AN EXPERIMENTAL INQUIRY INTO THE PATHOLOGY OF GASTRIC TETANY.*

BY

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"GASTRIC TETANY," or tetany associated with dilatation of the stomach, has in recent years received considerable attention. This has been due not merely to the rarity of the complaint, but also to its high mortality, and to the vague nature of its etiology and pathology. The association of this nervous disorder with dilatation of the stomach was first described by Newman¹ in 1861, and shortly afterwards by Kussmaul,² and from that time up to the present frequent communications have been made on this subject. Most authors, however, have confined themselves to the minute description of cases, and few have made observations of an experimental nature so as to throw light on the causation of this obscure malady. We have recently had the opportunity of examining the gastric contents from a case of tetany with dilatation of the stomach, and of observing the results after their injection into animals.

We publish these results as we believe them to be of pathological importance, not because we desire to draw positive conclusions from a single case, but rather to indicate some of the lines of research which should be followed in the future.

I.

We have to acknowledge our indebtedness to Dr. Finlayson, of Glasgow, for giving one of us the opportunity of seeing this case, and for allowing us to experiment with the vomited matter. We regret, however, that we were unable to obtain the vomited material during the tetanoid seizure. The contents were procured during a partial convalescence.

The patient was a gentleman about middle life who had suffered from "his stomach" for fully fifteen years. Within the last few years he had experienced severe pain after food, which was, as a rule, relieved by the vomiting of a large quantity of sour-smelling material. He had consulted various physicians of note, and from their reports it was found that hydrochloric acid was seldom present in excess. On one examination it was absent, but it was generally normal in amount. Sarcinae were usually present, but in various samples they were absent. He had gastric ulcer when a young man. For the last three years he has used the stomach tube two or three times a day.

The onset of his present illness was sudden, and apart from a severe frontal headache and a tingling and numbness of his fingers, he was in his usual health except for some undue constipation. He had been taking no liberties with his diet, nor had he indulged in any way in alcoholic beverages. He is totally unaware of the cause of this recent illness.

When first seen he was semi-conscious, but soon he passed into a state of coma which lasted for fully thirty-six hours. By the use of drastic medicines and injections high up into the bowel an evacuation was obtained which quickly caused the nerve symptoms to abate. The hands and fingers were in a state of contracture, forming the usual and characteristic appearance of the "accoucheur's hand." The hands were equally affected on the two sides, but the feet were free. There were no spasms of the hands and fingers (as is so often the case), but a long continual cramp or contracture which lasted during the whole period of unconsciousness. After the contracture abated the cardinal signs of Erb, Trousseau, and Chvostek could not be elicited. The heart and lungs were normal. The stomach was markedly dilated, the greater curvature passing well down below the umbilicus. The peristaltic wave was readily obtained. The urine during the tetanoid seizure contained a trace of albumin and also acetone. After the cessation of the spasm, these substances passed away and gave place to a trace of sugar. The specific gravity

averaged 1028. The vomit contained acetone, hydrochloric, acetic and butyric acids, but no sarcinae.

The following note we have from Dr. Finlayson:

After recovering sufficiently to return to his home in England the patient was operated upon by-and-by, apparently with great success; his appearance and his report in February, 1901 (a few months after his illness), when he showed himself to Dr. Finlayson, was very satisfactory in every respect.

II.

This case presents several interesting features:

(a) The dilatation of the stomach resulted most probably from the cicatrization of an old-standing gastric ulcer causing pyloric stenosis. Hydrochloric acid was found in excess in only one previous examination. It was once absent, but as a rule it was present in almost normal proportion. Sarcinae were not always present in the contents, although they were frequently found. The chemical condition of the gastric contents may in part be accounted for by the prolonged use of the stomach tube. The patient remembers having had tingling and creeping sensations along the arms and down to the finger-tips, associated with headache and often a feeling of nausea. We believe that these were the premonitory symptoms of tetany, which were prevented from increasing in severity by gastric lavage. We have frequently observed cases of dilated stomach, or even cases of distension of the stomach associated with hyperacidity due to hydrochloric acid, where these premonitory symptoms were present, and we believe that in all such cases gastric lavage should at once be performed.

(b) Associated with a strong clonic contracture of the arms and hands there was complete loss of consciousness for thirty-six hours. Although the leg muscles were not affected, we think that this case might well be classed with those of the third degree of Bouveret and Devic,³ where symptoms resembling an epileptic attack with unconsciousness and coma are present, without, however, any convulsive phenomena. This form is not so grave as that of the second degree, when the tetanic contractures are more or less general, often without loss of consciousness, but where the muscles of the thorax become involved in the contracture, and death from asphyxia results.

