VARIATIONS IN THE HYDROCHLORIC ACID OF THE GASTRIC CONTENTS IN CASES OF CARCINOMA IN MAN

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In the Proceedings of the Royal Society (Series B., Vol. 76, p. 138) Professor Moore published a series of observations which he, together with Messrs. Alexander, Kelly and Roaf, had made on the gastric contents of patients who were suffering from carcinoma situated in various parts of the body. As the result of these observations they came to the conclusion that the well known absence of free HCl in Carcinoma Ventriculi was due to the presence of Carcinoma in the body rather than to its presence in the stomach itself, for they found that the free HCl was very greatly diminished wherever the carcinoma might be situated in the body.

Working on the same lines and using the same methods,² except in a few small details, I have examined fourteen malignant cases and seven non-malignant cases; my results agree very closely with those obtained by Moore and his colleagues and are, I think, worthy of publication as further evidence in support of their conclusions.³ It will be seen in my deductions that the examination of non-malignant cases shows that the effect of diet and residence in a surgical ward considerably influences the gastric secretion and may be largely responsible for the diminution of free HCl in malignant cases.

1. The expenses of these experiments were defrayed by Dr. Pembrey from a sum granted by the Royal Society.

2. Further details and a review of the literature of the subject will be found in a paper to be published in the next volume of the Guy's Hospital Reports, Vol. LX.

3. In a paper published in *The Bio-Chemical Journal* for June, 1906, Moore, Alexander, Kelly, and Roaf incorporate the cases discussed in their previous paper of May, 1905, with a further series of cases. They also point out the influence of diet, etc., on the resulting estimations. My thesis for the M.D. degree, of which this paper is an abstract, was submitted on May 24th, 1906, and accepted on June 14th.

I have also endeavoured to discuss this question from its clinical aspect and have given details of my cases to enable some idea to be formed of the relation of the acidity to the condition of the malignant disease.

ROUTINE OF EXAMINATION

Before the patient was given his test meal he fasted for 14 hours, as by this means it was assured that the stomach was empty ; unless, indeed, its mobility were very much impaired, an unlikely event as the patient examined complained of no gastric symptoms. A light supper consisting of bread and butter and milk or soup was given at 6 p.m., and nothing more was allowed till 8 a.m. the following morning, when the patient was given a slice of buttered toast and a pint of weak tea with a few drachms of milk and a little sugar. This differs from the ordinary test meal given by Ewald in containing more proteid, as he gave no sugar, milk or butter. As my purpose was to estimate the active HCl in the gastric juice and, as Pawlow has demonstrated that plain bread produces a much smaller flow of gastric juice than does proteid, in order to conduct the experiment under more advantageous conditions, I considered it advisable to introduce some proteid into the meal. I avoided, however, the heavy proteid meals advised by some observers, as the organic bases so introduced into the stomach combine readily with the HCl present.

Another of Pawlow's discoveries also influenced me in the choice of a test meal. He proved that gastric secretion varies directly with appetite, as was demonstrated by his well known experiment of feeding a dog by suggestion. Now a more unappetising diet than dry bread and milkless tea cannot possibly be imagined, but the addition of butter and milk increased the patients' appetites and so, therefore, their gastric secretion.

After an interval of an hour and a quarter to an hour and a half the stomach tube was passed, and some of the gastric contents siphoned off. In the majority of cases the mere act of passing the tube was sufficient to cause a gastric contraction which set up a siphon action which, once started, continued for about a minute. It is quite

unnecessary to remove the products of digestion by any aspiration or 'expression,' but occasionally it is difficult to start the syphon action and then a Higginson syringe, with a glass tube fitted into the receiver, can be applied for a few seconds and gently worked until the gastric contents begin to flow in the tube, when the syringe should be at once detached.

