstein and Schiff [1] who worked with larger dilutions and found the method very satisfactory.

The chief objections to the use of this method - which has been largely tried in this Laboratory - are :-

(1) the trouble of preparing the albumen tubes.

(2) the long time required for the process and

(3) the lack of sharpness in the reading of results.

In the matter of preparation of the capillary tubes it was found that unless the glass tube was cut evenly and transversely the surface

of albumen presented to the peptic solution was a very variable one indeed and of course the results are only comparable when this surface is the same in each case. Then again a very active agent against a ferment's action is the accumulation of that action and in a capillary tube this is at its maximum, diffusion alone being responsible for their dissemination.

Of course it must be understood that in practically all laboratory tests with ferments this accumulation of the results of the ferments' action is the greatest handicap and unfortunately it cannot be reduced to the terms of a formula and allowed for.

The second method tried was that of Jacoby [2] and Solnes where the substratum employed was Ricin. This however was not at all satisfactory, the solution of ricin was difficult to make and still more difficult to keep and the results varied very widely according to whether or not the substratum Ricin solution was freshly prepared. Differences amounting in some cases to almost 100% were got when the ferment solution - in this case urine or gastric contents - was tested with two solutions of Ricin one freshly prepared and the other a fortnight old in the latter case the results were higher than the former. In this test also sharpness is lacking in reading results - pepsin clears up the solution when complete digestion occurs but the line of demarcation is not sharp.

The next method tried was the Casein method of Gross. [3] The Casein solution was however difficult to keep and possessed no advantage over the method of Fuld and Levison. As a matter of fact the end reaction is never so clear with the Gross method as with the latter.

The method found to have the most to recommend it and which therefore has been used in the following tests was that of Fuld [4]. In the case of the gastric contents a method following Fuld and Levison [5] has been used.

The method of procedure was as follows :- An Ewald test breakfast was given to the patient to be examined - in some cases where it was deemed necessary the stomach was washed out the previous evening. After 45 minutes the gastric contents were drawn off by means of an ordinary stomach tube and suction bottle.

The amount recovered was noted and then filtered through a double filter paper very carefully by means of an air pump. The acidities free and total were then determined. A dilution of 1 in 10 or in some cases 1 in 20 was then made of the gastric juice and in cases of hyperacidity where even in the diluted solution a positive reaction was got with Congs red paper, no HCl. was added. In most of the cases examined however there was subacidity or anacidity and 5 ccm. of $\frac{N}{1}$ HCl. was added to 45 ccm of the diluted gastric juice - the solution was therefore in most cases :-

Gastric Content 5 ccm or 2'5 ccm.

Ag. dest. 40 ccm or 42'5 ccm.

N/1 HCl. 5 ccm 5ccm.

This having been done a series of test tubes was taken and by means of graduated pipettes, decreasing amounts of the solution were measured into the tubes thus - 3 ccm. 2'8 ccm. 2'4 ccm. and so on down to '05 ccm. Into each tube then was pipetted 2 ccm. of a 1%. Edestin Solution. The tubes were then shaken and allowed to stand in a rack at room temperature.

The Edestin Solution is prepared as follows - 1 gram of powdered edestin - Hemp seed protein - is dissolved in a 1000 ccm. of N/33 HCl., boiled and kept in the cold in a tightly stoppered bottle - a layer of Toluol on top to prevent entrance of organisms. Such a solution is good after weeks but to ensure greater certainty it was found better to make a fresh solution at least once a week.

When the test tubes have lain at room temperature - 20° Cent. - for half an hour, '3 ccm of saturated solution of Sodium Chloride is added to each tube, and in the tubes where digestion has been complete no turbidity occurs whereas in the tubes where digestion has not been complete a white cloudiness appears and a white precipitate gradually falls to the bottom of the tube. The tube higher in series to the first cloudy one contains just sufficient pepsin to digest the edestin and it is taken as the Limit. Thus supposing on addition of salt solution the tube containing '3 ccm of a tenfold dilution shews a cloudiness while the tube next it

containing '4 ccm of the same dilution remains clear this second tube is the Limes and P.i.e. the number of "Peptic Units" in 1 ccm of Gastric Contents

$$P \frac{20^\circ C.}{30 \text{ mins}} = \frac{10 \text{ (dilution)} \times 2 \text{ (ccm of edestin sol)}}{'4}$$

$$= \frac{200}{4}$$

$$= 50$$

Fuld and Levison allowed the solution to act on the Edestin Solution for $\frac{1}{2}$ hour only but this time I have found to be too short and for purposes of comparison with the values of pepsinogen in urine which is incubated for 1 hour, the ferment action has been allowed to take place always for 60 minutes at 20° C.

The method however and the calculation are quite the same as outlined above. So far as the addition of the Sodium Chloride solution is concerned it has been mentioned above that '3 ccm of solution was added, this is sufficient for the tubes containing a small quantity of fluid but to each of the tubes containing more than '8 ccm or 1 ccm some more salt solution must be added in gradation and proportion to ensure proper precipitation . This is important because when too little salt solution is added the results got are too high.

As stated above in all the cases gastric contents were used after an Ewald test breakfast, and this of course gives us merely a practical indication of the chemical activity of the stomach so to speak only for a point of time while it is a matter of urgent necessity that we should have a means of testing its peptic activity for a period of time by some such method as Sahli's Desmoid-pillen &c.

## Peptic Action of the Urine.

It has long been known that the urine of certain patients could exercise some peptic activity as for instance Grutzner [6] shewed. His method of demonstrating this phenomenon was by the use of fibrin masses impregnated with Carmine. These masses

he placed in urine for a time and then transferred them to a solution of Hydrochloric Acid. The fibrin masses were found to undergo digestion and in a general way the extent of this could be measured by the tinge of the Acid coloured by the Carmine. This method was of course crude but it sufficed to shew that peptic action in the urine could be demonstrated.

This was not due at all to organismal infection of the urine &c., and was clearly peptic digestion. As such it was accepted and the action was attributed to Pepsin and for long no attempt was made to probe the matter further.

Lately, however, it has excited a good deal of interest and Jacoby and Solnes performed many estimations in urine. Wilenko [7] used the Ricin method but as here a solution is being used which is never perfectly clear, and is not constant in concentration, there is too little constancy in the results.

In all the estimations of peptic activity in urine here recorded the method used was that of Fuld and Hirayama.[8] In this method the substratum used is the same as in Fuld and Levison's method for gastric contents. The urine was filtered in every case and sufficient $\frac{N}{1}$ HCl. added to give a definite positive reaction with Congo red paper. The urine was pipetted into a series of test tubes in gradually decreasing quantities. Then to each tube was added 2 ccm of the 1‰ Edestin Solution. The tubes were shaken and placed at once in a beaker containing water at 40°C. The time was noted and the tubes transferred to a rack and placed in the incubator at 38°C. for one hour. The tubes were placed in warm water first for the short period as it was found that the temperature was raised to body heat more quickly and uniformly than if they were placed in the incubator at once. This initial raising of the temperature is necessary since the Edestin Solution is kept in ice cold water.

