CONTRIBUTIONS TO THE EXPERIMENTAL PATHOLOGY OF THE STOMACH

I. EXPERIMENTAL PYLORIC STENOSIS *

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The sequence of events responsible for the clinical and pathological findings in disease of the stomach is often difficult if not impossible to analyze. The difficulty is directly proportional to the number and complexity of the processes involved. For example, in chronic gastric ulcer one attempts to analyze and properly coordinate the increase or decrease of gastric acidity, secretion, and motility; pyloric spasm or stenosis; dilated or hypertrophied stomach, etc. Through long clinical custom certain views are current as to the cause and effect of these interrelating processes, without much question as to the validity of these views or without subjecting them to experimental proof.

It has seemed to us that in view of the complexity of the problem of chronic ulcer of the stomach, these several processes should be separated and studied individually, a method, as Bolton[1] points out, which has not hitherto been adopted.

The following paper is presented as the first of a series of reports concerning the experimental pathology of the stomach and contains the results of producing primary partial stenosis of the pylorus in a series of twenty-nine dogs. It includes incidental reference to the relation of pyloric obstruction to chronic ulcer, a question which will be discussed at greater length in a subsequent paper.

METHODS

Small male and female dogs weighing from 6 to 8 kg. were used exclusively. Under usual surgical asepsis and complete surgical anesthesia an upper abdominal incision is made somewhat to the right of the mid line to insure easy access to the pyloric region. The stomach and antrum are pulled up into the wound and a fairly heavy silk ligature passed under the pylorus with the aid of an aneurysm needle and tied as near as possible to the duodenopyloric junction, avoiding the compression of large blood-vessels. The ligature is tied suffi-

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* From the Morris Institute for Medical Research.
1. Bolton: Proc. Roy. Soc. London, 1909-10, lxxxii, B 241.

ciently tight to produce permanent obstruction as evidenced by deep peristaltic waves in the antrum, cramp of the pylorus with temporary anemia, antiperistaltic waves, etc. Considerable experience is necessary to produce proper tension of the ligature, as in some instances it is tied too loosely, producing little, if any, obstruction, or too tightly, causing complete stenosis with death of the animal within from two to five days. The high mortality in many of our earlier dogs is to be attributed to this latter cause.

After experimenting with various test-meals and methods of introducing and withdrawing them, the following method was chosen as a routine: The dogs were fasted from eighteen to twenty hours over night and in the morning were given 100 gm. chopped lean beef and 300 gm. milk introduced by stomach-tube. In from fifty to sixty minutes 1/20 grain apomorphin hydrochlorid is injected hypodermatically, resulting in two to three minutes in the emesis of the test-meal, which is collected in a large evaporating dish. In the obstructed animals there is present, in addition to the meat and milk residue, large rests of beef, cartilage, bones, potatoes, carrot, etc. of food eaten days before. The apomorphin method possesses advantages over other methods of withdrawal by tube in obtaining total residue of stomach. The meals were examined for total quantity, free and total acidity, the finer chemical and microscopic examination being dispensed with as unessential.

In many of the dogs a second laparotomy was made in intervals of from ten days to three weeks, when 1 or 2 c.c. of 5 per cent. silver nitrate was injected at various points (pylorus, fundus, lesser curvature) producing acute ulcers. In four dogs (Nos. 11, 30, 31, 13) the pyloric ligature and injections were made simultaneously, resulting in all instances in complete obstruction and death of the animal. Two dogs (Nos. 44, 52) were injected daily with 1/5 grain pilocarpin hydrochlorid and 1/50 grain eserin sulphate respectively, to produce recurring stenosis from pyloric spasm.

RESULTS

The results of pyloric occlusion may be grouped in three divisions, dependent on the degree of obstruction.

GROUP 1.—Moderate stenosis (ligature tied loosely) resulting in little change in gastric acidity, motility or size (ten dogs—Table 1).

GROUP 2.—Marked obstruction (ligature tied sufficiently tight to cause marked peristalsis and anemia) resulting in definite change in motility (decrease) acidity (increase) and size (dilatation and hypertrophy) (nine dogs—Table 3).