The fluid so obtained generally contained but little mucus, and the solid contents were usually finely divided. They were filtered through ash free filter paper—the ash of ordinary filter paper being capable of taking up some of the free HCl. For example, 20 c.c. of a solution of HCl were passed through an ash free paper, when it was found that 5 c.c. required $3.59 \frac{N}{100} \text{NaOH}$ to neutralise; on the experiment being repeated with an ordinary filter paper, 5 c.c. required only $3.41 \frac{N}{100} \text{NaOH}$; thus, for every 5 c.c. passed through it, the ordinary filter paper absorbed $.18 \text{ c.c. } \frac{N}{100}$ more than the ash free paper.

The effective acidity of this fluid was then estimated by measuring the concentration of hydrogen ions present in the solution. This was done by means of the methyl acetate method which estimates the amount of acetic acid produced from the methyl acetate in a given time when it is in the presence of the gastric contents. This method was used by Moore and his colleagues in their investigations, and I have closely followed the technique described by them in their paper in the Proceedings of the Royal Society.

It is not necessary to further describe this technique but I shall point out a few differences which I introduced in the course of my investigation. Moore used a temperature of 45° for the thermostat in which he kept his solutions, and Hoffmann, in his original paper, used higher temperatures still; but the higher the temperature the greater the evaporation, and so I used a temperature of 37°C. , at which the evaporation is almost nil, and thus avoided the necessity for making up the solution to its original volume before titration. Moreover, it is probable that at higher temperatures some of the HCl in combination with proteid is dissociated therefrom, and goes to swell the total free HCl.

As the fluid was yellow or brownish in colour some difficulty was

experienced in judging the exact point of neutralisation, so control solutions were used for comparison in each titration, and as sufficient fluid was not always obtained to provide these controls, the fluid had occasionally to be diluted exactly before estimation, and the results multiplied accordingly. In the table the figures given for titration in cases V, VI, VIII, XV are those actually obtained, and the values of C in the next column, the values for the original solutions, are obtained by multiplying those figures accordingly.

Sex	Age	Disease	Period of Digestion in Hours	Titration with Decinormal Soda and Phenol-phthalein			Period of Incuba- tion = t	Constant of Velocity of Reaction 10°C	Effective Acidity in HCl percentage	
				Initial	Final	Difference = x				
I	M.	56	Epithelioma Linguae	1½	3.3	9.54	6.24	5½	39.820	.1218810
II	M.	56	Epithelioma Linguae	1½	.53	.653	.123	5	.7469	.0022861
III	F.	46	Carcinoma of Colon	1¼	2.31	3.237	.927	5½	5.2061	.0159348
IV	M.	61	Carcinoma Recti	1½	2.188	2.397	.209	6	1.0596	.0032432
V	F.	43	Carcinoma Mammae	1¾	.85	.90	.05	4½	.744 ¹	.0022772
VI	M.	66	Epithelioma of Lip	1½	.053	.124	.071	5	2.1535 ²	.0065914
VII	F.	62	Carcinoma Mammae	1½	.941	1.038	.097	5¾	.5195	.0015901
VIII	M.	48	Epith. Floor of Mouth	1¼	.57	1.507	.937	5	28.9490 ²	.0886070
IX	M.	64	Carc. of Oesoph.	1	.44	.44	.00	5	.0000	.0000000
X	M.	62	Epithelioma Penis	1¼	.194	.33	.136	5	.82613	.0025286
XI	M.	63	Epith. Floor of Mouth	1¼	2.012	2.026	.014	5	.0848	.0002595
XII	M.	57	Epithelioma of Lip	1¼	1.68	1.77	.09	5	.5462	.0016781
XIII	M.	59	Epithelioma Penis	1¼	1.643	1.694	.051	6	.25769	.0007887
XIV	M.	57	Melanotic Sarcoma	1¼	2.702	6.118	3.416	6	18.6091	.0569583
XV	M.	33	Pyo Nephrosis	1½	.254	.288	.034	4¾	1.0847 ²	.0033201
XVI	M.	44	Simple Stricture Recti	1	.91	3.29	2.38	5½	13.8050	.0422543
XVII	F.	29	Chronic Mastitis	1¼	.60	.66	.06	5	.3639	.0011138
XVIII	M.	48	Conjunctivitis and Keratitis	1¼	3.17	4.8	1.63	6	8.5216	.0260830
XIX	M.	29	F.W.M.P.	1	2.19	7.39	5.2	5½	32.2898	.0998300
XX	M.	28	A.S.M.P.	1	2.16	7.09	4.93	5½	30.40321	.0930572
XXI	M.	28	T.W.	1½	2.39	6.69	4.3	6	23.9283	.0732390
Average									.0887087	
N 10 HCl				..	..	..	..	..	119.2543	.365

1. The value of 10°C here given is twice that obtained from preceding columns as contents were diluted twice.

2. " " " " five times " " " " " " " " five times.