At the end of one hour in the incubator the tubes were placed in cold water to inhibit the action, and then saturated sodium

chloride solution was added as in the case of the gastric contents. The result was read off as in the stomach tests and P.i.e. the peptic index of 1 ccm of urine calculated as in that case, e.g. supposing the last tube remaining clear after Na Cl has been added contains '5 ccm urine, then $\frac{P_{60\text{ minutes}}^{38^\circ C.}}{} = \frac{2(\text{ccm. Edestin Sol})}{\text{'5 ccm urine}} = 4$ units

In this case one had first to decide as to the necessity of adding Hydrochloric Acid to the urine, and the amount to be added, and in this connection it was found that although the amount varies, most probably with the concentration and alkalinity of the urine, 1 ccm of $\frac{N}{1}$ HCl. to 9 ccm of urine gave a sufficient degree of acidity.

For example :-

| | Quantity of Urine. | Quantity of HCl. | Result. |
|---|---|---|---|
| (1) | 20 ccm. | 0. | Cloudy without adding Na.Cl. |
| (2) | 20 ccm. | '5 ccm. | Doubtful : cloudiness from start in tubes with more than 1'2 ccm. |
| (3) | 20 ccm. | 1 ccm. | P - '6 ccm. |
| (4) | 20 ccm. | 1'5 ccm. | P - '5 |
| (5) | 20 ccm. | 2 ccm. | P - '5 |
| (6) | 20 ccm. | 2'5 ccm. | P - '5. |

It will thus be seen that up to a certain degree of acidity the values got are too low and in addition to this precipitation is apt to occur on the addition of the Edestin Solution, which of course vitiates the whole test. Thus in (1) of the table given above all the test tubes of the series showed turbidity on the addition of the Edestin. In (2) of the same table turbidity occured only in these which contained more than 1'2 ccm of the urine. This left the other tubes clear but of a necessity made it impossible to read the result obtained on the addition of NaCl. Solution. In (3) of same table the result is more definite and here the peptic index is near that which was got and which, remaining constant in the three successive tests (4) (5) and (6), is taken as the peptic capacity of the urine for this particular case.

In regard now to the meaning of the action, it is obvious that it may be an expression of the action of pepsin or of a propepsin or pepsinogen. When the action was discovered it was considered as being without much doubt due to pepsin, but this probably is not the case.

Wilenko had the idea that the pepsinogen was absorbed from the glands - the peptic index did not rise after feeding with stomach pepsin - Acidol pepsin. Ellinger and Scholz [9] also concluded that the substance must be a propepsin - they attempted to adduce proof from other sources e.g. the addition of pepsin to the solution.

To demonstrate the correctness of the hypothesis that the agent is present really as a proferment is a very difficult matter as we do not know any essential difference in constitution between a ferment and its precursor and in this case the medium is also the activating agent.

Fuld and Hirayama tried to demonstrate that it is a proferment by shewing that in the case of Rennin in the urine - this is present really as prorennin and they assumed that it was the same with the peptic ferment, they consider Rennin and Pepsin identical and so consider this proof.

The strongest evidence in favour of its proferment nature is the fact that on standing in neutral or alkaline solution it loses very little of its efficiency whereas a solution of a ferment loses its potency very rapidly on standing.

Pepsin is much more easily affected by alkalis than its precursor pepsinogen - the action being due to the number of H. ions present, and the same is true of neutral solutions to a less degree.

The solution of the "ferment" - in this case the urine - was therefore taken and activated by means of HCl. and its potency estimated. It was then kept for three days under Toluol having been neutralized, and an unactivated sample was kept under the same conditions and with the same precautions. The potency of both was tested at the end of that time - the unactivated sample being activated just before the investigation.

The results shewed that the specimen preserved "activated" which according to this reasoning contained pepsin only had lost much more of its activity than the unactivated specimen which contains its ferment mostly in the form of pepsinogen.

Stomach contents also lost their potency much more quickly than the unactivated urine i.e. in comparison of course - the stomach ferment being mostly in the form of pepsin. It seems therefore practically certain that the pepsinogen hypothesis is the correct one - that we are dealing with a proferment which is absorbed not from the lumen of the stomach but directly from the pepsin - producing glands of the gastric mucous membrane.

## Excretion of Pepsinogen - daily variations.

Assuming then that the theory of Wilenko and others is correct and that there is possible a twofold destination of pepsinogen - one destination into the lumen of the stomach where it is "activated" and performs peptic digestion, the other into the blood stream, daily variations are to be expected. These in fact are found and are as follow :-

In the first specimen of urine passed in the morning we find that the peptic activity is greatest. This urine is of course most concentrated but even making allowance for this as has been done below it is probable that most pepsinogen is excreted during the night. During the morning and forenoon the peptic index steadily declines and in the afternoon is at its lowest point, rising again gradually in the evening to reach its maximum during the night.

This is shewn very well by the tables and graphs given below.

These results practically agree with those of Fuld and Hirayama.

| | 10-5 a.m. | 12-15 p.m. | 4-30 p.m. | 6-20 p.m. |
|---|---|---|---|---|
| I. Dr. R. (1) | 2'5 | 2 | 1 | 1'5 |
| | 7 p.m. | 10 p.m. | | |
| | 1'6 | 1'6 | | |
| (2) | 9 a.m. | 11-15 a.m. | 1-10 p.m. | 3 p.m. |
| | 2'5 | 1'8 | 1 | 1'4 |
| | 6 p.m. | 9 p.m. | | |
| | 1'5 | 1 | | |

Meals :- Breakfast 9-30 a.m.

Lunch. 1-30 p.m. Dinner. 7 p.m.

Tea. 4-0 p.m. Supper. (glass of milk) 11 p.m.

II M. : healthy - previously anterior Poliomyelitis.

(1) 9 a.m. 12-30 p.m. 3-20 p.m. 6-50 p.m. 8 p.m.