GROUP 3.—Complete obstruction (from occluding ligature or edema from silver nitrate injection) resulting in inanition, vomiting, convulsions and death of the animal in from forty-eight to one hundred and twenty hours (ten dogs—Table 4).

Group 1.—This is perhaps the most interesting of the series, demonstrating the resisting power of the dog's stomach, as indicated by maintenance of normal acidity, motility, and size in the presence of a pyloric ligature tied for obstruction and producing at time of operation definite pyloric obstruction. For the most part these animals showed no loss in weight or cachexia, ate their food greedily

TABLE 1.—MODERATE—

Dog No.	Test Meal Before Operation			First Operation	Test Meal After First Operation		
	Date	Amount	Total Acid	Pyloric Ligature	Date	Amount	Total Acid
41	12/23	200	37	12/26	.....	.....	.....
51	2/5	200	51	2/6	2/17	350	54
35	.....	.....	.....	11/25	.....	.....	.....
36	.....	.....	.....	12/20	.....	.....	.....
42	.....	.....	.....	1/8	1/26	250	55
43	.....	.....	.....	1/15	1/26	450	26
7	.....	.....	.....	6/20	.....	.....	.....
6	.....	.....	.....	6/26	.....	.....	.....
26	.....	.....	.....	11/20	.....	.....	.....
28	.....	.....	.....	11/25	.....	.....	.....

without apparent discomfort, grew fat and sleek in spite of their occluding ligatures, and had every evidence of good care and health in marked contrast to their appearance on entrance into the laboratory.

Test-Meals: We found for the most part a slight increase in total quantity and total acidity within from ten to fourteen days after pyloric obstruction. Two dogs (51, 42) following a primary hyperacidity gave a secondary drop to normal within six weeks of the original operation. Necropsy in one to three months after ligation revealed a slightly or moderately dilated stomach, the latter occurring in those dogs whose test-meals had shown hyperacidity. In Dog 41, however, in spite of an increase from 37 to 52 total acid in two months, the stomach was found of normal size.

The control test-meal findings in dogs in which no preliminary meal has been given, were obtained from a series of six normal dogs as shown in Table 2:

Most of the animals were necropsied in approximately two months after ligation. In every instance the silk ligature was found in place,

buried usually in the serosa or muscularis coats and covered with connective tissue and adhesions, and adherent to the under surface of liver or gall-bladder.

Group 2.—In these animals, as a result of more securely tied ligature with marked pyloric obstruction, the changes of hyperacidity, hypersecretion, motor insufficiency, dilated and hypertrophied stom-

—Pyloric Stenosis

Second Operation	Test Meal After Second Operation			Necropsy			
$AgNO_3$	Date	Amt.	Total Acid	Date	Stomach	Ulcer	Scar
.....	2/13	425	25	2/28	Small	No ulcer	No scar
2/19	3/17	200	30	3/20	Small	No ulcer	No scar
12/18	1/26	150	38	2/20	Small slight hypertrophy	Two small healing ulcers	
12/30	1/26	350	26	2/20	Slightly dilated	Chronic pyloric ulcer	
.....	2/29	325	36	3/8	Slight dilatation	No ulcer	No scar
2/13	2/24	550	50	3/23	Slightly dilated; slight hypertrophy.	Chronic pyloric ulcer	
.....	.....	.....	.....	7/26	Fundus dilated; pyloric hypertrophy.		
.....	.....	.....	.....	7/10	Slight dilatation and hypertrophy		
12/13	.....	.....	.....	12/27	Small	Two acute ulcers	
12/10	.....	.....	.....	12/30	Slight dilatation	Both ulcers healing	

TABLE 2.—Test-Meal Findings in Six Normal Dogs

Dog No.	Total Quantity	Free Acid	Total Acid
1	150 c.c.	0	30
2	250 c.c.	0	31
3	350 c.c.	0	27
4	150 c.c.	0	25
5	200 c.c.	0	35
6	100 c.c.	0	32
Range—100-350 c.c.		Range—25-35	
Average—200 c.c.		Average—30	

ach were more marked. The dogs appeared ill at ease, grew thin and emaciated, refused food as if in pain, later became toxic and unable to stand, finally dying in from three weeks to two months from inanition and toxemia.