(c) Albumin was present in the urine during the tetanoid seizure, while it completely disappeared after its cessation. Albuminuria has been noted by many observers in gastric tetany. In some cases a chronic nephritis was discovered *post mortem* (Trevelyan),⁴ while in others the kidneys were healthy (Dreyfus Brissac,⁵ Muller,⁶ Loeb⁷). We consider that the presence of albumin in the urine during the tetanoid seizure, with its disappearance after the attack has abated, is an indication of the severity of the storm, the albuminuria being caused by an irritation of the parenchyma of the kidney by the poison circulating at the time in the blood. We are not disposed to entertain the idea of uræmia being the cause of the tetanoid seizure, although Jurgensen⁸ has recently described such a case. Acetone was present in small quantity in this patient's urine. Biscaldi⁹ describes a case of tetany where acetone was found in the urine, and which was considered by him to be the cause of the disease.

Numerous investigations have been made on the urine in such cases. Fenwick¹⁰ discovered sugar in the urine, while Ewald and Jacobson,¹¹ and later Albu found an alkaloidal substance, which they described as a picric salt, and to which they attributed the cause of tetany. Oddo and Sarles¹² found indican, while Gumprecht¹³, after a series of elaborate investigations, found that the urotoxic co-efficient was increased in certain cases of tetany. He was unable, however, to separate the poison in such cases from the urine, so that his results were for the most part negative.

(d) In our patient the tetanoid seizure passed off, and during the interval of convalescence he underwent an abdominal operation. Since the operation he has been well, and he has had no return of the tetanic symptoms. Operations in such cases were clearly put before us a few years ago by Mayo Robson¹⁴. After a series of operations he was able to state definitely that an immediate operation of the nature of a pylorotomy or a gastro-enterostomy relieved the symptoms, and prevented the recurrence of this grave disorder. We believe that such treatment, by preventing the retention of food stuffs in the stomach and consequently preventing their ab-

* In the following paper Dr. Halliburton is only responsible for the experiments recorded.

sorption into the blood, will be a radical means of curing this malady, and thus allow tetany to become a curable disease.

We would advocate, however, such operative intervention before the disease has manifested itself in the form of a nervous disorder, provided that those nerve symptoms

Fig. 1.—Fall of arterial blood pressure and slowing of heart in cat produced by injection of fluid from a case of tetany prepared as described in the text. The time tracing indicates seconds. In subsequent figures where the time tracing is omitted, the rate of movement of the blackened paper was the same as in this one. The raising of the abscissa (lowermost line) indicates the period during which the injection took place. This and all subsequent tracings read from left to right.

Fig. 2.—Injection of the same amount of the same fluid after the two pneumogastric nerves of the cat had been cut.

deeply coloured brown, but gave no spectroscopic bands. This fluid was evaporated once more to dryness, but on this occasion the residue was taken up with normal saline solution. After filtration the solution was used for injection experiments. The original tetany fluid had a strong chloroform smell, was extremely acid, and the substance or substances which we investigated were odourless and soluble both in alcohol and physiological saline solution. We did no experiments with the insoluble residues or volatile materials.

IV.

This tetany fluid then, prepared as above, was injected into an animal.

Experiment A.

A cat was anaesthetised with A.C.E. mixture, and 5 c.cm. of the saline solution were injected into the external jugular vein; this was equal to 20 c.cm. of the original gastric fluid. No spasms or convulsions were produced; whether these would have occurred had not the animal been anaesthetised it is impossible to say. We are inclined to believe, however, that the alcoholic extract was weak, owing to its having been prepared from gastric fluid after the ces-

do not abate under gastric lavage. Moreover, it appears to us that all cases of gastric dilatation with a history of gastric ulcer should be operated on without delay, when the possibility of such a complication is imminent.

III.

The contents of the stomach from this case of gastric tetany were prepared in the following manner: The gastric contents were emptied into a beaker, and to them was added six times their volume of rectified spirit. The mixture was allowed to stand for twenty-four hours and then filtered; the filtrate was evaporated on a water bath to dryness. The residue was taken up with alcohol, filtered, and the filtrate a second time evaporated to dryness. This process was repeated twice more. The fluid was still

Fig. 3.—Injection of the same amount of fluid after neutralisation in another cat.

sation of the tetanoid seizure during the convalescence of the patient. As will be seen from the tracing (Fig. 1) there was considerable heart slowing and a large fall of arterial pressure (taken from the carotid with mercury manometer).

The pressure slowly recovered its original height, but the heart beat faster than before the injection. After the blood pressure had regained its original force, the vagi were cut, and soon after 5 c.cm. of the tetany fluid were again injected. The result showed an almost negative response (see Fig. 2).

The main fall of blood pressure was therefore due to an action on the cardio-inhibitory centre, though whether the action on the centre was direct or reflex we cannot say. The fluid was acid, giving the colour tests for hydrochloric, but not for lactic acid. The amount of total acidity reckoned as hydrochloric acid, estimated by titration with standard alkaline solution was = 0.115 per 100 c.cm. of original gastric contents.