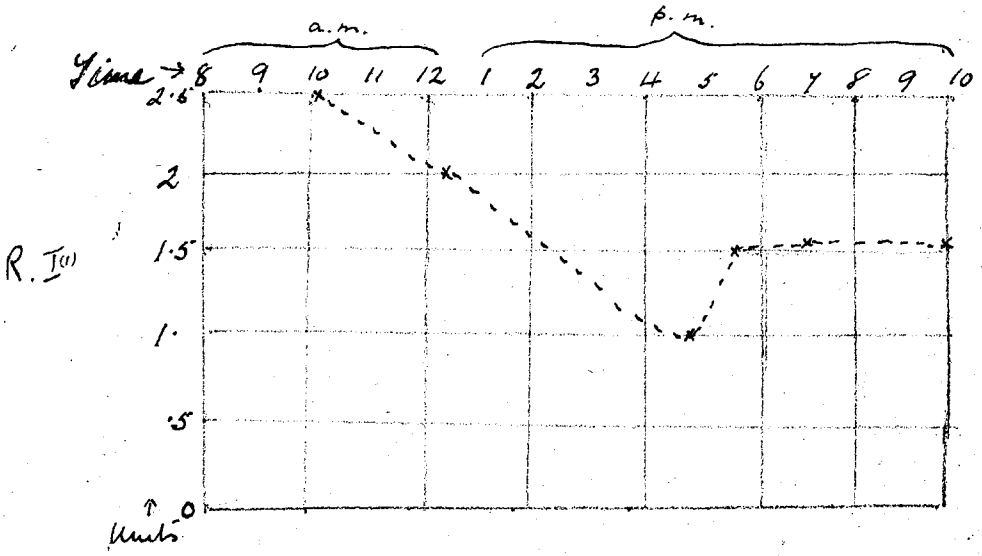
2'5 2 1'8 1'5 1'8

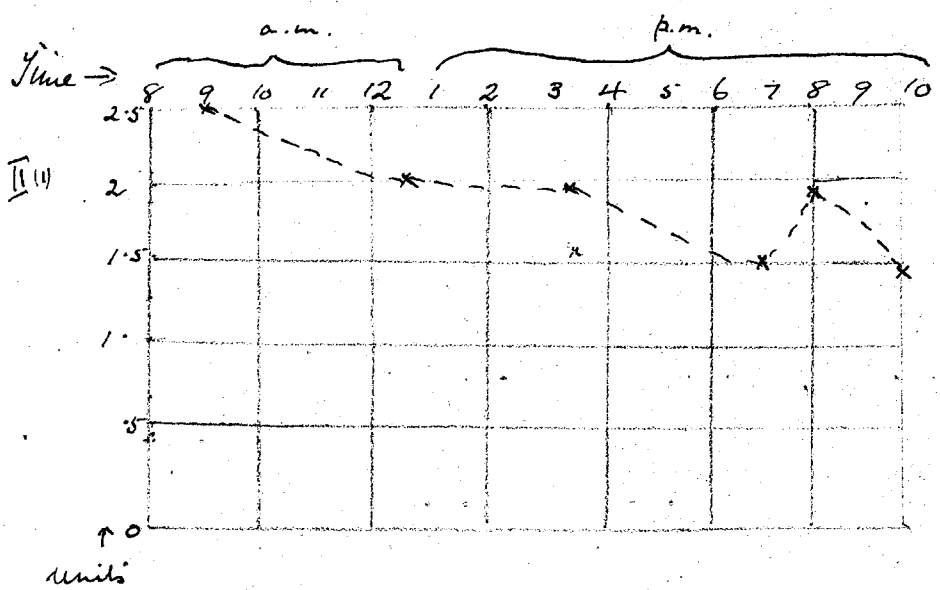
10 p.m.

1'4

(2) 8-30 a.m. 12 noon. 4-5 p.m. 7 p.m. 10 p.m.

2'6 2'2 1'6 1'4 1'7



It is conceivable and in fact more than probable that the results set out above are dependent on or at least concomitant with the scheme of meals named, and most common in this country and in any case variations are all within limits and it is probable that the peptic index for the whole twenty-four hours is constant in so far as any expression of any living process is constant for each individual in health.

The lowered peptic index which has been found prevalent in the urine of the daytime may be due to one or two causes.

(1) The watery portion of the urine may dilute it to such an extent that although the total ferment excretion may be normal - the peptic index of a ccm may be diminished.

Fuld and Hirayama made the (to the writer) astounding statement that they did not find dilution of the urine made much difference. This seems practically inconceivable when talking of an index of the urine as concentration of urine varies so widely.

(2) The other possible cause is simply that during the daytime less proferment can be spared to find its way into the bloodstream, as more of it may be required to perform peptic digestion of the stomach contents. This I have not been able to prove. I have tried to secure the night urine of a night worker who had to take meals during the night but so far have not succeeded; but there seems to be little doubt that the result in such a case would give a graph the reverse of those normal ones shewn above.

From the fact that we are dealing with a proferment we are practically reduced to the hypothesis of Wilenko and others that the absorption into the bloodstream takes place from the glands for producing pepsin. This I consider proved by the experiments of J. Wohlgemuth [13] who estimated pepsin in the urine of dogs and then resected the stomach and found that the excretion of pepsin in urine ceased at once.

Wilenko tried to increase the amount of urinary pepsin by giving a patient Acidolpepsin - and found no increase, but such a method of proof that the agent is pepsinogen and that its

absorption takes place from the pepsin forming glands is not conclusive. In the first place the quantity of Acidolpepsin administered must be very small and the part of it absorbed must be still smaller and consequently can only increase the peptic index to a minute degree; and then again the presence of Acidolpepsin in the gastric lumen may be sufficient to neutralise the stimulus on the gland cells to throw out pepsin into the gastric lumen - in other words to give these cells a period of rest during which time their accumulated products are being absorbed into the bloodstream as an internal secretion and excreted in the urine. Thus a positive result of such a method of experimentation would have proved nothing for or against.

A far more reasonable proof of the proferment nature of the agent is provided by the experimentation given above, with specimens of urine to which have been added increasing quantities of HCl.

The urine was tested at once on the addition of the HCl and it is probable that the low Indices in these cases where less than the "optimum" amount of HCl. had been added may be due to the fact that the activation of the proferment requires some time unless a sufficiently excessive amount of HCl. has been added - to produce activation at once and produce an excess of H.ions. Assuming then, and it seems a reasonable assumption, that the agent excreted in the urine is a proferment we are driven to the conclusion that its absorption can occur only from the peptic glands into the bloodstream where being inactive it circulates until thrown out of the body by the Kidneys, and is continuous and independent, as the other peptic supply, on stimuli by food &c.

Thus we arrive at the conception of a continual and constant formation of pepsinogen by the only glands in the body so far as we know, capable of its formation - with one of two possible destinations before it. The hypothesis is not unreasonable as practically all, if not all, living tissue gives to the bloodstream a substance analogous to that given by special glands and designated for that reason - internal secretion.

These thoughts now lead to the consideration of the variations of the "peptic index" of urine - unfortunately from the nature of blood plasma, its richness in albumen and in antiferment - it is as yet impossible to ascertain a "peptic index" of the blood - which are not of physiological origin and may therefore be called pathological .

In the first place I have found no urine of a healthy individual which on activation by means of Hydrochloric Acid did not shew evidence of peptic activity and therefore I consider "peptic action" of the urine an essential concomitant of healthy existence.