Test-Meals: A marked increase in total quantity up to one liter of contents (five times normal) much of this being food residue

but more supernatant fluid (hypersecretion). In all a marked primary hyperacidity was found, many showing later a secondary relative decrease (hypacidity) the total quantity remaining the same or

TABLE 3.—MARKED—

Dog No.	Test Meal Before Operation			First Operation	Test Meal After First Operation		
	Date	Amount	Total Acid	Pyloric Ligature	Date	Amount	Total Acid
55	2/5	200	44	2/12	2/24	950	56
38	1/14	250	26	1/23	2/2	550	36
50	2/5	300	59	2/6	2/18	250	75
48	.....	.....	.....	1/15	1/26	450	26
39	.....	.....	.....	1/16	1/26	800	62
37	.....	.....	.....	12/18	.....	.....	.....
22	.....	.....	.....	10/9	.....	.....	.....
21	.....	.....	.....	10/8	.....	.....	.....
5	.....	.....	.....	6/5	6/26	100	23

TABLE 4.—COMPLETE—

Dog No.	Date	Operation	Postoperative Condition and Course
4	5/27	Pyloric ligature	Sudden death in 72 hours with convulsions
2	5/20	Pyloric ligature	Constant vomiting, gradual inanition
9	7/17	Pyloric ligature	Progressive inanition. Death in 96 hours
17	9/4	Pyloric ligature	Sudden death in 96 hours with convulsions
19	9/11	Pyloric ligature	Sudden death in 48 hours
24	11/27	Pyloric ligature and $AgNO_3$	Sudden death in 72 hours
13	8/22	Pyloric ligature	Sudden death in 96 hours
31	12/4	Pyloric ligature and $AgNO_3$	Sudden death in 96 hours
30	12/4	Pyloric ligature and $AgNO_3$	Sudden death in 48 hours
11	8/6	Pyloric ligature and $AgNO_3$	Sudden death in 72 hours

becoming higher. Number 48 showed a late hyperacidity of 50 without previous increase.

Group 3.—The animals in this series died more or less suddenly in from forty-eight to 120 hours. A few refused food, vomited what

little water they drank and succumbed from progressive inanition and weakness. Most of the dogs were found dead in their cages in the morning, having been in good condition the previous evening,

—Pyloric Stenosis

Second Operation	Test Meal After Second Operation			Necropsy		
$AgNO_3$	Date	Amt.	Total Acid	Date	Stomach	Ulcer
2/26	3/24	1050	42	4/13	Markedly dilated	Chronic pyloric ulcer
2/13	.....	.....	.....	2/26	Markedly dilated	No ulcer or scar
2/19	3/20	600	64	3/21	Markedly dilated and hypertrophied	Superficial pyloric ulcer
2/13	2/24	550	50	3/23	Slightly dilated—Marked hypertrophy	Two duodenal ulcers — two chronic pyloric ulcers
.....	2/24	525	62	2/28	Markedly dilated and hypertrophy	No ulcer or scar
12/27	1/26	350	50	2/20	Markedly dilated	Chronic pyloric ulcer
10/30	.....	.....	.....	11/20	Markedly dilated	Unhealed pyloric ulcer, healing lesser curv. ulcer
.....	.....	.....	....	10/30	Markedly dilated and hypertrophy	
7/17	.....	.....	.....	8/21	Markedly dilated	Chronic pyloric ulcer

—Pyloric Stenosis

Necropsy			
Date	Stomach	Pylorus	Stomach Contents
5/30	Slightly dilated	Complete obstruction	Moderate amount clear fluid
5/25	Markedly dilated	Edema of all coats	Glairy mucus covering fundus
7/21	Small	.....	Small amount thick mucus
9/8	Small	Tightly contracted	50 c.c. thin milky fluid
9/13	Small	Strongly contracted	Mucoid fluid in stomach
11/30	Small	Thick and edematous	Four acute ulcers
8/26	Small	.....	Small amount frothy mucus
12/6	Small	Edema of antrum	
8/9	Small	Firmly contracted	Little fluid in stomach

eating their food, standing and walking about the cage, etc. Two of them (Nos. 4 and 16) were seized suddenly with tonic convulsions resembling tetany and died within five minutes. The condition of these dogs suggests the clinical picture of gastric tetany seen occasion-

ally in benign pyloric obstruction and is in accord with the experimental findings of Kaufman,[2] MacCallum[3] and others.