Experiment B.

In view of the question whether the acid substance or substances might cause the fall in blood pressure, the original tetany fluid was injected as before into the external jugular vein, after neutralisation (Fig. 3).

The injection only produced a slight fall of pressure, which may be due to the fact that potash was used for neutralisation instead of soda. After section of the vagi there was a similar slight effect as a result of the injection. Some acid substance, then, we take it, appears to be responsible for the marked fall of pressure in the first tracing.

V.

Bouveret and Devic,¹⁵ in their inquiries, injected solutions of hydrochloric acid into animals. They commenced with a solution of 0.1 per cent., but made observations with solutions up to 0.9 per cent. Solution 0.1 per cent. caused a fall of temperature from 39.3° to 38.6°, but the animal was little affected by the injection. Solution 0.6 per cent. caused a fall of temperature from 39.3° to 37.8°, but likewise caused no grave symptoms. Solution 0.9 per cent. caused general convulsions and death. The temperature rapidly fell from 38.6° to 37.6°. At the necropsy a sero-sanguineous discharge was found in the peritoneum. They found that the dose of hydrochloric acid which causes death is 0.40 per kilogramme of the weight of the animal. Their researches then proved that hydrochloric acid, when present in fairly normal proportions (0.2 to 0.3 per cent.), if injected into the vein of an animal, caused little disturbance.

We made experiments to see the effects of the injections of free hydrochloric acid of the same strength as that of the tetany fluid:

Experiment C.

The animal was anaesthetised as before, and 2.5 to 10 c.cm. of HCl. of strength 0.2 to 0.4 were injected into the external jugular vein (Fig. 4).

Fig. 4.—Effect of injecting 0.2 per cent. hydrochloric acid. The upper tracing was the result of an injection of 2.5 c.cm., the lower tracing of 5 c.cm. The abscissa is not shown, but the height of the tracing above it was about the same as in Fig. 5.

There is an insignificant fall of pressure, which is not abolished by section of the vagi.

It therefore appears to us to be clear from the results of these three experiments that the tetany fluid contained a substance much more poisonous than the hydrochloric acid itself, but which was distinctly acid in reaction.

VI.

The results obtained by the injections of pepsin and peptones into the blood have been studied by various physiologists,¹⁶ but these substances do not produce convulsions or tetanoid contractions, except when injected in very large doses. We did not repeat these experiments, but we are satisfied that the symptoms produced by these substances are different from those produced by the tetany fluid. Certainly

no peptone or pepsin was present in the fluid we injected, because it had been so repeatedly treated with alcohol. Alcohol itself does not produce convulsions when injected into animals. Bouveret and Devic¹⁷ found that a dose sufficient to kill an animal produced narcosis without convulsive phenomena. The fluid we injected was free from alcohol.

To conclude our research we injected into animals the gastric contents obtained from patients in health or suffering only from mild dyspepsia. (Experiments D and E.) The gastric contents were prepared in exactly the same manner as above, so that 5 c.cm. of the solution injected corresponded to 20 c.cm. of the original gastric fluid.

Experiment D.

The acidity of the vomit was 0.06 free HCl. The animal was anaesthetised as before. Injections were made before and after sections of the vagi. (See Fig. 5.)

Fig. 5.—Effect of injecting the same amount of fluid from a case of mild dyspepsia.

The effect is an insignificant fall of arterial pressure (Fig. 5) whether the vagi were cut or not.

Experiment E.

The acidity of the vomit was 0.13 free HCl. Four experiments were performed in this case. 1.5 c.cm. of the fluid (= 20 c.cm. of the original normal gastric contents) were injected into the animal, with the result that there was a slight fall of blood pressure, accompanied by the expansion of the intestinal blood vessels. (See rise of intestinal plethysmogram. Fig. 6.)

Fig. 6.—Effect of injecting the same amount of fluid from another case of mild dyspepsia. The slight fall noticed here and in Fig. 5 is about equal to that produced by dilute hydrochloric acid. The upper line is the intestinal plethysmogram; expansion of vessels is seen; dilute hydrochloric acid causes the same vascular dilatation. The abscissa of the blood pressure is omitted.

2. 5 c.cm. of 0.2 per cent. HCl were injected, giving a result almost similar to the above.
3. Vagi were cut, and 5 c.cm. of 0.2 per cent. HCl was injected, causing a rather more pronounced fall in blood pressure than in 1.
4. After vagi were cut, 5 c.cm. of gastric fluid were injected, with result similar to 3.

In these experiments the intestinal plethysmograph of Edmunds¹⁸ was used to ascertain whether the fall of blood pressure in these cases was due to dilatation of the splanchnic blood vessels.