The first and probably the most common interference with the excretion of pepsinogen in the urine is due to defective function of the Kidney. Pepsinogen as well as the other ferments found in the urine has a high molecular weight and is of complicated composition. That being so ferments are among the first bodies, normally present in the urine, which are held back by defective action of the Kidney. So much has this been proved to be the case that J. Wohlgemuth [12] has devised a test for Kidney efficiency using the urinary content of diastatic ferment as the indicater. The same is true of pepsinogen and we must look upon renal efficiency as one of the most common causes of the decrease of pepsinogen in the urine.

This is found in practically all cases of Nephritis, acute and chronic, as can be seen from the tables given below. It is difficult to estimate this factor of disturbance in order to eliminate it and this possible error must remain until some more efficient method of estimating Kidney function has been evolved.

In these cases of renal disease pepsinogen was never or only very seldom found to be totally absent. It may be that where albumen is present in the urine, by using Edestin solution as substratum we are not performing a fair test as the pepsinogen when activated by HCl. probably first attacks the native albumen present in the urine. Edestin of course is an absolutely foreign albumen. The native albumen present in the urine may therefore

bind up the pepsin or most of it and only the small quantity free to act on Edestin is estimated which is not at all satisfactory.

By allowing the urine to act on the native albumen for twenty-four hours and then precipitating by Uranyal Acitate I have attempted to get a ferment precipitate which was dissolved and estimated by its action on edestin as usual. The attempt failed for the same reason that all ferment extractions fail. The loss is so great that even if we do succeed in getting a ferment in a little purer condition than before, the 'yield' is useless for purposes of quantitative estimation.

This presence of renal inadequacy which holds back pepsinogen is a factor then always to be considered. As to whether the converse is true in some cases of increased permeability of the Kidneys I do not know for the reason that such conditions probably always allow quantities of albumen into the urine as well.

In one of the cases where a persistence of a strikingly low Peptic index was got that of C.-- Table VI No. 10. In this case, with no digestive symptoms whatever, there was practically an absence of pepsinogen in the urine. Albumen was present in small amount, together with some hyaline casts and the case was thought to be one of Granular Kidney. There was indefinite swelling on the left side in the renal region but no blood, pus or bacilli were ever found in the urine. The peptic index was lower than in any case of nephritis examined, and the diastatic ferment index of the urine was also very low when estimated by Wohlgemuth's most recent method.

Autopsy revealed a large sarcoma involving the whole of the left Kidney so that no active Kidney substance remained, while the right Kidney was small and granular. In this case the conclusion arrived at that only one Kidney was functioning was borne out by the autopsy but the clinician under whose care the patient was, held different views, and no operation was advised.

In this case the test of ferments in the urine afforded practically all the information necessary for a diagnosis and of course without any of the inconvenience to the patient entailed by segregation of the urine or cystoscopy with colour tests. Estimations of peptic and diastatic content of the urine must

therefore be regarded as the most sensitive indices to the function of the kidneys.

The other variation of 'peptic index' of the urine is variation in the producing organ, in this case the gastric mucous membrane , and it was to find if possible any relationship between changes of the peptic index of the urine and pathological conditions of the gastric mucous membrane that the investigation was undertaken.

It stands to reason that if no pepsinogen be absorbed by the bloodstream none can be excreted by the kidney, but short of this it might be that changes could give variations which of course would be an indication of these changes.

This search is the more justifiable because at present we have in many cases no symptom or sign on which we can depend to any extent for a differential diagnosis between Achylia gastrica of benign and that of malignant origin. How far the peptic index of the urine alone or in conjunction with the peptic index of the gastric contents recovered after a test breakfast may help us in this or other directions in differential diagnosis of stomach conditions will be discussed later.

A third factor causing variations of the peptic index of the urine is one which we find hard to estimate or even to determine as existing, namely the presence of antiferments or anti-bodies in the urine.

This is a question whose decision is of extreme importance in this matter. A few years ago Brieger [15] and Trebing demonstrated in plasma the existence of antitryptic bodies which were specially increased in the blood of cancer patients. The same factor was established to the satisfaction of most if not all observers as being present in the urine. In that case demonstration was a more simple matter than in the case of peptic antibodies, although it is likely that there exists bodies in antagonism to peptic as to tryptic action.

In some of the cases here examined urine was found containing no peptic bodies at all notably in one or two cases of Carcinoma Ventriculi and with one of these the following experiment was performed. The urine of a healthy individual - Dr. R.- was taken

and its peptic activity carefully estimated. Then using urine of a patient with cancer of the stomach which contained little or no pepsinogen - also carefully determined - some of this was added to the first specimen and the peptic activity of the mixture was estimated.

The results were as follow :-

| Tubes. | Edestin Sol. | Healthy urine. | Cancer urine. Unactivated. | Activated. | Digestion |
|---|---|---|---|---|---|
| 1. | 2 ccm. | 1 ccm. | - | - | Complete. |
| 2. | 2 " | '8 " | - | - | " |
| 3. | 2 " | '6 " | - | - | Incomplete |
| 4. | 2 " | 1 " | 1 ccm. | - | " |
| 5. | 2 " | '8 " | 1 " | - | " |
| 6. | 2 " | '6 " | 1 " | - | " |
| 7. | 2 " | 1 " | '8 " | - | " |
| 8. | 2 " | '8 " | '8 " | - | " |
| 9. | 2 " | '6 " | '8 " | - | " |
| 10. | 2 " | 1 " | - | 1 ccm. | " |
| 11. | 2 " | '8 " | - | 1 " | " |
| 12. | 2 " | '6 " | - | 1 " | " |
| 13. | 2 " | 1 " | - | '5 " | " |
| 14. | 2 " | '8 " | - | '5 " | " |
| 15. | 2 " | '6 " | - | '5 " | " |

The cancer urine in this case by itself shewed practically no peptic activity, '5 of a unit downwards in a series of three tests. The healthy urine alone shewed 2'5 units; with the cancer urine added it shewed less than 2 units in each case whether the latter was activated or not.

