AN EXPERIMENTAL INQUIRY INTO THE QUANTITY OF VOLATILE ACIDS IN THE STOMACH.

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Of late years the chemistry of the stomach has come to play a very important part in the diagnosis of the different forms of disease that are loosely designated as dyspepsia. Most of the researches, however, have been more or less confined to estimating the quantity of hydrochloric acid, and very little has been done in the quantitative analysis of the organic acids that are formed under certain pathological conditions. It is known, however, that under pathological conditions, even when free hydrochloric acid is entirely absent, the acidity of the stomach may be very great, entirely owing to the formation of volatile acids.

It therefore appeared to be of some interest to make an investigation into the quantity of volatile acids present in the apparently normal stomach contents. Before this research could be carried out it was necessary to find out some method by which the volatile acids could be more or less easily estimated. In the past lactic acid has been that principal organic acid which has drawn the attention of investigators in this line of medicine.

To estimate the volatile acids, however, Hermann Strauss¹ introduced a method by which fresh, unfiltered gastric contents were poured into large sterilised fermentation tubes. These were placed in an incubator at 37° C. for twenty-four hours. The proportional amount present was estimated as follows:

One or more bubbles of gas; very slight fermentation.
Tube filled to one-fifth with gas; slight fermentation.
Tube filled between one-fifth and one-half; moderate fermentation.
Tube filled between one-half and three-quarters; much fermentation.

It is obvious that this method is not very accurate; at the same time, Strauss considered it accurate enough for ordinary clinical work. G. Hoppe-Seyler² believed this method to be misleading, for the gastric contents are under totally different conditions from the normal, and are removed from such modifying influences as the gastric secretion, saliva, and mucus. The other method which has been introduced for the estimation of volatile acids is Töpfer's which was the one advocated by G. Hoppe-Seyler. It consists in titrating the filtered gastric contents with a decinormal solution of sodium hydrate, various indicators being employed. Experimentally we have found this method does not yield very accurate results, for control analysis of the same substance yielded quantities which did not tally with great accuracy. Moreover, the method does not take into consideration the acid phosphates that are normally present in the stomach.

For some six years there has been employed in the Pathological Chemistry Department at University College a method which has yielded very satisfactory results when controls are done, and is sufficiently easy for clinical work. The following is a description of the method with some of the results obtained in apparently normal gastric contents:

Method for Estimating Total Volatile Acids in the Gastric Contents.

Gastric contents were in all cases obtained by means of the ordinary soft stomach tube one hour after the patient had taken Ewald's test breakfast. A certain quantity—preferably about 25 c.cm.—of unfiltered gastric contents are poured into a distillation flask; about 100 or more c.cm. of water are then added, and a current of superheated steam is driven through the flask, and a small flame is placed underneath it. The steam, raising the contents to boiling point, drives off the volatile acids, which distil over through a condenser into an Erlenmeyer containing about 10 c.cm. of a decinormal solution of sodium hydrate. After about thirty minutes the Erlenmeyer is removed, and after the addition of a few drops of neutral litmus solution the sodium hydrate solution is titrated with a decinormal solution of sulphuric acid. The quantity of decinormal sodium hydrate neutralised by the volatile acids is thus obtained. Multiplying the number by four,

if 25 c.cm. of gastric contents were taken, will give us the percentage of volatile acids in the gastric contents. This method is somewhat similar to the method employed originally by von Mering and others, in which the gastric contents with water are distilled, and when boiled down to about one-third fresh water is added, and again boiled to a third, and this process repeated some four or five times, the volatile acids being collected in a titrated sodium hydrate solution.

By von Mering's method possibly the same accuracy can be obtained, but when it was employed by one of us it was not found to be extremely accurate. In our method is the danger, as in von Mering's, that on heating the gastric contents not only the volatile acids will be distilled over, but possibly some of the organic matter, as proteids or fat, may be broken up by the superheated steam, and lead to a too high quantity of volatile acids. At the same time even if this is the case, the quantities broken up when control analyses are done, are equal.

For the purpose of showing the accuracy of this method we here give results of four analyses taken at random (Table I),

TABLE I.—Showing the Accuracy of the Method Employed for the Quantitative Estimation of the Volatile Acids, and the Total Percentage Volatile Acidity Expressed in C.cm. of $\frac{1}{10}$ N. Na OH.