In obtaining the various values of the constant velocity of reaction I have used common logarithms instead of the Napierian logarithms used by Moore, so that all the figures in this column are lower than the corresponding figures obtained by him. The figures in the last column are, however, obtained in each case from the *ratio* of the figures in the preceding column and so correspond exactly to the figures obtained by Moore.

The actual titrations were performed with centi-normal soda, and the results expressed in terms of deci-normal.

DISCUSSION OF THE RESULTS

1. Of the thirteen cases of non-gastric carcinoma which were examined only two showed effective gastric acidity to a normal degree. They were a case of epithelioma linguae, in which it was above normal, and a case of epithelioma of the floor of the mouth, in which it was almost exactly normal—where normal is taken as equivalent to the mean of observations taken on three healthy young men.

2. Of the remaining eleven cases, one showed one-sixth the normal effective acidity; while the rest were all below one-fourteenth, most were below one-fortieth, several were below one-hundredth of normal. Thus, in the majority of the cases examined, the effective acidity was very greatly reduced, almost as much as in cases of carcinoma ventriculi. I suspect, indeed, that if a similar series of cases of carcinoma ventriculi were examined by the same method the results would be almost identical.

This would point to the conclusion that the diminution of HCl in cancer of the stomach is due to the presence of carcinoma in the body, and not to the position of that carcinoma in the stomach itself. And so far as my results go they uphold the views of Moore and his colleagues, although exceptional cases occur. It is interesting to notice that in the first series of ten cases which they investigated by this method a case of cancer of the tongue gave the highest percentage, 0.1239, though some of our lowest results also came from cases of tongue and floor of mouth.

3. It is well known that psychical influences play a great part in gastric secretion. Appetite, in the case of Pawlow's dog, increased the secretion of HCl, and a worried man is so often a dyspeptic, that I thought for some time that in this condition lay the solution of the low results which Moore and I obtained. I thought that the dread of approaching operation, or the horror of cancer always present in the lay mind, might cause the diminution. But in case VIII, although the man was extremely worried and harassed, his free HCl was normal, while in case X, the free HCl was one-fortieth of normal, and yet never was there a happier patient or one more free from dread. Psychical influences alone do not seem to be the cause of the diminished secretion.

4. It is interesting to discuss the stage at which carcinoma affects the gastric secretion, and the evidence of my results shows that this change is not necessarily delayed till the later stages of the disease. Only four of my cases could be described as inoperable—I, III, IV, XI, and yet the free HCl in case I was more than normal, and in case III, though much less than normal, yet it was the third highest value obtained. On the other hand, case V, which gave one of the smallest estimations, exhibited a very small growth.

5. In only one case could cachexia be said to exist, and that was a case of oesophageal stricture, the gastric secretion from which contained no free HCl. The majority of patients were healthy so far as one could judge from external appearances, so that cachexia cannot be the direct cause of the diminution.

6. The only case of sarcoma which I examined was one of melanotic sarcoma, probably the most malignant form of sarcoma; and yet it showed nearly normal free HCl, or very much more than eleven out of the thirteen cases of carcinoma.

7. I also examined four patients who were suffering from various non-malignant surgical affections and in two of them obtained very low readings, as low as in most of the malignant cases, while the other two were also less than normal. These cases are not sufficient in number to justify definite statements, but they certainly impair the value of the investigation of stomach contents as an aid to diagnosis,

and suggest that the diet and life in a surgical ward lead to some diminution in the gastric secretion.