## Tables.

### I Healthy Individuals.

| | Free HCl. | Total acidity. | Peptic index (F & L) | Do. (F & H) |
|---|---|---|---|---|
| (1) W--. | | | | |
| (a) | 24. | 46. | 40. | 1'6 units. |
| (b) | 26. | 48. | 33'6. | 1'4 " |

| | Free HCl. | Total acidity. | Peptic Index (F & L) | Do. (F & H) |
|---|---|---|---|---|
| (2) M-- (anterior poliomyelitis) | | | | |
| (a) | 18. | 33. | 33'3 | 1'8 units. |
| (b) | 26. | 50. | 30. | 2 " |

II Patients with Carcinoma Ventriculi.

| | Free HCl. | Total acidity. | Peptic Index. F & L. | Peptic index. (urine) F & H. |
|---|---|---|---|---|
| (1) H-- | 0 | 12. | 10. | 1'6 units. |
| (2) H-- | 0 | 5. | (a) 20<br>(b) 6'6 | '9 " |
| (3) E-- | Trace. | 20. | 50. | '9 " |
| (4) M-- | - | - | 20. | 2. " |
| (5) B-- | 39. | 84. | 66'6 | '8 to nil. |
| (6) L-- | 16. | 68. | 28'5 | '7 " " |
| (7) H-- | 30. | 90. | 20. | '8 " " |
| (8) C-- | 10. | 26. | 10. | 1. |
| (9) W-- | 0. | 5. | less than 10. | Nil. |
| (10) R-- (Cancer of Pylorus and first part of duodenum) | 44. | 98. | 33'6 | Nil. |
| (11) C-- | 14. | 46. | 20. | " |
| (12) R-- | 2. | 5. | less than 10. | " |
| (13) W-- | 18. | 36. | less than 10 | " |
| (14) | 16. | 30. | 20. | '8 |
| (15) | 5. | 36. | under 20. | '5 and under. |

III Cases of Carcinoma Ventriculi where only the peptic index (P) of the urine was estimated.

| | Patient. | P. |
|---|---|---|
| (1) | J. -- | 1'25 units. |
| (2) | S. -- | 1'6 " |
| (3) | T. -- | 1'5 " |
| (4) | U. -- | 1'6 " |
| (5) | D. -- | 1'8 " |
| (6) | F. -- | 1'2 " |
| (7) | T. -- | '8 " |

III continued.

| | Patient. | P. |
|---|---|---|
| (8) | W. -- | '8 units. |
| (9) | H. -- | less than '75 " |
| (10) | C. -- | 1'2 " |
| (11) | M. -- | 1. " |
| (12) | J. -- | '7 to Nil. |
| (13) | B. -- | '8 unit. |
| (14) | W. -- | '7 " |
| (15) | S. -- | practically nil. |
| (16) | H. -- | '9 unit. |
| (17) | L. -- | '7 to nil. |
| (18) | O. -- | nil. |
| (19) | N. -- | 1. unit. |
| (20) | C. -- | '6 " |

---

IV Cases of other gastric conditions.

| | Free HCl. | Total acidity. | Peptic index. F. & L. | Peptic index. (urine) F. & H. |
|---|---|---|---|---|
| (1) H.-- Chronic Anacid Gastritis - operated on. | | | | |
| | 0 | 12. | 10 units. | 2'5 units. |
| (2) W.-- Chronic Gastritis. | | | | |
| | 20 | 36 | 33'3 " | 2. " |
| (3) T.-- Cholelithiasis with Acute Gastritis. | | | | |
| | 60. | 88'8 | 18'2 units. | 2. " |
| (4) T.-- Pyloric Stenosis (benign) : dilatation of stomach : Neurosis. | | | | |
| | 54. | 114. | 20. units. | 1'4 units. |
| (5).M.-- Pyloric Stenosis (benign) | | | | |
| | 32. | 82. | 25. " | 1'4 " |
| (6) A.-- Enteroptosis :- some albuminuria. | | | | |
| | 48. | 106. | 40 " | nil. |
| (7) P.-- Chronic Constipation : vomiting. | | | | |
| | 14. | 58. | 16'6 " | 1'1 " |
| (8) D.-- Nervous Dyspepsia - Hysteria. | | | | |
| | 12. | 62. | 28'57 " | nil. |

IV. Continued.

| | Free HCl. | Total acidity. | Peptic Index. F. & L. | Peptic Index. (urine) F. & H. |
|---|---|---|---|---|
| (9) K.-- Simple Gastric Ulcer. | 59. | 79. | 50. | 2. units. |
| (10) N.-- Atrophic Gastritis with dilatation of Caecum : Neurosis. Before operation - (removal of ascending and Transverse Colon) | 0. | 3. | nil (20 dilution) | '6 unit. |
| (11) R.-- Subacid Gastritis - chronic : benign. | 6. | 20. | 10. | 1'1 units. |
| (12) M.-- Subacid Gastritis with dilatation. | 3. | 15. | 10. | '9 " |

---

V. Cases of Chronic Gastritis where only urinary Peptic Index was estimated.

| | Patient. | Peptic Index. |
|---|---|---|
| (1) | E. -- | 2'3 units. |
| (2) | B. -- | 1'6 " |

---

VI. Other conditions. - only urinary peptic index estimated.

| | Patient. | Disease. | P. (urine) |
|---|---|---|---|
| (1) | K.--- | Arterio Sclerosis. | '9 unit. |
| (2) | R.--- | Arterio Aneurysm. | 1'5 units. |
| (3) | T.--- | Diabetes Mellitus. | 1'25 " |
| (4) | R.--- | " " | 1'6 " |
| (5) | S.--- | Tabes Dorsalis. | 4. " |
| (6) | T.--- | " " | 1'2 " |
| (7) | D.--- | Chronic Nephritis. | 1'25 " |
| (8) | F.--- | " " | 1'25 " |
| (9) | B.--- | " " | 1'4 " |
| (10) | C.--- | Renal Tumour and granular kidney. | '4 to nil. |
| (11) | M.--- | Nephroptosis and Hydronephrosis. | '5 unit. |
| (12) | T.--- | Cholelithiasis. | 2. units. |

---

Reviewing the tables of results given above.

In the investigations carried out, the urine of upwards of 50 patients was examined and more than 200 tests performed, and in the tables the results stated are the average of several determinations.

These results however have been found to vary within very small limits as for instance in the case of R.--- Table VI. No.(2) suffering from Aneurysm of the Aorta, where the results obtained on twenty successive days were as follow :-

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| (1) | 1'1 units. | (7) | 1 units. | (13) | 1'1 units. | (19) | 1'2 units. |
| (2) | 1'2 " | (8) | 1'4 " | (14) | 1'1 " | (20) | 1'1 " |
| (3) | 1'2 " | (9) | 1'2 " | (15) | 1. " | | |
| (4) | 1'4 " | (10) | 1'1 " | (16) | 1'1 " | | |
| (5) | 1'6 " | (11) | 1. " | (17) | 1'2 " | | |
| (6) | 1'6 " | (12) | 1. " | (18) | 1'3 " | | |

S.--- Table VI. No.(5) suffering from Tabes Dorsalis gave the following results.

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| (1) | 3'3 units. | (3) | 5. units. | (5) | 3'3 units. | (7) | 2'6 units. |
| (2) | 3'3 " | (4) | 5. " | (6) | 3'3 " | (8) | 3. " |

C.--- Table III. No.(10) suffering from Carcinoma Ventriculi gave the following results.

| | | | |
|---|---|---|---|
| (1) | 1'4 units. | (4) | 1'6 units. |
| (2) | 1'1 " | (5) | 1'4 " |
| (3) | 1'4 " | (6) | 1'6 " |

These results are taken at random from the list to shew that the average result is not the average of a series which included wide extremes but was in most cases practically the result which was obtained in each examination. Any little variation is probably due to difference in the concentration of the urine.