At necropsy the pyloric antrum is tightly contracted as if in tonic spasm, the fundus slightly dilated, the stomach of usual size, containing a small amount of thin fluid and glairy mucus. In one case (No. 2) in which there had been constant vomiting, with progressive inanition and loss in weight, the animal living for five days, the stomach was quite markedly dilated.

DISCUSSION

The interpretation of the motor insufficiency, continuous secretion, hyperacidity, hypertrophy and dilatation of stomach produced by pyloric obstruction, we believe to be the following: As a result of the narrowed pyloric canal, food normally propelled into the duodenum within from six to twelve hours is retained twenty-four hours or even several days. During this time the pylorus is in a state of continuous peristaltic activity in attempts to drive the contents, through the obstruction, on into the intestines—a prolongation and intensification of the normal peristalsis described by Cannon.[4] The grinding and churning of the food caused by this increased peristalsis presses the gastric contents with increased violence against the pyloric mucosa, stimulating the production of a chemical stimulant by the gastric mucosa, which Edkins[5] has shown is responsible (after its absorption into the blood) for the continued secretion of gastric juice. We have found that as late as forty-four hours after test-meals, the obstructed dog's stomach contained large quantities of contents with high free (34) as well as total (90) acidity, a condition never seen in normal dogs. We conclude, therefore, that the hyperacidity resulting from obstruction is really a hypersecretion (continuous secretion) produced as described and persists as long as food is present in the stomach. The histology of hyperacidity will be reported on later.

The explanation of the hypertrophy and dilatation is not so clear, some dogs with marked obstruction having small stomachs with hypertrophied walls, others having marked dilatation, while dogs with only slight obstruction have very markedly dilated stomachs. In all probability the gastric muscle tonus plus a possible subacute or chronic gastritis are additional factors, although it may be entirely a muscle affair analogous to the response of the heart to a stenosis. Micro-

2. Kaufmann: Am. Jour. Med. Sc., 1908, cxxvii, 606.
3. MacCallum: Zentralbl. f. allg. Path., 1905, xvi, 385.
4. Cannon: Mechanical Factors of Digestion, 1911, Chapter VI. Effect of Stomach Movements.
5. Edkins: Jour. Physiol., 1906, xxxiv, 133.

scopic examination of the stomach wall is necessary to substantiate this. The results will be reserved for later publication.

In the dogs with *successful* partial pyloric obstruction (motor insufficiency, continuous secretion) the acute ulcers produced by silver nitrate injection were in many instances prevented from healing, or became chronic and progressive, particularly the pyloric ulcers (see Bolton). We believe that the constant mechanical trauma of the retained food, grinding forcibly back and forth on the raw surface, plus the continuous corrosive action of free hydrochloric acid (the stomach never being free from acid) are two of the most important factors in the production of chronic experimental ulcer.

CONCLUSIONS

1. Moderate pyloric stenosis in dogs (ligature around pylorus tied loosely) causes little or no change in stomach motility, acidity or size.

2. Marked obstruction (ligature tied sufficiently tight to produce marked peristalsis and anemia of the pylorus) causes motor insufficiency, continuous secretion (hyperacidity) and hypertrophy and dilatation of the stomach.

3. Complete occlusion (ligature or silver nitrate injection causing secondary occluding edema) results in inanition, vomiting, convulsions (gastric tetany) and death of the animal in from forty-eight to 120 hours.

4. The pyloric ligature (stenosis) results in a motor insufficiency with food retention which in turn sets up a continuous secretion with the constant presence of free hydrochloric acid.

5. Pyloric obstruction with resulting motor insufficiency and continuous secretion are probably the most important factors in the production of *chronic* experimental ulcer.

6. While the foregoing results concern *experimental* chronic ulcer, it is more than likely that primary partial pyloric stenosis (from whatever cause) with secondary motor insufficiency and continuous secretion are largely responsible for the progression and delayed healing of chronic ulcer in man.

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