8. The almost complete absence of any symptoms of dyspepsia in all my cases was very striking, a phenomenon which Ewald explains by supposing a substitution of intestinal for gastric digestion.

SHORT DESCRIPTION OF CASES

- I Thomas H., 56. A large inoperable epithelioma involving both sides of the tongue. Irritation from a tooth had been noticed for 6 months, but the tumour only 2 months. Much glandular enlargement, but no cachexia or wasting, he looked healthy and had no dyspepsia.
- II William M., 56. A small epithelioma on anterior part of tongue which was easily removed. Six weeks' history—some glandular enlargement. No dyspepsia, does not think he has lost weight.
- III Hannah C., 46. Carcinoma of Hepatic Flexure of Colon involving Peritoneum, which it had been found impossible to remove on laparotomy a few weeks before her stomach contents were examined. She said she had wasted and become paler—slight dyspepsia.
- IV William H., 61. Large definite carcinoma of rectum for which a colotomy was subsequently performed. History of only 3 months' symptoms, and yet radical treatment was impossible.
- V Leah L., 43. A small carcinoma of breast without much glandular enlargement. Only 5 months' history. She looked very healthy and was not at all wasted. Slight dyspepsia.
- VI Thomas G., 66. A small epithelioma of lower lip, which had started as a pimple 7 months before. There were some glands which were found to be inflammatory, and the man was healthy and well nourished.
- VII Hester N., 62. A small carcinoma of the left breast giving a few small glands. 12 months' history. Not wasted.
- VIII Alfred E., 48. Extensive epithelioma involving floor of mouth, lower jaw and submaxillary glands. He was wasted, though there was only a four months' history, and very worried and nervous about his operation which was going to take place on the morrow.
- IX Charles B., 64. An oesophageal stricture which was considered to be malignant—the bougie passing about 12 inches. Swallowing had been painful for about six weeks, and he was very wasted.
- X Henry M., 62. A very large growth at end of penis, which had been growing for 12 months. There was no loss of weight and no cachexia. This man was particularly cheerful—assured me that it was not 'cancer' and that no operation was necessary.

- XI William W., 63. Large epithelioma which involved most of the right side of the floor of his mouth and caused much difficulty in swallowing. Only two months' history, and yet it was inoperable.
- XII Job T., 57. Fairly large epithelioma of the tongue, with a history of two months. There was no wasting and he was a healthy looking man. Operation refused.
- XIII Edwin B., 59. A very large foul epithelioma at end of penis which had been growing for 6 months. There was no cachexia, but he had lost half a stone in 6 months. His general condition was good in spite of the growth, and he denied all symptoms of dyspepsia.
- XIV Charles B., 57. A large melanotic sarcoma which had started growing from a mole on abdominal wall near umbilicus 12 months before, and had already given secondary deposits in the axilla. The man was very fit, not at all wasted, and had no dyspepsia.
- XV Walter S., 33. A large pyonephrosis on the right side, which had produced haematuria for 4 months and frequency of micturition for 2 months. The kidney was thought to be malignant, but operation proved it to be a simple pyonephrosis—probably tuberculous. The man was very healthy in appearance and general condition—appetite good, no dyspepsia, no wasting, and a good colour.
- XVI Richard W., 44. A simple stricture of the rectum, which had given symptoms for 13 years. He was very slightly dyspeptic and had lost 23 lbs. in 6 months.
- XVII Emily F., 29. A case of mastitis following prolonged lactation, the tumour had suppurated and produced several indolent sinuses. Patient was very well, fat, and denied all dyspepsia. After scraping, the breast healed up very well.
- XVIII Richard G. S., 48. A case of conjunctivitis and keratitis with corneal ulcers.
- XIX, XX, XXI. Healthy young men leading an active life.

In the above cases the diagnosis was usually made by the examination of microscopical sections of the growth, but in those cases where it was not possible to examine them histologically, the surgeon's diagnosis has been given. I am much indebted to the Surgeons of Guy's Hospital for their kind permission to utilise the clinical material in their wards.