Appraisal of Gastric Freezing by the Use of Experimentally Produced Gastric Ulcer*

By

Tetsuhiko Hatafuku

From the Department of Surgery, Tohoku University School of Medicine, Sendai; Director: Prof. T. Makii

and

From the Department of Surgery, Wayne State University College of Medicine, Detroit, Michigan, U.S.A.; Director: Prof. A.P. Thal

(Received for publication, December 25, 1964)

The present study was designed to determine whether the gastric freezing promotes the healing of peptic ulcer or not. Except for the control group, all the dogs were subjected to the gastric freezing and a standard experimental gastric ulcer was created afterwards at the varying intervals of 1, 3 and 6 months respectively. Control dogs were subjected to the ulcer operation only. Three weeks postoperatively the dogs were sacrificed and the healing of ulcer was studied. Initially, experimentally produced gastric ulcers showed a tendency of healing due to the depression in acid peptic power of the gastric juice. This, however, was followed by the gradual increase of perforation and persistent ulceration when observed up to 6 months following the date of the gastric freeze. These observations lead to conclusion that although the gastric acid pepsin secretion is temporarily depressed by gastric freezing, its return to the control level can be expected with the lapse of time. Problems of gastric freezing technique were also discussed.

Since Wangensteen and his associates1–3 reported the technique of gastric freezing in 1962 which in their words is called “physiological gastrectomy”, appraisal of this technique has become the center of our attention.

The aim of the present experiment is to determine whether the gastric freezing depresses the acid peptic power of the stomach, thus promoting the healing of an experimentally produced gastric ulcer. The basis of the experiment arose out of our previous study in the management of duodenal perforation by the use of onlay jejunal patch.4 In this instance the jejunal serosa of the patch graft regularly became covered by proliferating duodenal mucosa4 but
when the jejunal patch was applied to a full thickness defect of the stomach, the majority of cases showed a perforation as an evidence of acid peptic activity.

At the present time, although the exact pathogenesis of gastroduodenal ulcers is not yet clear, it is our general belief that the gastroduodenal ulceration is promoted due to acid peptic autodigestion.

The present study deals with the change of the acid peptic power following gastric freeze, which as a whole determines the fate of an experimentally produced gastric ulcer.

**METHOD**

Initially, gastric freezing was carried out in all dogs except in the control group; then the standard size defect was created on the anterior wall of the body of the stomach at varying intervals after the freeze, namely 1, 3 and 6 months respectively, the jejunal patch graft was applied and the healing was studied (Fig. 1). If the gastric freezing were truly to depress the acid peptic secretion of the stomach we would expect the majority of the experimental ulcers to heal.

Fig. 1. Schema of the experimental production of a standard gastric ulcer.
A. A full thickness defect of 2.5 cm diameter is created by rotating a cork borer.
B. Completion of the procedure.
C. A loop of jejunum is held up and the defect is sealed by means of two layer sutures. The first row is a Connell type chromic catgut suture and the second row is interrupted Lembert sutures. Now the seromuscular layer of the jejunum constitutes the ulcer base.
1. Technique of gastric freezing

Young mongrel dogs of both sexes weighing between 14 and 24 kg were used in this study. Food was withheld for 24 hours. Then the dogs were lightly anesthetized by the intravenous injection of 25 mg/kg of Nembutal.

The dog was laid on the table supinely, gastric lavage was done and the stomach was thoroughly washed until the aspirating water became completely clear. Then a Levine tube was placed in the stomach.

Swenko Gastric Hypothermia Machine (Swenko Research and Development Company, Minneapolis, Minnesota, U.S.A.) which has the flow rate of 1,500 ml/min and the cooling efficiency of reservoir temperature as low as −25°C under 20°C of room temperature was employed throughout this experiment.

A standard stomach shaped latex balloon, with an esophageal portion of which was shortened, was secured to the end of the outer tube by #00 silk ligature. Although the original inner tube was used initially, many incidences of necrosis and perforation were seen on the anterior wall of the stomach along the greater curvature and later a modified inner tube which has fewer holes facing the greater curvature was employed. Since then, the incidence of post-freezing complication could almost be abolished. This will be discussed later.

The hypothermia machine was turned on at least 30 minutes prior to the actual freeze so as to pre-cool the coolant in a reservoir down to −22 to −23°C, and inflation and deflation of the balloon was repeated several times to evacuate the air from the circulating system.

Introduction and Placement of the Gastric Balloon

A small midline abdominal incision was made prior to the introduction of the balloon so that the correlation between the inflated balloon and the stomach could be examined later with fingers inserted through the incision.

The introduction of the balloon and attached tubing system was done as was previously described by Peter et al. The double lumen tube was intussuscepted into the balloon, flap portion of the balloon was wrapped around the tube, lubricated with surgical jelly and was introduced into the stomach with the dog in semi-Fowler position. Then the dog was placed on its right side and balloon was filled very slowly with approximately 300 ml of coolant. Ninety-five per cent of alcohol was used as a coolant. The tube was pulled out until a slight resistance was encountered. The table was then changed from the semi-Fowler to the Trendelenburg position and the balloon was inflated with 450 to 800 ml of total coolant capacity according to the size of the dog. Gastric contents as well as the remaining air was evacuated and the Levine tube was removed.