1	...	...	3.6	...	...	2.8 control.
2	...	...	3.2	...	...	2.8 "
3	...	...	7.0	...	...	7.5 "
4	...	...	7.0	...	...	7.0 "

two being with small quantities of volatile acids and two with large. To determine how the volatile acids vary under apparently normal conditions, thirty-six examinations were made on apparently normal individuals; that is to say, patients who were free from all stomach symptoms.

TABLE II.—Showing the Amount of Volatile Acids in 36 Analyses in which the Stomach Contents appeared normal.

Total percentage Volatile Acidity expressed as C.C. of 1 to 10 N NaOH.											
1	...	2.00	10	...	4.0	19	...	5.00	28	...	6.40
2	...	2.20	11	...	4.0	20	...	5.00	29	...	6.40
3	...	2.40	12	...	4.2	21	...	5.00	30	...	7.50
4	...	2.40	13	...	4.4	22	...	5.25	31	...	7.50
5	...	2.80	14	...	4.7	23	...	5.25	32	...	7.50
6	...	3.00	15	...	4.8	24	...	5.50	33	...	9.13
7	...	3.00	16	...	5.0	25	...	5.75	34	...	10.30
8	...	3.20	17	...	5.0	26	...	6.00	35	...	11.00
9	...	3.25	18	...	5.0	27	...	6.30	36	...	11.00

In Table II the analyses are placed together, graduating them from the lowest amount to the highest, and it is seen that the percentage of volatile acids varies from 2 to 11 c.cm. of decinormal sodium hydrate. It would therefore seem to follow that in the normal stomach there is a certain amount of fermentation going on which leads to the evolution of volatile substance, since the diet and the period after taking food in all cases were the same.

The next question to decide was whether the quantities of volatile acids found in these thirty-six analyses were influenced by anything in the chemistry of the stomach.

The method employed for the estimation of the hydrochloric acid was that of Prout-Winter, by which it is possible to estimate not only the free hydrochloric acid, but also that combined with the proteids, and the hydrochloric acid present as salts. Other methods which have been introduced for this work, such as Töpfer's, have in our hands not proved nearly so accurate. To show the accuracy of this method the following results (Table III), obtained in

TABLE III.—Showing the Accuracy of the Prout-Winter Method.

No.	Total HCl.	Free HCl.	Proteid HCl.	Mineral HCl.
1	0.32 0.31 (control)	0.020 0.010 (control)	0.23 0.23 (control)	0.070 0.070 (control)
2	0.32 0.32 "	0.020 0.020 "	0.25 0.24 "	0.050 0.050 "
3	0.30 0.28 "	0.006 0.006 "	0.27 0.25 "	0.025 0.025 "
4	0.32 0.31 "	0.004 0.007 "	0.27 0.27 "	0.050 0.040 "

four analyses taken at random from our notebook, are given. By other methods we have used we have never obtained any results that so closely tallied.

In the next experiments, not only is the total (free) proteid and mineral hydrochloric acid separately given, but as both the hydrochloric acid loosely combined with the proteids and that in the free state are capable of acting in digestion, these two are given together in a separate column. As far as the volatile acids are given, this acidity is expressed in c.cm. of one-tenth normal sodium hydrate solution.

In Table IV the examination of normal gastric contents in which the motility of the stomach was proved to be normal, shows (in group A) those cases in which the volatile acidity was less than 5 c.cm. We see that the volatile acidity really varied from 2 c.cm. to 4.8 c.cm., and the total hydrochloric acid, as well as the free and combined, varied very considerably.

In the next group, B, comprising eight experiments, the volatile acidity was more than 5 c.cm. Here were also great variations, from 5.5 c.cm. to 11 c.cm. of volatile acids being

TABLE IV.—Normal Gastric Secretion and Motility.

Group A.—Results of Nine Examinations in which the Volatile Acidity was below 5.