The tables include 3 cases of healthy hospital residents.

1 case of Aortic Aneurysm.

2 cases of Diabetes Mellitus.

2 cases of Tabes Dorsalis.

1 case of Arterio-Sclerosis.

3 cases of Chronic Nephritis.

1 case of Kidney Tumour.

1 case of Nephroptosis and Hydronephrosis.

1 case of Duodenal Ulcer.

49 cases of Gastric troubles.

Among the cases of Carcinoma Ventriculi, 35 in number, full estimations of peptic activity of stomach contents and urine were carried out in 15 : urine examinations alone were done in the remaining 20 cases.

In the series of 14 cases of gastric conditions other than Carcinoma full stomach and urinary estimations were done in 12, and urinary examinations alone in the other two which were both cases of Chronic Gastritis. These 12 cases included 2 cases of Anacid Gastritis (operated on - see later) : 4 cases of Subacid Gastritis : and 1 Gastric Ulcer. The remaining 5 cases were of Gastritis of nervous origin.

The results in the three healthy cases were on an average :-

Case I. '75 ccm. - P - 2'8 units.

Case II. 1'2 " - P - 1'8 "

Case III. 1'2 " - P - 1'8 "

Average P - 2'1 units.

In the case of Aortic Aneurysm where P - 1'3 units the arteries were affected with arteriosclerosis but there was no albumen in the urine.

The two cases of Diabetes Mellitus shewed :-

Case I. P - 1'25 units.

Case II. P - 1'6 "

Average P - 1'4 units.

Neither of these two cases had albumen in the urine but No. II had a very large quantity of sugar and much Diacetic Acid.

The first case of Tabes Dorsalis, which had no gastric crises gave an index of P - 4 units, a very high reading and in contra-distinction to what was found in the other - a more advanced case - where the stomach symptoms were then those of Achylia Gastrica, and the average index was P - 1'2 units.

This condition is probably a result of nerve changes which cause atrophy of the glands of the gastric mucous membrane, or at least a diminished activity on the part of these glands.

The three cases of Chronic Nephritis gave rather surprising results. The average index was P - 1'3 units. This is low but hardly as low as one might expect, but the permeability of the kidneys for bodies of high molecular weight is of course very variable and it would require a very large number of estimations in cases of Chronic Nephritis to determine an average constant, if such is possible.

The one case of Renal Tumour, to which reference has previously been made, is of sufficient interest to be fully reported here.

The results in this case were as follow.

| | Date. | Tubes. | Result. |
|---|---|---|---|
| C.-- | 11-12-12. | 2'6 ccm. down to 4. ccm. | All cloudy on addition of Edestin : i.e. digestion incomplete. |
| | " " " | 4'6 " " " 2'6 " | |
| | 13-12-12. | 5. " " " '4 " | |
| | 16-12-12. | 5. " " " " " | |
| | 17-12-12. | 5. ccm down. | All cloudy except tube 1 containing 5 ccm. P. : - '4 unit. |
| | 18-12-12. | 5. ccm down. | No digestion occur |
| | 20-12-12. | 5. " " | " " " |
| | 31-12-12. | 5. " " | " " " |

5-1-13. Post Mortem - Nothing abnormal was found in the stomach.

The left kidney and suprarenal body were practically replaced by tumour-(sarcoma): No secreting tissue left : The right kidney was granular. The spleen was enlarged and contained metastases.

In this case unfortunately no test breakfast was given, a procedure which might have allowed the lowering effect on the peptic index of renal inadequacy to be more clearly demonstrated.

During the whole period of examination there was practically no pepsinogen excreted in the urine.

The patient suffering from Nephroptosis and Hydronephrosis (proved by Laparotomy) had a very low index.

P - '5 unit - a sign of renal insufficiency.

In the case of the patient suffering from Cholelithiasis the index was practically normal - P - 2 units.

The urine of two patients who presented the clinical signs and symptoms of duodenal ulcer were examined. In the first - Morley, the peptic index of the urine was P - 2 units a value which is if anything lower than might be expected in duodenal ulcer. This case came to operation and was found to be one of malignant disease of the first part of the duodenum. It may here be noted that the stomach contents after a test meal shewed per ccm. P = 20 units (Fuld and Levison) which is quite that found usually in the cases of Carcinoma Ventriculi examined.

The second case Haworth was simple ulceration of duodenum also proved by operation and in this case the peptic index of the urine was P = 2'5 units - a practically normal result.

## Cases of Carcinoma of the Stomach.

The peptic activity of the gastric contents and urine was estimated in 15 cases of Carcinoma Ventriculi. Most of these cases were fairly early, most of them being verified at operation and a few at autopsy later, in the few unconfirmed cases the clinical diagnosis was fairly certain and X ray examination gave confirmatory signs. Doubtful cases have been intentionally omitted.

In these cases - Table II - looking first at the Hydrochloric acid values in the stomach content there is little to be remarked. In only two cases (5) and (10) were the values much greater than normal. Case (10) was Carcinoma of duodenum and case (5) was probably one of Carcinoma superimposed on an ulcer.

The free Hydrochloric value in the remaining cases was either normal or much lower than normal and in general there was no free Hydrochloric.

With regard to the total acidity there was nothing of remark found.

The peptic index estimated in Fuld and Levison units of the gastric contents varied within very wide limits.

It may be remarked here that even in normal stomachs this investigation has never given values the equivalent of those found by continental writers. Fuld and Levison [8] themselves put the

average peptic index of a normal stomach content after a test breakfast at 100 units as so also did Wolff and Tomaszewski. 17

In cases where the fluid was washed out from a fasting stomach the figures were even higher.

In no case was an index of 100 units found during this investigation, the value being much lower than that stated varying in normal cases from 33'3 units to 50 units.

On account of the disparity between these results and those of others every possible care was exercised to eliminate error, and the conclusion has been arrived at that the continental observers must have added too little salt solution to their tubes, or were working in higher temperature.

It is interesting to remark that Allanson working under Dr. Craven Moore 14 in the Ancoats Hospital Laboratory, Manchester found results which were even lower than those found by me.

The result of the investigation detailed above shews that the peptic capacity of 1 ccm of stomach contents varied from less than 10 up to 66'6 units.

Averages in such cases as have been investigated here are valueless, but generally speaking the value has been much below normal.

In no case has the peptic activity of a gastric juice of a Carcinomatous stomach been absolutely absent and although in three cases the value has been put down as less than 10 units there was evidence in every case of peptic action having taken place to some degree.