This apparatus has the advantage over the plethysmograph of Bayliss¹⁹ and that of Hallion and François Frank,²⁰ in that the oncometric medium is air instead of oil or salt solu-

tion. In these experiments there was a rise of the plethysmograph with each fall of pressure which indicated vascular dilatation, the result, we have no doubt, of the acid in the gastric fluid.

VII.

The pathology of gastric tetany has given rise to much speculation. Some observers have confined their attention to the alterations in the cerebro-spinal system, but their investigations have been for the most part negative. Slight alterations of brain structure have been observed, with thickenings of lining membranes and inflammatory exudations, but the changes in themselves cannot account for the nervous symptoms of tetany. The theory of dehydration of the tissues generally, from the constant bouts of vomiting and from the permanent hypersecretion of the gastric juice into the stomach, has now been discarded. The reflex theory likewise receives little support from recent investigations.

We are convinced that the only plausible theory is that of autointoxication. A poisonous substance is formed in the stomach, which, when absorbed into the blood stream in sufficient amount, gives rise to the tetanoid contractures and other concomitant symptoms which are well known in this disease.

Bouveret and Devic²¹ uphold this view, and although their results have not been confirmed by some other observers, we think that their elaborate investigations have done much to clear up the uncertain prevailing ideas on this affection. Their results are briefly as follows: they associate this form of tetany to that condition of the stomach in which there is a constant hypersecretion of gastric juice. Tetany, they say, results from an autointoxication, the poisonous substance or substances being produced by a chemical change in the stomach in presence of excess of hydrochloric acid.

They differ from Brieger,²² who considers that a peptotoxin is produced in the normal peptonisation of proteids, but they believe that in the presence of alcohol such a substance can be obtained. They found that the introduction of this peptotoxin, so prepared, caused violent tetanic convulsions of a nature precisely similar to those observed in man, and if introduced in weaker doses produced the ordinary contractures of tetany. They believe that in a dilated stomach, where there is an excess of free acid, this peptotoxin can be obtained, which when injected into animals causes convulsions. They proved this on several occasions. They do not know the nature of this peptotoxin, but they do not consider it to be either an ethylamine hydrochlorate or an ethylene-diamine. They believe it to be a form of syntonin to which new properties have been added by the action of alcohol.

Gumprecht²³ declines to believe that autointoxication is the underlying cause in such cases, as he has failed to produce convulsions in animals by intravenous injection, although he has been able to separate an albumose which had toxic properties, but which he could not discover in the urine.

Ewald²⁴ has recently described a case where there was an entire absence of hydrochloric acid; and Sievers,²⁵ after making a survey of 27 cases, believes that hyperchlorhydria is not essential for the causation of gastric tetany.

We have found that a toxic substance existed in the stomach in the case under consideration, which when injected into an animal produced a marked fall of blood pressure and slowing of the heart beat. This substance was not present in the normal gastric contents of health; and, moreover, after neutralisation of the tetany fluid, practically no fall of pressure was obtained. We do not know what this toxic substance is; it has a marked acid reaction. Whether the brown colour and chloroform-like smell of the alcoholic solution are due to this material we cannot say. It is soluble in alcohol and in normal saline solution. By its injection into animals it causes either direct or reflex excitation of the cardio-inhibitory centre. It is, therefore, by no means improbable that other centres in the brain or cord are similarly excited.

As we mentioned before, the gastric contents were obtained after the patient was in a state of partial convalescence, and it is possible that had the fluid been obtained during the period of coma with contracture, this poisonous substance would have been present in greater amount, and would, when injected into the veins of an animal, have produced convulsions and death.

VIII.

We append a bibliography in chronological order. This is necessarily limited, and is confined almost entirely to reports on cases of gastric tetany. Special attention has been given to the more recent works on this interesting subject.

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CHANGES IN THE NEURONAL CENTRES IN BERI-BERIC NEURITIS.

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By most writers on the subject of beri-beri the statement is made that there are no changes in the proper cells of the central nervous system. It seems incredible, in view of the profound changes in the spinal sensory and motor cells, that are now known to accompany the peripheral neuritis of alcoholism, which in so many respects resembles beri-beric neuritis, and experimental section or destruction of the axonal portion of neurons.

Scheube,¹ who appears to have missed no important point in the clinical and pathological aspects of the disease, has in a table of 20 cases recorded no lesion of the spinal cord more marked than "im mittleren Dorsalmarke Atrophie und theilweiser Schwund der Ganglienzellen der Vorderhorner." And, further, in his last published work on the subject² he has not changed his opinion in the matter. In fact the only authorities who appear to have observed central changes are Pekelharing and Winkler,³ although they failed to investigate the extent and to appreciate the significance of them. The relatively imperfect methods of their day for the investigation of cellular changes in the central nervous system was undoubtedly the reason.

My experience leads me to differ from most observers who have studied this disease. For in a careful examination of 8 cases of beri-beri I have found changes in those posterior