	Total HCl.	Free HCl.	Proteid HCl.	Mineral HCl.	Proteid + Free HCl.	Volatile Acidity in c.cm. $\frac{1}{10}$ N. NaOH.
1	0.350	0.016	0.270	0.050	0.296	2.0
2	0.320	0.020	0.245	0.050	0.265	2.2
3	0.320	0.020	0.240	0.000	0.260	2.4
4	0.340	0.006	0.260	0.070	0.266	2.4
5	0.315	0.020	0.265	0.029	0.285	3.0
6	0.315	0.015	0.230	0.070	0.245	3.2
7	0.360	0.022	0.260	0.080	0.282	4.0
8	0.325	0.037	0.245	0.040	0.282	4.7
9	0.305	0.006	0.270	0.045	0.276	4.8
Average	0.328	0.019	0.254	0.055	0.273	3.2

Group B.—Results of Eight Examinations in which the Volatile Acidity was above 5.

	Total HCl.	Free HCl.	Proteid HCl.	Mineral HCl.	Proteid + Free HCl.	Volatile Acidity in c.cm. $\frac{1}{10}$ N. NaOH.
1	0.320	0.007	0.280	0.0350	0.287	5.5
2	0.325	0.010	0.260	0.0400	0.270	5.5
3	0.275	0.030	0.218	0.0370	0.248	6.4
4	0.285	0.007	0.220	0.0550	0.227	7.5
5	0.335	0.015	0.265	0.0500	0.280	7.5
6	0.305	0.006	0.255	0.0400	0.261	7.5
7	0.290	0.006	0.260	0.0250	0.266	10.3
8	0.310	0.004	0.235	0.0650	0.249	11.0
Average	0.305	0.012	0.249	0.0430	0.261	7.6

present; but only on two occasions was there more than 7.5. The hydrochloric acid, however, also showed a tendency to fluctuate. If the average of the two groups be compared it will be seen that the volatile acids have an average of 3.2 in the first case, and 7.6 in the second. It would seem that when the quantity of hydrochloric acid is high, the quantity of the volatile acids tends to be low. This is well brought out on comparing the free hydrochloric acid or the free and proteid together so that one would be led to believe from these averages that deficiency of hydrochloric acid tends to cause an increased formation of volatile acids in the stomach, agreeing with Hoppe-Seyler and Bunge. We now turn to a group in which the chemical composition of the stomach contents was found practically normal, belonging to slightly neurotic persons who suffered from no gastric symptoms whatsoever, yet the gastric motility was distinctly diminished, so that the stomach, instead of emptying itself after Leube's test meal in from four to six hours, took from seven to eight or even nine hours. Here again the table is divided into two groups, one in which the volatile acid is below 5 and the other in which it is above 5.

TABLE V.—Normal Gastric Secretion: Motility Diminished.

Group A.—Results of Five Examinations in which the Volatile Acidity was below 5.

	Total HCl.	Free HCl.	Proteid HCl.	Mineral HCl.	Proteid + Free HCl.	Volatile Acidity in c.cm. $\frac{1}{10}$ N. NaOH.
1	0.319	0.016	0.167	0.136	0.183	2.8
2	0.285	0.011	0.176	0.099	0.187	3.0
3	0.280	0.007	0.160	0.110	0.167	4.0
4	0.329	0.033	0.186	0.109	0.219	4.2
5	0.348	0.041	0.182	0.124	0.223	4.4
Average	0.312	0.022	0.174	0.115	0.196	3.7

Group B.—Results of Five Examinations in which the Volatile Acidity was above 5.

	Total HCl.	Free HCl.	Proteid HCl.	Mineral HCl.	Proteid + Free HCl.	Volatile Acidity in c.cm. $\frac{1}{10}$ N. NaOH.
1	0.390	0.020	0.250	0.120	0.27	5.20
2	0.319	0.011	0.207	0.101	0.218	5.75
3	0.276	0.016	0.168	0.092	0.184	6.30
4	0.379	0.020	0.254	0.105	0.274	9.13
5	0.390	0.020	0.270	0.100	0.290	11.00
Average	0.351	0.017	0.229	0.104	0.247	7.47

In Table V (Group A) the results of five analyses are given, and it is seen that the volatile acidity varies from 2.8 to 4.4 c.cm. of 1 in 10 normal sodium hydrate—that is to say, an average of 3.7—very closely corresponding with what we found in the cases of normal motility. In Group B, showing the result of five analyses with an acidity above 5.0, we find that it varies from 5.2 to 11.0 c.cm., yielding an average of 7.47. On comparing these averages, we find that in this case the lowest volatile acidity corresponds with the smallest amount of total hydrochloric acid, and is apparently contradictory to the former results (Table IV).