With regard to the rise and fall of the Hydrochloric value and the peptic capacity together some interesting results fall to be recorded. In the work cited above from the Ancoats Laboratory the findings shewed that normally the HCl. and peptic values rose and fell together.

In the Carcinomatous cases here recorded we find as follows :-

I. Cases with no free HCl.

| | Free HCl. | Peptic Units (F. & L.) |
|---|---|---|
| (1) | 0. | 10. |

I. Cases with no free HCl. continued.

| | Free HCl. | Peptic Units (F. & L.) |
|---|---|---|
| (2) | 0. | (a) 20.<br>(b) 6'6 |
| (3) | Trace. | 50. |
| (9) | 0. | 10- |
| (12) | 0. | 10- |

---

II. Cases with HCl. under 20.

| | Free HCl. | Peptic Units (F. & L.) |
|---|---|---|
| (6) | 16. | 28'5 |
| (8) | 10. | 10. |
| (11) | 14. | 20. |
| (13) | 18. | 10. |
| (14) | 16. | 20. |
| (15) | 5. | 20. |

---

III. In cases with HCl. over 20.

| | Free HCl. | Peptic Units (F. & L.) |
|---|---|---|
| (5) | 39. | 66'6 |
| (7) | 30. | 20. |
| (10) | 44. | 33'6 |

---

The chief conclusion which is arrived at from these findings is that with no or practically no HCl. free in the stomach juice the peptic value may be quite normal e.g. case (3), and practically never disappears. This is an evident result of the conditions in a cancerous stomach where the alkaline bases exuded from ulcerated cancerous surfaces and the extreme proteolytic products due to abnormal ferments from cancer tissue as shewn by Emerson [16] and lately substantiated in this laboratory by Dr. W. J. Reid, and possibly back flow from the duodenum, combine with the free HCl. and leave the pepsin free to act so long as the reaction of the

medium i.e. the concentration of H ions will permit the action.

In a general way cases like (5) and (10) with a high free HCl. value have a normal peptic index.

It is interesting in this connection to compare with the above the tables of results got in conditions other than Cancer of the Stomach.

In these we find,

I. Cases with free HCl. under 20.

| | Free HCl. | Peptic Units. (F. & L.) |
|---|---|---|
| (1) | 0. | 10. |
| (10) | 0. | 0. |
| (11) | 6. | 10- (Atrophic Gastritis) |
| (12) | 3. | 10- |
| (7) | 14. | 16'6 |
| (8) | 18. | 28'5 |

---

II. Cases with Free HCl. over 20.

| | | |
|---|---|---|
| (2) | 20. | 33'3 |
| (3) | 40. | 18'2 |
| (4) | 54. | 20. |
| (5) | 32. | 25. |
| (6) | 48. | 40. |
| (9) | 59. | 30. |

---

Here we find the results generally higher than in the cases of Carcinoma Ventriculi, but the values of HCl. are also generally higher, and when the free HCl. value is over 20 there is no probability even that the peptic value will be normal or over. The HCl. and peptic values in such pathological stomachs may progress quite independently. This is not found in normal stomachs as shewn by Moore and Allanson (loc. cit.).

With regard to the urinary peptic index - this being really - as pointed out above - the Pepsinogen index, case No. (4) Table II with Carcinoma just beyond Pyloric ring gave an average index of

2 units, but with this exception the highest value found in the cancer series was 1'6 units and many cases gave nil.

The following tables have been prepared in order to see whether gastric and urinary peptic indices run a parallel course.

I. Cases of Carcinoma.

A. where P (gastric) - 10 units and under (F & L)

| | Units (F & L) | Units (F & H) |
|---|---|---|
| (1) | 10. | 1'6 |
| (2) | (b) 6'6 | '9 |
| (8) | 10. | 1. |
| (9) | 10. | nil. |
| (12) | 10 - | " |
| (13) | 10 - | " |

B. over 10 units (F & L)

| | | |
|---|---|---|
| (2) | (a)20. | '9 |
| (3) | 50. | '9 |
| (4) | 20. | 2. |
| (5) | 66'6 | '8 to nil. |
| (6) | 28'5 | '7 " " |
| (7) | 20. | '8 " " |
| (10) | 33'6 | nil. |
| (11) | 20. | " |
| (15) | 20 - | '5 and under. |

Among these cases of cancer of the stomach then it seems a high Peptic index in the stomach content need not be followed by a high index in the urine as a matter of course but a case with a high index in the stomach content may have no index at all in the urine.

In the series of cases of Cancer of the stomach where the gastric contents for any reason were not examined we find the Peptic index of the urine ranging from nil up to 1'8 units i.e. from total absence up to the lower limit of normal content.

In the cases of gastric conditions other than Carcinoma we find :-

I. Where the Peptic index of stomach contents is 10 units (F & L) and under.

| | Units (F &L) | Units (F & H) | |
|---|---|---|---|
| (1) | 10. | 2'5 | |
| (10) | 0. | '7 and under | - Atrophic Gastritis |
| (11) | 10 - | 1'1 | |
| (12) | 10 - | '9 | |

---

II. Where P - more than 10 units (F & L)

| | | | |
|---|---|---|---|
| (2) | 33'3 | 2. | |
| (3) | 18'2 | 2. | |
| (4) | 20. | 1'4 | |
| (5) | 25. | 1'4 | |
| (6) | 40. | nil. | - albuminuria |
| (7) | 16'6 | 1'1 | |
| (8) | 28'5 | nil | |
| (9) | 50. | 2. | |

The two cases of Chronic Gastritis in which the peptic index of the gastric contents was not examined gave urinary indices of

(1) 2'3 units.

(2) 1'6 units.

In the above series we see that there are two cases with urinary Apepsia, while in one the index is '7 and under - Case (10) Atrophic Gastritis which shewed also gastric Apepsia.

Case (6) which also shewed absence of peptic activity in the urine had 40 units F. & L. in the gastric contents : this patient had albumen in the urine and renal inefficiency might be put down as the cause.

Case (8) had 28'5 units in the gastric contents and nil in the urine. The case was one of nervous trouble and Hysteria with Vasomotor disturbances - flushing and irregular sweating - and it may be that we have got here the result of some nervous effect on the kidneys.

The other cases all had pepsinoegn in the urine in quantities up to normal and in these cases the urinary pepsinogen kept parallel in a general way with the gastric pepsin - this is in contrast with the results found in the series of cancer patients shewn above where without any evidence of renal inefficiency the urinary pepsinogen is present only in small amount or totally absent even when there is a fair peptic index of the stomach contents.

This fact is very striking and deserves further investigation than could be bestowed on it in this short work, and may possibly require animal experimentation. Most recent writers on the subject have explained the phenomenom by putting it down to destruction of the peptic glands of the stomach by cancer directly involving and destroying them. This explanation is perhaps sufficient in cases where there is no pepsin or practically none found in the gastric contents after a test breakfast. Where the quantity is small in the gastric cavity we might find that the small amount of pepsinogen getting into the bloodstream could be very easily destroyed and so the urine shew no peptic activity.