In the latter half of this experiment, a thermocouple was introduced together with the balloon and was placed between the balloon and corpus mucosa of the stomach alongside the greater curvature to measure the temperature of
the place.\textsuperscript{5}

The position of the dog was then changed to supine and the table was replaced to the horizontal position.

When the introduction and the placement of the balloon was done properly as described above, digital correction of the position of the balloon was not necessary in the majority of cases. However, the thermocouple had to be frequently replaced during this procedure.

\textit{Gastric Freezing}

As soon as the balloon was filled and its position examined, circulation was started. The dog was covered with a hot water pad so as to prevent the fall of body temperature. Readings from the thermocouple placed between balloon and mucosa of the stomach (T.B.M.),\textsuperscript{5} inflow and outflow temperature as well as rectal temperature were recorded every 5 minutes. Fig. 2 shows the frozen stomach. In this case, the abdominal incision line was extended to visualize the entire stomach.

Total freezing time was between 45 and 60 minutes depending upon the temperature reading of the thermocouple in the latter half of the experiment. When the thermocouple was not used the duration of the freeze was determined by

\begin{figure}[h]
\centering
\includegraphics[width=0.5\textwidth]{fig2.jpg}
\caption{Picture of the frozen stomach at the termination of the freeze. Ice crystal formation is seen all over the anterior wall of the stomach. In the actual freeze, however, anterior wall of the stomach was covered by the abdominal wall, thus lessened the cooling efficiency due to the heat conduction from the anterior gastric wall to the abdominal wall.}
\end{figure}
Fig. 3. Temperature readings during the gastric freeze. T.B.M.: Temperature of the space between balloon and gastric mucosa.

Throughout the entire experiment, the outflow temperature was maintained between $-11^\circ C$ and $-14^\circ C$ and the inflow temperature reading was between $-17^\circ C$ and $-20^\circ C$. Under this condition, average T.B.M. temperature reading was found being about $7^\circ C$. Thus the duration of the freeze was controlled depending upon what the T.B.M. temperature reading was. For example, when the T.B.M. temperature dropped more than $2^\circ C$ or $3^\circ C$ below the $7^\circ C$ level in the middle of the freeze and under the constant outflow temperature, the freezing time was reduced. On the contrary, when the T.B.M. temperature had stayed higher than $7^\circ C$, a longer freezing time was given. Fig. 3 shows a typical graph showing mutual correlations of these temperature readings. At the termination of the freeze, cooling and main switches were turned off and the balloon was left in place for at least 10 minutes and then the balloon was deflated very slowly taking about 10 minutes. The tube was also removed very carefully. Dogs were kept under hot water pad until the rectal temperature rose to the prefreezing level and then they were returned to the kennel. After the freeze, meat and milk diet as well as water were given.

2. Experimental production of a standard gastric ulcer

To see the effect of gastric freezing upon the healing of a gastric ulcer created
afterward, all the dogs were subjected to the operation as described below.

Under Nembutal anesthesia, the abdomen was entered through a midline abdominal incision. Using a cork borer, a full thickness defect of 2.5 cm diameter was created on the anterior wall of the body of the stomach adjacent to the antral border and alongside the greater curvature (Fig. 1-A). To seal this defect, a loop of jejunum was brought up keeping enough distance from the ligament of Treitz and using 000 chromic catgut, a Connell type suture was started tacking the seromuscular layer of the jejunum around the edge of the defect (Fig. 1-C). The suture line was again secured by means of interrupted 5-0 silk Lembert sutures. Fig. 1-B shows the completion of this procedure.

Care was taken to maintain the jejunal continuity. Often few additional sutures were necessary to prevent kinking of the elevated jejunal loop. Thus a standard size of a gastric ulcer was produced with its ulcer base consisting of the jejunal serosa which is very sensitive to the acid peptic power.

Postoperatively the dogs were kept on meat and milk diet for 3 weeks and then were sacrificed for histological study.

Control dogs were subjected to this operation only without the preceding gastric freeze. In the remaining dogs, gastric freezing was done first, and then 11 dogs were operated upon 1 month after the gastric freeze, 8 dogs were operated upon 3 months after the freeze and 10 dogs were operated upon 6 months after the freeze, respectively.

3. Histamine stimulation of the gastric secretion

Ten control and a total of 15 frozen dogs were given intramuscular injection of 50 mg of histamine dichloride in beeswax to augment the continuous gastric secretion. A daily injection was started on the first postoperative day and was continued for 3 weeks until the date of sacrifice.

RESULTS

In essence if the digestive power of the stomach were depressed by freezing, healing of the experimental ulcer would be expected, whereas had there been no interference with acid peptic secretion following gastric freezing a high incidence of persistent ulceration or perforation would be expected. The results were summarized in Tables I and II. When the ulcer base, which consisted of the jejunal wall with its serosal layer facing toward the lumen of the stomach was continually bathed in acid gastric juice, a further ulceration occurred progressing in some to complete perforation (Fig. 4). In the 2 tables, “persistent ulcer” means that there was an absence of regeneration over the ulcer base or there was further ulceration of the jejunal wall, but it was not perforated. Fig. 5 is one of those histological specimens which show persistent ulceration.