In Table V, with an average volatile acidity of 3.7 c.cm., the total hydrochloric acid is only 0.312, while with an average volatile acidity of 7.47 it was no less than 0.351. At the same time, when one compares absolutely free hydrochloric acid one finds that the smallest volatile acidity occurs with the largest amount of free hydrochloric acid—0.022 as against 0.017. So that, although at first sight this table seems contradictory to the other, this is not quite the case. In both groups the volatile acids vary in proportion to the amount of free hydrochloric acid.

TABLE VI.—Delayed Motility Due to Migraine.

	Total HCl.	Free HCl.	Proteid HCl.	Mineral HCl.	Proteid + Free HCl.	Volatile Acidity in c.cm. $\frac{1}{10}$ N. NaOH.
1	0.330	0.010	0.270	0.050	0.280	16.0
2	0.310	0.014	0.235	0.065	0.249	11.0
3	0.335	0.015	0.265	0.050	0.280	8.0
4	0.345	0.042	0.225	0.080	0.267	6.0
Average	0.330	0.020	0.249	0.061	0.269	10.0

Before concluding we desire to give in the following table the results of four observations on a stomach which had been frequently examined previously, and found that its secretion and motility were normal. On these four occasions when

there was some nausea and migraine it was found that the motility of the stomach was very markedly delayed.

In this case (Table VI) we see that although the stomach contents, as far as hydrochloric acid was concerned, were practically normal, the volatile acidity on the contrary was very markedly increased; in fact, the average was not less than 10, and in one examination the volatile acidity was as high as 16. We thus see that in a normal stomach during an attack of migraine, when the motility, no doubt from purely nervous causes, is delayed without any corresponding diminution in either the quantity of the free or proteid hydrochloric acid, there is a distinct increase in volatile acids.

In conclusion we can now briefly consider what appears to have been brought out. In the first place there is a method of estimating the volatile acids that is sufficiently simple, and at the same time accurate, as to be of value in the quantitative analysis of the stomach contents for clinical purposes.

The possible fallacy of the breaking up of proteids, etc., by the superheated steam leading to an increased quantity of volatile acids over that which ought really to be found, can apparently be negatived, in that in the first place the diet in all cases was exactly the same, and the period of time allowed after the tea and toast had been taken being exactly the same, one would expect, all things being equal, the amount of proteids would not vary very much, and in the next place, which is well borne out in Table I, the method yields results in the four control analyses, given in the table, which correspond so closely that for all purposes of comparison they are similar.

It is seen that the apparently normal stomach contains a certain amount of volatile acids, but so long as the quantity of free hydrochloric acid secreted by the stomach is sufficient and the gastric motility is not interfered with, this quantity averages not over 3.2. If, however, the free hydrochloric acid is decreased from any cause, even in spite of the motility being normal, the volatile acidity averages 7.6.

When we turn to cases in which the gastric secretion is apparently normal, although the motility is diminished, we find here that with a small excretion of hydrochloric acid the average is 3.7 of volatile acids, that is slightly higher than the average with normal motility, while when the free hydrochloric is low the volatile acids average 7.47.

In a case of migraine, where the chemical composition of the stomach is little altered as far as hydrochloric acid is concerned; in consequence of delayed motility there was a tendency to an increase in volatile acidity. So that these experiment with a more accurate method of estimating the volatile acids than others that have been employed, confirm the results of G. Hoppe-Seyler, etc., that the quantity of free hydrochloric acid influences the quantity of volatile acid in the stomach. The practical value of this in the treatment of stomach cases is, therefore, too apparent to need any comment.

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CASE OF MALIGNANT ŒDEMA: AMPUTATION AT THE THIGH: RECOVERY.

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IN a recent number of the BRITISH MEDICAL JOURNAL Drs. Tubby and Wright gave a most instructive account of a disease which they rightly say is nowadays very rare, namely, malignant œdema. They state that as they could not obtain any antitoxin for malignant œdema they decided to use the antistreptococcic serum, and they say "it is difficult to explain the *modus operandi* of the injections of the antistreptococcic serum except on the supposition that the presence of the streptococcus is essential to the rapid development of the bacilli of malignant œdema." I would suggest that the antistreptococcic serum had little or nothing to do with the happy ending of their case. For when one bears in mind the characteristics of the bacillus of malignant œdema, that it is an anaërobic organism, we can at once see that in free oxygen we have an antidote to its growth, the value of which is far greater than can be that of any antitoxin. The fact that the

bacillus was not found in the discharge on the gauze is not to be wondered at, because, as they state, it does not usually appear in the blood till some fifteen or twenty hours after death; moreover, the wound, I take it, had been carefully washed with an antiseptic solution.