In cases like (5) Table II where the peptic index of the gastric contents after a test meal was 66'6 units and the peptic index of the urine at its highest was only '8 unit and was mostly absent altogether, the theory above enunciated seems hardly sufficient, else whence can so much pepsin find its way into the gastric cavity ?.

The explanation is much more likely to be in the action of an antibody in the blood or in the urine or in both. The demonstration of such an antibody may appear at first sight an easy matter, but this is not so. In the first place the antibody if present must be united with the pepsinogen and only an excess of the latter over the former can be estimated. It seems improbable that Hydrochloric Acid should destroy the antibody and leave the pepsinogen.

The only feasible method of proof seems, to the writer, to lie in an attempt to obtain a cumulative effect.

It has been shewn above that a cancerous urine containing only a small quantity of pepsinogen was able to inhibit to some slight degree the action of a specimen of urine from a healthy individual,

and probably rich in pepsinogen. Making allowance in such a case for any effect possible from the increased dilution - the result to be expected was an increased peptic activity something approaching the sum of the peptic activity of the two specimens. Instead of this, however, it was found that a diminution of peptic activity had taken place and this is probably due to the presence of an antibody in the urine of patients suffering from Cancer of the stomach. The blood and urine of Cancer patients generally have been shewn to be specially rich in Antitrypsin and this is considered by many to be not a true Antitrypsin but a body whose action is to inhibit the action of proteolytic ferment generally. To the writer it seems probable that such is also the case in the matter of pepsinogen in cancer cases.

There is always the possibility that what we are dealing with in urine is not really a proferment - pepsinogen - but a combination of pepsin and the antipepsin which is present in the blood and by combining with the ferment acts as a convoy in its journey through the body. This explanation however is not so probable as that put forward (on page above of this paper) by the writer.

As to the diagnostic importance of these findings we again find ourselves on difficult grounds. Fuld and Hirayama say that in sure cases of Carcinoma of the stomach absence of urinary pepsin seems to be constant. --- More important also the presence of pepsin in the urine in cases of Achylia Gastrica is against a diagnosis of Carcinoma, even if not conclusively.

Takeda [10] agreed also with Fuld and Hirayama and Wilenko that pepsin is always found in the urine in Apepsia Gastrica.

He found that the peptic activity of the urine in Carcinoma depends on the extent and site of the growth - there being less peptic activity in the urine where the pylorus is most affected.

Bieling [11] working with the Ricin method found practically no peptic activity in the urine of advanced Carcinoma Ventriculi but does not regard the sign as of great or constant value in early cases.

The writer believes that an estimation of the peptic activity

of stomach contents after a test breakfast should be a routine procedure and only by this means can we become acquainted with the gastric function in pathological conditions and it is a fallacy to assume that in such conditions free HCl. and pepsin go together, they are absolutely discrete.

I am of opinion also that a fair peptic index in the gastric juice with low free HCl. value is a sign in favour of a diagnosis of early carcinoma of the stomach, though the presence of blood may here be a disturbing factor in inhibiting peptic action.

In cases of Achylia Gastrica and in Anacid and Subacid cases generally we find the pepsin and free HCl. in stomach contents diminishing side by side, and these eventually reach the vanishing point together as in the case of Atrophic Gastritis recorded above.

This has bot been found to be the case in Carcinoma Ventriculi, the peptic activity always remaining if only to a slight degree. This is to be considered essential in the differential diagnosis of these conditions - Atrophic Gastritis and Carcinoma Ventriculi - which is otherwise practically one of the hardest problems of Clinical Medicine.

In the matter of the peptic activity of the urine some observers, as shewn in the few references given above, have claimed by this method to be able to differentiate between Carcinoma Ventriculi and Subacid or Anacid Gastritis from any cause other than Carcinoma.

Thus in Anacid or Subacid Gastritis from any benign cause the peptic activity of the urine has persisted, in other words P has never fallen to nil while the latter state of affairs is the rule in Cancer of the Stomach.

With the object of testing the value of this pronouncement the cases reported here have been selected with the utmost care - cases which were doubtful being rejected unhesitatingly.

In cases of Anacid Gastritis from benign cause it has been shewn above that some peptic activity was always present in the urine. The one case of Atrophic Gastritis gave continuously a very low index - never exceeding '7 unit - but some activity was always present.

Accordingly such a case was most likely to be one of Cancer of the stomach - yet operation shewed there was no cancer present and

from the gastric analyses both before and after operation it was shewn to be a case of benign Achylia Gastrica probably Atrophic Gastritis.

In this case note the complete Apepsia in the gastric contents - a very important factor against a diagnosis of cancer.

Apart from this and from those cases where there was a doubt of the renal efficiency these investigations shew a urinary peptic index of normal or very little reduced from normal in gastric conditions other than Cancer. In cancer cases on the other hand it was invariably reduced - except in one case Table II (4) where the growth was however duodenal.

The presence of these low values is very striking and their constant occurrence should be utilized as an aid to diagnosis. Of course it is not suggested that all cases which have Apepsia of the urine and suffer from gastric symptoms should be put down as Carcinoma Ventriculi, but where the diagnosis rests between Subacid or Anacid Gastritis of benign and malignant origin the presence of a very diminished peptic index of the urine or complete apepsia of the urine with renal efficiency should be an additional signpost on the route to a diagnosis of Cancer.

The fact that even in the most experienced and expert hands, the use of the stomach tube is terrifying to some patients, is sufficient to make us look to any method of enquiry that helps us whereby we can dispense with it. It is to be deplored however that more examinations of stomach contents are not performed even to the discomfort of the patient, and in all cases such as those described the peptic index of gastric contents and urine should be estimated. From a comparison of these two where the kidneys are healthy much can be learned and the writer considers that a moderate index in the stomach or even a fairly low index with alow index in the urine is in favour of diagnosis of cancer. Atrophic Gastritis sufficient to give complete Achylia and Apepsia of the urine must be a very rare condition.

Inefficiency of the kidney must of course as pointed out above vitiate the value of the estimations completely. In cases where there is a doubt as to whether an Apepsia of the urine is due to

kidney inefficiency or not it is useful to perform Wohlgemuth's diastatic estimations as related above. The absence of diastase as well as the absence of peptic function, except in very rare and acutely severe cases of pancreatitis is a sign that the kidneys are at fault and the tests cannot then be relied on.

In time it may be that this difficulty may be circumvented by the use of blood serum instead of urine.

I have to acknowledge here with thanks the courtesy of Dr. W.J. Reid, Director of the Cancer Research Laboratory of the Manchester Royal Infirmary under whose direction the work embodied in this paper was performed.

James M. Scott, M.B.

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