Among the non-histamine group, there was 61 per cent (8/13) perforation in
TABLE I. Results of Non-histamine Group

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>1 month</th>
<th>3 months</th>
<th>6 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of dogs</td>
<td>13</td>
<td>5</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Perforated</td>
<td>8 (61%)</td>
<td>1 (20%)</td>
<td>1 (25%)</td>
<td>2 (40%)</td>
</tr>
<tr>
<td>Persistent ulcer</td>
<td>4 (31%)</td>
<td>2 (40%)</td>
<td>3 (75%)</td>
<td>2 (40%)</td>
</tr>
<tr>
<td>Healing</td>
<td>1 (8%)</td>
<td>2 (40%)</td>
<td>0 (0%)</td>
<td>1 (20%)</td>
</tr>
</tbody>
</table>

TABLE II. Results of Histamine Group

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>1 month</th>
<th>3 months</th>
<th>6 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of dogs</td>
<td>9</td>
<td>6</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Perforated</td>
<td>7 (78%)</td>
<td>4 (67%)</td>
<td>4 (100%)</td>
<td>5 (100%)</td>
</tr>
<tr>
<td>Persistent ulcer</td>
<td>2 (22%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Healing</td>
<td>0 (0%)</td>
<td>2 (33%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

Fig. 4. Picture of the perforated ulcer. The dog was sacrificed 6 months after the freeze. The dog was given daily histamine injection for 3 weeks.
of Gastric Freezing 271

Fig. 5. Histological specimen of a persistent ulcer 3 months after the freeze. (10 ×, Gomori’s modification of Masson’s stain.) Ulceration is reaching to the muscular layer of the jejunum. Several microthrombi are seen in the submucosal layer.

the control dogs, 20 per cent (1/5) perforation in the dogs operated upon 1 month after the freeze, 25 per cent (1/4) perforation after 3 months and 40 per cent (2/5) perforation after 6 months, respectively (Table I). These results indicate an initial depression of gastric digestive power followed by a progressive recovery.

Among the dogs which were given daily histamine injection, there was 87 per cent (7/9) perforation in the control dogs, 67 per cent (4/6) perforation after 1 month, 100 per cent (4/4) perforation after 3 months and 100 per cent (5/5) perforation after 6 months (Table II). These results indicate that while parietal and chief cell secretion was temporarily depressed they could be stimulated to maximum secretion by histamine. Possibly a temporary inhibition of extrusion of pepsinogen granules is produced by the freeze.

Microscopic examination of the specimens other than the perforated cases revealed that there were frequent findings of submucosal edema and some microthrombi among animals examined during the first month after the freeze.

DISCUSSION

Several investigators have reported the hazard of gastric freezing in its clinical application.6-9 Most of the problems seem to be related to the freezing technique. In the beginning of our study, when the original inner tube which came
Fig. 6. Perforated stomach due to the ununiform gastric freeze. Close location of the inner tube resulted in a profound partial deep freeze of the corpus wall along the greater curvature. The dog expired 6 days after the freeze.

from the manufacturer was used, incidence of necrosis, perforation, or mucosal ulceration was often seen; and several dogs expired. Fig. 6 shows a typical example of the partially necrotized stomach followed by a perforation.

This, it was later understood, was due to the close location of the inner tube with its jet streams of coolant striking the gastric wall alongside the greater curvature and the anterior wall of the corpus where the freezing efficiency was greater owing to relatively less thermal conductivity to the adjacent organs or tissues.

To eliminate these hazardous complications, a modified inner tube was made. Regarding the fact that most of the time the inner tube was located close to the greater curvature, fewer holes were made, which eject the coolant toward the greater curvature, and more holes were placed superiorly so that the better uniform cooling effect could be obtained. Thus, the incidence of necrosis or perforation could be nearly eliminated, although the cooling effect of the antral
mucosa was less.

Abrupt deflation and removal of the balloon may cause another serious complication of massive bleeding damaging the fragile gastric mucosa. Deflation and removal of the tubing system should be started at least 10 minutes after the termination of the gastric freeze and very slowly allowing enough time for thawing of the gastric wall.

Reviewing the data obtained from the present study, it has become clear that the acid peptic power returns progressively after the freeze. This is shown by the gradual rise of the perforation rate from 20 per cent up to 40 per cent during the period of 6 months, although it did not reach the control level of 61 per cent (Table I).

The histamine injection group, however, showed rapid regain of the perforation rate, and it even exceeded the control level after 3 months, showing that the potential for the secretion of highly potent acid pepsin is not reduced by this technique (Table II).

These findings seem to suggest that the gastric freezing produces a transient inhibition of gastric acid pepsin secretion and there is restoration of full digestive activity within 3 months after the gastric freeze in the cases where the gastric secretion is continually stimulated, and within a little over 6 months under non-stimulated condition.

References