CASE I.—A healthy boy, aged 11, fell off a truck at a brickyard; the wheel of the waggon passed over his right leg in such a way that all the soft parts were peeled off the tibia from the ankle to the knee, and the freshly-cut tissues seem to have been rubbed along the surface of the ground. The boy was carried some three miles from the scene of the accident to my house. He was almost unconscious from loss of blood and shock when I saw him. The wound was carefully washed with 1 in 2,000 perchloride solution and the parts brought together by wire sutures. Constant irrigation was applied; but within twenty hours the foot showed signs of gangrene, which spread up the leg most rapidly. Dr. Anson saw the case with me about eight hours later, and by that time the skin was quite brown and emphysematous, and cracking could be felt as high up as the eighth rib on the right side. The boy was quite collapsed and unconscious. The limb was much distended with gas, and as the stitches were cut through the characteristic smell of malignant œdema was very apparent. An hour was allowed to elapse in order to see if any amelioration of the symptoms would take place; then amputation was decided upon, not with much hope of saving his life, but rather that he should not die without something being done. There being a small patch of uncoloured skin on the inner aspect of the thigh, I at first thought of doing an amputation at the hip; but, as there would not have been sufficient sound tissue to cover the wound, we decided to simply cut away the dead part, and I amputated about 2 inches above the knee. As indicating the condition of the parts, I may say that there was not the slightest bleeding, and I did not require to tie any vessels. The boy passed a bad night, and on two occasions seemed about to die, but the free exhibition of brandy by the bowel pulled him through. Within ten hours the emphysema disappeared from the chest and abdomen, and three days later, with the help of Dr. Anson, I did an amputation 2 inches higher up, in order to get a good flap. There was rather free bleeding at the second operation, but the boy made an uninterrupted recovery, with this exception, that the ligature on the femoral cut its way through, and I had to tie it higher up. He is quite well now, and has a very good stump.

In the fact that the bacillus is an anaërobic organism lies one of the great difficulties of cultivating it unless we have an apparatus by which pure hydrogen can be poured over the colony. I managed to raise a weak colony by sinking pieces of tissue deep in the nutrient media to which I added some glucose to act as an absorber of the oxygen. A small portion of this was injected into two guinea-pigs with the result that death took place in about 48 hours, with all the symptoms of malignant œdema. A solution was made of the soil from the place of the accident, and a portion of this was injected over the inside of the thigh of another guinea-pig. This again caused death in 44 hours, with the usual *post-mortem* signs of malignant œdema. The fact that we had to deal with an organism which can only thrive in the absence of oxygen accounts fully for the great and immediate benefit which resulted from the removal of the dead part of the limb and the consequent exposure of the stump to pure air. Reasoning back, I should advise the free use of hydrogen peroxide in the treatment of such a case, because the liberation of free oxygen would be offering the bacillus of malignant œdema the very set of conditions under which it cannot exist.

MEMORANDA:

MEDICAL, SURGICAL, OBSTETRICAL, THERAPEUTICAL, PATHOLOGICAL, Etc.

THE DANGERS OF CHLOROFORM NARCOSIS.

It is a decided mistake to think that death or threatened death from chloroform must always be from the same cause, as a matter of fact this is not so. When lecturing upon this subject in Queen's College it is my custom to include under the "dangers" of anaesthetics six heads:

1. Sudden death at the beginning of inhalation ascribed to "irritation of the peripheral nervous system, accumulation of CO₂ in the blood, and stoppage of the heart." Bartholow says that in his opinion it is due to the fact that the first chloroform inhaled which reaches the cardiac ganglia paralyzes them, they being in an abnormal state of susceptibility from certain undefined causes.

2. Epileptiform syncope, described by Richardson. Death in this case is due to tetanic rigidity of the respiratory muscles, prior to muscular relaxation, consequently interfering with the pulmonary circulation, with venous engorgement and stoppage of the heart. In this case respiration ceases before the heart beats.